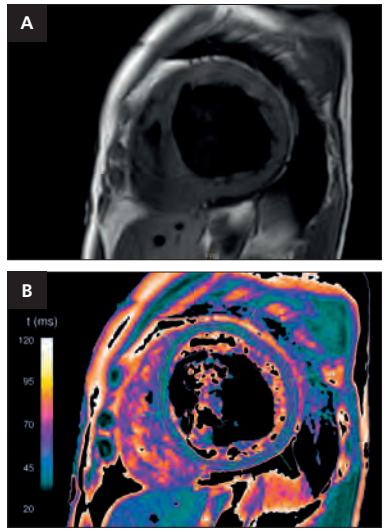
ČESKÁ KARDIOLOGICKÁ SPOLEČNOST
THE CZECH SOCIETY OF CARDIOLOGY

ČESKÁ SPOLEČNOST KARDIOVASKULÁRNÍ CHIRURGIE
CZECH SOCIETY FOR CARDIOVASCULAR SURGERY

Ročník | Volume 67 • Číslo | Number 3 • Červenec/Srpen | July/August 2025

ISSN 0010-8650 (print), ISSN 1803-7712 (online)

Cor et Vasa



Ukázka měření T2 relaxačního času myokardu (A) a T2 mapy (B) ve středním segmentu levé komory v krátké ose u pacienta s výraznou dilatací obou komor a difuzní hypokinezí. Bez detekce edému nebo prodloužených hodnot T2 relaxačního času. Globální T2 čas byl 53,9 (6,8) ms. *(Štípalová T, Panovský R, Mojica-Pisciotti M, Krejčí J. Využití magnetické rezonance srdce ve stratifikaci nemocných s dilatační kardiomyopatií. Přehledový článek, str. 386–392).*

ČESKÁ KARDIOLOGICKÁ SPOLEČNOST

10.– 11. října 2025 | Hotel Passage, Brno

XXVIII.

Konference České asociace srdečního selhání

Těšíme se na setkání s Vámi!

Registrujte se na www.kardio-cz.cz

Cor et Vasa

S PŘÍLOHOU Kardio

Časopis České kardiologické společnosti a České společnosti kardiovaskulární chirurgie *Cor et Vasa* vychází šestkrát ročně a pokrývá všechny aspekty kardiologie, angiologie, kardiovaskulární chirurgie, kardiovaskulárního zobrazování, pediatrické kardiologie, hypertenze, kardiovaskulární prevence a některé z aspektů intervenční radiologie.

Obsahuje úvodníky, původní sdělení, přehledové články i krátká sdělení z klinické a experimentální kardiologie. Počínaje rokem 2012 jsou v *Cor et Vasa* publikovány také souhrny (5 000 slov) z doporučených postupů Evropské kardiologické společnosti, připravené předními českými odborníky. Od roku 2025 časopis *Cor et Vasa* **nepřijímá kazuistiky.** Pokud byste měli zájem, můžete své kazuistiky zaslat do sesterského časopisu *Cor et Vasa Case Reports*, který najdete na adrese https://www.kardio-cz.cz/coretvasa-case-reports/.

Příloha *Cor et Vasa* Kardio přináší recenze knih, abstrakta z vybraných kongresů, zprávy z kongresů a konferencí, voleb a diskusí, polemiky, komentáře, informace z České kardiologické společnosti, České společnosti kardiovaskulární chirurgie a Evropské kardiologické společnosti i aktuální mezinárodní zprávy a témata.

Příspěvky jsou publikovány v češtině, slovenštině anebo v angličtině.

Časopis vychází ve dvou verzích se stejným obsahem: online a tištěné verzi. *Cor et Vasa* je dostupná v plném rozsahu také na webu ČKS.

Cor et Vasa je citována v databázích EMBASE, Scopus, Bibliographia medica Čechoslovaca, ESC Search Engine, Emerging Sources Citation Index společnosti Thomson and Reuters, Web of Science a Journal Citation Reports – impakt faktor 0,9 za r. 2024.

Příspěvky do časopisů zpracované podle pokynů autorům zasílejte prosím prostřednictvím systému ACTAVIA – vstup do něj je na adrese: http://actavia.e-coretvasa.cz/. Příspěvky do Kardia můžete zasílat také na adresu vedoucího redaktora nebo odpovědné redaktorky.

Adresa pro korespondenci s vedoucím redaktorem časopisu *Cor et Vasa*
Prof. MUDr. Michael Aschermann, DrSc., FESC, FACC (vedoucí redaktor)
II. interní klinika kardiologie a angiologie,
1. lékařská fakulta Univerzity Karlovy a Všeobecná fakultní nemocnice,
U Nemocnice 2, 128 08 Praha 2, Česká republika
E-mail: Aschermann@seznam.cz, Aschermann@e-coretvasa.cz

Vychází 6× ročně (+ 2 suplementa)
Povoleno Ministerstvem kultury ČR E 18519.
ISSN 0010-8650 (print), ISSN 1803-7712 (online)

Vydavatel
Česká kardiologická společnost, z. s.
Netroufalky 6b, 625 00 Brno

Předseda
Prof. MUDr. Petr Ošťádal, Ph.D., FESC

Odpovědná redaktorka
Mgr. Klára Procházková
Tel.: +420 607 932 545
E-mail: ProchazkovaKlara@email.cz,
redakce@e-coretvasa.cz

Inzerce
Mgr. Denisa Ebelová
Tel.: +420 725 777 880
E-mail: ebelova@kardio-cz.cz

Distribuce, předplatné
Distribuce vydaných čísel bude zajištěna cestou mailingu všem členům společnosti.

Pro členy ČKS je roční předplatné tištěného časopisu 2 400 Kč, pro nečleny ČKS 3 000 Kč, v případě zájmu kontaktujte prosím paní Mgr. Denisu Ebelovou: ebelova@kardio-cz.cz

Vydavatel neručí za kvalitu a účinnost jakéhokoli výrobku nebo služby nabízených v reklamě nebo jiném materiálu komerční povahy.

Pre-press
Studio Franklin Praha
E-mail: franklin@franklin.cz

Tisk
Tiskárna Knopp s.r.o.
Nové Město nad Metují

Cor et Vasa

WITH SUPPLEMENT

Kardio

Cor et Vasa, the journal of the Czech Society of Cardiology and Czech Society for Cardiovascular Surgery, publishes 6 times a year and covers all aspects cardiology, angiology, cardiovascular surgery, cardiovascular imaging, pediatric cardiology, hypertension, cardiovascular prevention and some aspects of interventional radiology.

It features editorial, original articles, review articles, as well as short communications from clinical and experimental cardiology. Beginning 2012, *Cor et Vasa* has also been publishing summaries (5 000 words) of the European Society of Cardiology guidelines, developed by leading Czech experts in the field. Beginning 2025, *Cor et Vasa* **does not accept case reports**. Should you be interested in publishing a case report, please submit your contribution to Cor et Vasa Case Reports, a sister journal of Cor et Vasa, to be accessed at https://www.kardio-cz.cz/coretvasa-case-reports.

Its supplement, *Cor et Vasa* Kardio offers book reviews, abstracts from elected congresses and conferences, elections and discussions, polemics, commentaries, information from the Czech Society of Cardiology, Czech Society of Cardiovascular Surgery and European Society of Cardiology as well as topical international news items.

Contributions appear in the Czech, Slovak or English language.

The journal publishes in two version with identical contents: online and printed versions. Fulltext *Cor et Vasa* is also available at the Czech Society of Cardiology website.

Cor et Vasa is indexed in the EMBASE, Scopus, Bibliographia medica Čechoslovaca, ESC Search Engine databases, Emerging Sources Citation Index, the indexing database of Thomson and Reuters, Web of Science, and Journal Citation Reports – impact factor 0.9 for year 2024.

Please submit your contributions formatted as per Instructions to Authors through the ACTAVIA editorial system to be entered at http://actavia.e-coretvasa.cz/. Contributions to Kardio can also be submitted to Editor-in-Chief or Managing Editor.

The Publisher cannot be hold responsible for data or opinions presented by authors in their individual contributions or the factual and linguistic aspects of advertising material.

Address for correspondence with the Editor-in-Chief of *Cor et Vasa*
Prof. MUDr. Michael Aschermann, DrSc., FESC, FACC (Editor-in-Chief)
2nd Department of Internal Medicine – Cardiology and Angiology
School of Medicine I, Charles University and General University Hospital
U Nemocnice 2, 128 08 Prague 2, Czech Republic
E-mail: Aschermann@seznam.cz, Aschermann@e-coretvasa.cz

Published 6 times a year (+ 2 supplements)
Permission E 18519 granted by the Ministry of Culture of the Czech Republic.
ISSN 0010-8650 (print), ISSN 1803-7712 (online)

Publisher
Česká kardiologická společnost, z. s.
Netroufalky 6b, 625 00 Brno

President
Prof. MUDr. Petr Ošťádal, Ph.D., FESC

Managing Editor
Mgr. Klára Procházková
Tel.: +420 607 932 545
E-mail: ProchazkovaKlara@email.cz,
redakce@e-coretvasa.cz

Advertising information
Mgr. Denisa Ebelová
Tel.: +420 725 777 880
E-mail: ebelova@kardio-cz.cz

Distribution, subscription
Published issues will be distributed to all society members through regular mail.

The annual subscription rate of the printed journal for the Czech Society of Cardiology members is 2,400 CZK, for non-members 3,000 CZK; for further information, please contact Mrs Mgr. Denisa Ebelová at ebelova@kardio-cz.cz.

Pre-press
Studio Franklin Praha
E-mail: franklin@franklin.cz

Print
Tiskárna Knopp s.r.o.
Nové Město nad Metují

Cor et Vasa

Cor et Vasa

Časopis České kardiologické společnosti & České společnosti kardiovaskulární chirurgie
Citován v databázích Scopus, EMBASE, BMČ, ESC Search Engine, Emerging Sources Citation Index společnosti Thomson and Reuters, Web of Science a Journal Citation Reports – impakt faktor 0,9 za rok 2024.

The Journal of the Czech Society of Cardiology & the Czech Society for Cardiovascular Surgery
Abstracted / Indexed in: Scopus, EMBASE, BMČ, ESC Search Engine, Emerging Sources Citation Index by Thomson and Reuters, Web of Science, and Journal Citation Reports – impact factor 0.9 for year 2024.

Obsah | Contents

Svazek | Volume 67 Číslo | Number 3

Původní sdělení | Original research articles

Přehledové články | Review articles

Kazuistika | Case report

Výsledky soutěže o nejlepší publikaci mladých autorů

Výbor ČKS a redakční rada časopisu *Cor et Vasa* vyhlásily pro rok 2024 soutěž o nejlepší publikaci mladých autorů v *Cor et Vasa*. Do soutěže byly zařazeny články publikované v roce 2024, jejichž první autor je člen ČKS a pracovní skupiny Kardio 35.

Všechny publikované články hodnotila tříčlenná komise složená ze členů výboru ČKS a jako nejlepší tři se umístily následující publikace.

První místo: Fibrilace síní u pacientů s hypertrofickou kardiomyopatií

Autoři: Veronika Puchnerová, Michael Jenšovský, Petr Ošťádal, Jiří Bonaventura; **pracoviště prvního autora:** Kardiologická klinika, 2. lékařská fakulta Univerzity Karlovy a Fakultní nemocnice Motol, Praha

Druhé místo: Použití multimodálního zobrazování u pacientů s mnohočetnými komorovými extrasystolami – pilotní výsledky

Autoři: Veronika Bednárová, Vladimír Kincl, Martin Pešl, Roman Panovský, Zdeněk Stárek, Věra Feitová, Jan Krejčí; **pracoviště prvního autora:** I. interní kardioangiologická klinika, Lékařská fakulta Masarykovy univerzity a Fakultní nemocnice u sv. Anny v Brně, Brno

Třetí místo: Stimulací indukovaná kardiomyopatie

Autoři: Roland Oravský, Andrej Nagy; **pracoviště prvního autora:** I. interní kardioangiologická klinika, Fakultní nemocnice u sv. Anny v Brně, Brno

Všem autorům nejlepších prací srdečně blahopřejeme, současně vyslovujeme poděkování všem kolegům, kteří publikovali v roce 2024 v soutěži jejich práce.

Za výbor ČKS a redakční radu Cor et Vasa,
prof. MUDr. Michael Aschermann, DrSc., FACC, FESC, šéfredaktor Cor et Vasa

Vyhlášení soutěže o nejlepší publikaci v roce 2025

Vážené kolegyně, vážení kolegové,

výbor České kardiologické společnosti a redakční rada časopisu *Cor et Vasa* vyhlašují pro rok 2025 soutěž o nejlepší publikaci mladých autorů v *Cor et Vasa*. Do soutěže budou zařazeny všechny typy článků – přehledové články, původní sdělení a kazuistiky – publikované v roce 2025, první autor pak musí být členem ČKS a pracovní skupiny Kardio 35 ve věku do 35 let. K rukopisu prosím přidejte informaci, že rukopis může být zařazen do této soutěže.

Publikované práce bude hodnotit tříčlenná porota tvořená členy výboru ČKS. Nejlepší práce bude ohodnocena odměnou 40 000 Kč, druhé místo odměnou 20 000 Kč a třetí místo odměnou 15 000 Kč. Vyhodnocení všech publikovaných článků bude provedeno v březnu 2026.

Za výbor ČKS a redakční radu Cor et Vasa,
prof. MUDr. Michael Aschermann, DrSc., FACC, FESC, šéfredaktor Cor et Vasa

Vážené autorky/vážení autoři,
chtěli bychom vás upozornit, že od letošního roku časopis *Cor et Vasa* nepřijímá kazuistiky. Pokud byste měli zájem, můžete své kazuistiky zaslat do sesterského časopisu *Cor et Vasa* Case *Reports,* který najdete na adrese https://www.kardio-cz.cz/coretvasa-case-reports/.
Moc děkujeme za pochopení.

Prof. MUDr. Michael Aschermann, DrSc., FESC, FACC,
šéfredaktor Cor et Vasa

Dear Author(s),
Please be advised that, beginning 2025, *Cor et Vasa* does not accept case reports. Should you be interested in publishing a case report, please submit your contribution to *Cor et Vasa Case Reports,* a sister journal of *Cor et Vasa,* to be accessed at https://www.kardio-cz.cz/coretvasa-case-reports.
Thank you for your understanding.

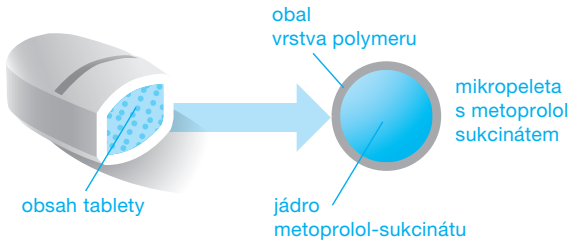
Prof. MUDr. Michael Aschermann, DrSc., FESC, FACC,
Cor et Vasa *Editor-in-Chief*

Seznam inzerentů

Betaloc® ZOK

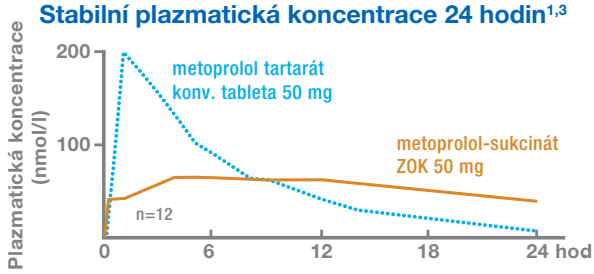
metoprolol-sukcinát

Stavba tablety Betaloc® ZOK[1,2]



Upraveno dle Plosker GL, Clissold SP. Drugs 1992;43:382-414

Dávkování 1× denně
Stabilní plazmatická koncentrace 24 hodin[1,3]



Upraveno dle Wieselgren I et al, J Clin Pharmacol 1990;30:S28 -32

Dávkování 1× denně[1]

Podávání léku 1× denně zlepšuje compliance pacientů.

Řízené uvolňování[1]

Potahované tablety s prodlouženým uvolňováním obsahují několik stovek mikropelet s jantaranem metoprololu. Každá mikropeleta je potažena vrstvou polymeru, která řídí rychlost uvolňování. Po spolknutí se tableta rychle rozpadá a mikropelety se dispergují v gastrointestinálním traktu a uvolňují léčivou látku po dobu asi 20 hodin. Tak je dosaženo rovnoměrných plazmatických koncentrací metoprololu po dobu 24 hodin (na rozdíl od konvenčních tablet s metoprololem).[1]

Dávkování u 7 schválených indikací[1]

Chronické srdeční selhání[1]

Doporučená počáteční dávka přípravku po dobu prvních dvou týdnů je 25 mg jednou denně. U pacientů třídy III-IV podle NYHA se doporučuje počáteční dávka 12,5 mg jednou denně po dobu prvního týdne. Doporučuje se dávku vždy po 14 dnech zvýšit na dvojnásobnou až na cílovou dávku 200 mg jednou denně (nebo nižší maximálně tolerovanou dávku.

Hypertenze[1]

50 mg 1× denně mírná až středně těžká hypertenze, 100–200 mg 1× denně při potřebě zvýšení dávky nebo kombinace s jinými antihypertenzívy.

Udržovací léčba po infarktu myokardu[1]

200 mg 1× denně

Angina pectoris[1]

100–200 mg 1× denně, lze kombinovat s jinými antianginózními léčivy

Srdeční arytmie[1]

100–200 mg 1× denně

Funkční srdeční poruchy s palpitacemi[1]

100 mg 1× denně, lze zvýšit na 200 mg

Profylaxe migrény[1]

100–200 mg 1× denně

Zkrácený souhrn charakteristických vlastností:
NÁZEV: Betaloc® ZOK 25 mg tablety s prodlouženým uvolňováním, **Betaloc® ZOK 50 mg** tablety s prodlouženým uvolňováním, **Betaloc® ZOK 100 mg** tablety s prodlouženým uvolňováním, **Betaloc® ZOK 200 mg** tablety s prodlouženým uvolňováním. **SLOŽENÍ:** Jedna tableta s prodlouženým uvolňováním obsahuje 23,75 mg, resp. 47,5 mg, resp. 95 mg, resp. 190 mg metoprol-sukcinátu (odp. 25 mg, 50 mg, resp. 100 mg, resp. 200 mg metoprolol-tartarátu). **DRŽITEL:** Herbacos Recordati s.r.o., generála Svobody 335, Rosice, 533 51 Pardubice, Česká republika. **TERAPEUTICKÉ INDIKACE:** Léčba hypertenze, anginy pectoris; poruch srdečního rytmu zahrnující zejména supraventrikulární tachykardii; po infarktu myokardu; funkčních srdečních poruch s palpitacemi; profylaxe migrény; léčba hyperthyreózy. **DÁVKOVÁNÍ A ZPŮSOB PODÁNÍ:** Doporučené dávkování je 100-200 mg jednou denně. Maximální denní dávka pro přípravek Betaloc ZOK je 400 mg. Betaloc ZOK je určen pro podávání jednou denně, nejlépe ráno před jídlem nebo v průběhu jídla. Tablety je nutné zapít vodou. Celé tablety nebo jejich poloviny se nesmějí kousat ani drtit. **KONTRAINDIKACE:** A-V blok druhého a třetího stupně, dekompenzovaná srdeční nedostatečnost, sinusová bradykardie (< 50 tepů/min.), sick-sinus syndrome, sinoatriální blok, kardiogenní šok a těžká periferní arteriální cirkulační insuficience, hypotenze (systolický TK nižší než 100 mm Hg), astma bronchiale a chronická obstrukční plicní nemoc (CHOPN) těžkého stupně, neléčený feochromocytom, metabolická acidóza. Metoprolol se nesmí podávat pacientům se suspektním akutním infarktem myokardu, pokud je tepová frekvence nižší než 50 tepů/min., P-Q interval je delší než 0,24 s nebo je systolický krevní tlak menší než 100 mm Hg (13,33 kPa). **ZVLÁŠTNÍ UPOZORNĚNÍ A OPATŘENÍ:** U pacientů, kteří jsou léčeni betablokátory; při léčbě pacientů s astmatem, nebo chronickou obstrukční plicní nemocí; u pacientů s A-V blokem; riziko ovlivnění metabolismu cukrů nebo maskování hypoglykémie; pokud je metoprolol podáván pacientům s feochromocytomem, mělo by být současně podáváno též alfa-sympatolytikum. **INTERAKCE**: Beta1-sympatolytika (např. oční kapky) a gangliioplegika; inhibitory monoaminooxidázy; betablokátory; blokátory kalciového kanálu; inhibitory CYP2D6; současná léčba indometacinem a jinými inhibitory prostaglandin syntetázy může snižovat účinek betablokátorů; při současném užívání s dalšími antihypertenzivy, tricyklickými antidepresivy, barbituráty nebo fenothiazinem dochází k prohloubení hypotenzního účinku; současné užívání se sympatomimetiky a xantiny vede ke vzájemné inhibici účinku; užívání betablokátorů vede k zesílení hypoglykemického účinku. **FERTILITA, TĚHOTENSTVÍ A KOJENÍ:** Metoprolol by neměl být podáván v průběhu těhotenství a kojení. V případě, že těhotná žena užívá metoprolol, se doporučuje provádět vhodné monitorování matky/plodu. **NEŽÁDOUCÍ ÚČINKY:** Mezi časté nežádoucí účinky patří bradykardie, posturální poruchy (velmi vzácně doprovázené synkopou), studené končetiny, palpitace. **ZVLÁŠTNÍ OPATŘENÍ PRO UCHOVÁVÁNÍ:** Uchovávejte při teplotě do 30 °C. **DATUM PRVNÍ REGISTRACE:** Betaloc ZOK 25 mg: 21. 3. 2001; Betaloc ZOK 50 mg: 20. 12. 2000; Betaloc ZOK 100 mg: 15. 4. 1998; Betaloc ZOK 200 mg: 20. 12. 2000. **DATUM REVIZE TEXTU:** 15. 01. 2025. **REGISTRAČNÍ ČÍSLA:** Betaloc ZOK 25 mg: 58/117/01-C.; Betaloc ZOK 50 mg; 58/628/00-C; Betaloc ZOK 100 mg: 58/015/98-C; Betaloc ZOK 200 mg: 58/629/00-C. **Před předepsáním přípravku si pečlivě prostudujte úplné znění Souhrnu údajů o přípravku, které naleznete na webových stránkách: *https://prehledy.sukl.cz/prehled_leciv.html#/leciva/0231690.* Výdej léčivého přípravku je vázán na lékařský předpis. Lék k vnitřnímu použití. Přípravek je hrazen z veřejného zdravotního pojištění.** Datum výroby materiálu: únor 2025. Kód materiálu:CZ-BET-2025-05-inzerce. **Tento materiál je určený pro odbornou veřejnost a interní účely společnosti**. **1.** SPC Betaloc ZOK leden 2025 **2.** Plosker GL, Clissold SP. Drugs 1992;43:382-414. **3.** Wieselgren I et al, J Clin Pharmacol 1990;30:S28-32.

RECORDATI

Původní sdělení | Original research article

Enhancing TAVI Patient Evaluation: A User-Friendly Tool for CT-Derived Body Composition Assessment

Marek Kantor[a], Jakub Balušík[a], Piotr Branny[a,b], Lubomír Blaha[a], Jan Hečko[a,c], Matej Pekař[a,d]

[a] *Complex Cardiovascular Center, Hospital AGEL Třinec-Podlesí, Třinec, the Czech Republic*
[b] *Cardiac Surgery, Faculty of Medicine, Palacky University, Olomouc, the Czech Republic*
[c] *Faculty of Electrical Engineering and Computer Science, VSB-Technical University of Ostrava, Ostrava, the Czech Republic*
[d] *Department of Physiology, Faculty of Medicine, Masaryk University, Brno, the Czech Republic*

ARTICLE INFO

Article history:
Submitted: 16. 12. 2024
Revised: 12. 1. 2025
Accepted: 14. 1. 2025
Available online: 9. 6. 2025

Klíčová slova:
Celkové přežití
Obezita
Sarkopenie
Tělesné složení
Transkatétrová implantace aortální chlopně (TAVI)

SOUHRN

Úvod: Analýza tělesného složení pomocí CT vyšetření se v současnosti ukazuje jako významný prognostický nástroj u pacientů s indikací k transkatétrové implantaci aortální chlopně (TAVI). Její rutinní využití v klinické praxi je však limitováno složitostí dostupného softwaru a vysokými technickými nároky. Naším cílem bylo vyvinout a validovat webovou aplikaci, která by zjednodušila používání existujícího softwaru AutoMATiCA při hodnocení tělesného složení v rámci předintervenčního vyšetření před TAVI.
Metody: Vyvinuli jsme webové rozhraní integrující již validovaný software AutoMATiCA, který využívá umělou inteligenci pro automatickou segmentaci tkání. Systém analyzuje předintervenční CT snímky a automaticky vypočítává index kosterního svalstva, objem viscerálního a podkožního tuku. Aplikace zpracovává soubory DICOM a generuje přehledné reporty včetně segmentovaných snímků a kvantitativních parametrů.
Výsledky: Testování systému prokázalo průměrnou dobu analýzy 21 sekund od nahrání snímků po zobrazení výsledků. Uživatelské hodnocení pěti klinickými lékaři potvrdilo jednoduchost použití a klinickou využitelnost. Analýza ilustrativních případů odhalila významné rozdíly mezi hodnocením pomocí BMI a CT analýzou tělesného složení, například u případů sarkopenické obezity nebo zachované svalové hmoty, které by při použití samotného BMI zůstaly neodhaleny.
Závěr: Vyvinuté uživatelské rozhraní představuje praktické řešení pro hodnocení tělesného složení u pacientů před TAVI. Systém efektivně překlenuje mezeru mezi pokročilými analytickými možnostmi validovaného softwaru AutoMATiCA a klinickou praxí díky intuitivnímu uživatelskému rozhraní. Toto řešení by mělo v budoucnu umožnit přesnější stratifikaci rizika a individualizovanější přístup k pacientům s indikací k TAVI.

Keywords:
Body composition
Obesity
Overall survival
Sarcopenia
Transcatheter aortic valve implantation (TAVI)

ABSTRACT

Background: CT-derived body composition analysis has emerged as a powerful prognostic tool for TAVI patient outcomes. However, widespread clinical implementation remains limited by complex software requirements and technical expertise barriers. This study aims to develop and validate an accessible web-based interface that streamlines the implementation of existing AutoMATiCA's validated CT-based body composition assessment in the pre-TAVI evaluation workflow.
Methods: We developed a web-based interface integrating the validated AutoMATiCA's AI-driven segmentation software for automated body composition assessment. The system analyses pre-procedural CT scans to quantify Skeletal Muscle Index, Visceral Adipose Tissue, and Subcutaneous Adipose Tissue. The interface accepts DICOM files and patient data, generating comprehensive reports including segmented images and measurements.
Results: System evaluation demonstrated an average analysis time of 21 seconds from upload to results display. User experience assessment with five clinicians showed unanimous positive feedback regarding accessibility and utility. Technical validation confirmed accurate tissue segmentation and quantification capabilities. Analysis of illustrative cases demonstrated significant discrepancies between BMI-based assessment and

Address: MUDr. Matej Pekař, Ph.D., MBA, Complex Cardiovascular Center, Hospital AGEL Třinec-Podlesí, Konská 453, 739 61 Třinec 1, the Czech Republic, e-mail: matej.pekar@gmail.com
DOI: 10.33678/cor.2025.008

Please cite this article as: Kantor M, Balušík J, Branny P, et al. Enhancing TAVI Patient Evaluation: A User-Friendly Tool for CT-Derived Body Composition Assessment. Cor Vasa 2025;67:323–330.

CT-derived body composition analysis, revealing conditions such as sarcopenic obesity and preserved muscle mass that would be missed by BMI evaluation alone.
Conclusion: This technical solution provides an accessible, integrated approach to body composition assessment in TAVI patients. Building upon the validated AutoMATiCA software, the system successfully bridges the gap between complex analysis capabilities and clinical practicality through an intuitive user interface. This solution should enable more precise risk stratification and a more individualized approach to patients indicated for TAVI in the future.

Introduction

Transcatheter aortic valve implantation (TAVI) has revolutionized the treatment of severe aortic stenosis, particularly in elderly or high-risk patients who are not candidates for traditional surgical approaches.[1] Recent evidence suggests that body composition parameters, derived from routine pre-procedural computed tomography (CT) scans, can significantly impact patient outcomes and aid in risk stratification.[2] Specifically, the analysis of skeletal muscle index (SMI) and visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) characteristics at the third lumbar vertebra (L3) level has shown prognostic value for post-TAVI mortality.[3]

Currently, the assessment of body composition requires specialized software tools, such as AutoMATiCA developed by Paris et al., which utilizes artificial intelligence for automated segmentation of CT images.[4] While highly accurate and efficient, these tools often present a significant barrier for clinicians without extensive IT expertise, potentially limiting the widespread adoption of body composition analysis in clinical practice.

The importance of accessible body composition analysis in TAVI patients cannot be overstated. Our previous research has demonstrated that SMI is a significant predictor of mortality in male patients undergoing TAVI. Additionally, VAT density shows predictive value for both male and female patients, while SAT density provides additional prognostic information in male patients.[2]

To address the technical barriers and facilitate wider adoption of body composition analysis, we have developed a user-friendly web interface that simplifies the CT segmentation process. This interface integrates with the existing AutoMATiCA software, maintaining its analytical power while providing an intuitive user experience suitable for clinicians of all technical backgrounds.

The existing workflow for CT segmentation and analysis presents several obstacles: complex software interfaces requiring specialized training, time-consuming data input and analysis processes, limited accessibility across different clinical settings, and difficulty in integrating analysis results into clinical decision-making. Our web-based solution aims to overcome these challenges by providing a streamlined, intuitive user interface; automated data processing and analysis; clear and clinically relevant output presentation; and seamless integration with existing clinical workflows.

Material and methods

System architecture and implementation

Our system presents a web-based interface designed to simplify CT segmentation analysis for body composition assessment. The technical infrastructure operates on a Windows Server 2022 Standard (IP 10.2.111.20, port 5001), accessible to medical staff through the hospital's local network. The system integrates the existing AutoMATiCA's AI-driven segmentation capabilities with our user-friendly interface, making advanced analysis accessible to clinicians of all technical backgrounds. AutoMATiCA, the core segmentation engine, employs U-Net architecture and was validated in the study of Paris et al. on 893 patient scans (80% training, 10% validation, 10% testing). The system demonstrated excellent agreement between human and AI segmentations with processing speeds of ~350 ms per scan on modern hardware.[4]

Our implementation architecture consists of two primary components. The front-end component, developed using HTML, CSS, and JavaScript, provides comprehensive functionality for patient data management and result visualization. It enables clinicians to input patient parameters, calculate body composition metrics including SMI, VAT, SAT, and Whole Body Fat Mass (WBFM) measurements, and interact with analysis outcomes through interactive visualizations powered by Chart.js. The interface allows detailed inspection of processed CT scans with segmentation overlays while maintaining access to raw CT data for verification.

The back-end system, built with Python's Flask framework, implements a sophisticated processing pipeline. It manages HTTP request routing, integrates with AutoMATiCA's Convolutional Neural Networks based on U-Net architecture, and handles comprehensive data security protocols. All data is stored securely on the hospital's local server and retained only during computation, with access restricted to authorized personnel within the hospital's local network.

Processing pipeline

The system employs a sophisticated multi-stage processing workflow. Initially, the system securely uploads and preprocesses DICOM files, followed by loading pretrained TensorFlow models utilizing U-Net architecture for rapid processing. The pipeline continues with image standardization through resizing and normalization protocols, preparing data for consistent analysis across different input sources.

The segmentation process generates detailed probability maps for each tissue type using CNNs, followed by refined post-processing through thresholding and filtering techniques. Hounsfield Unit analysis provides precise tissue characterization. The system then processes this data into JSON format for front-end presentation while maintaining strict anonymization protocols and efficient temporary file management. Additional computational processes generate comprehensive body composition parameters, including SMI calculations and both percentage and absolute WBFM measurements.

Output generation

Results are presented through a comprehensive single-page report integrating multiple data visualization elements. The interface generates interactive graphs and visualizations using Chart.js, alongside segmented CT images with customizable overlay options. Key metrics include SMI, VAT, and SAT areas and densities, and WBFM measurements in both absolute values and percentages. The system additionally provides survival probability estimations based on established study data.

Results

Our system performance evaluation revealed an average analysis time of 21 seconds from image upload to results display. The system consistently identified the L3 vertebra level in uploaded scans.

We conducted a technical expertise validation study with five experienced clinicians representing different specialties with varying technical expertise levels. Participants included two cardiologists, one cardiac surgeon, and two general surgeons. In terms of ease of use, all users successfully uploaded and analysed a CT scan on their first attempt without assistance, with an average time to run the interface and upload an image of 53 seconds. Previously, only one technically skilled clinician could use the AutoMATiCA software. Now, all clinicians in the study can easily utilize the new web interface, regardless of their technical background. The technical validation showed maximum interface satisfaction rating of 5/5, with all expert users rating the results display as "clear and informative". The most appreciated features were the one-page comprehensive report layout, visual representation of obesity and sarcopenia metrics, and immediate access to survival rate predictions. Regarding clinical utility, all clinicians reported that the tool would "significantly improve" their ability to assess TAVI patient risks. Key benefits cited included rapid risk stratification, objective quantification of body composition, and easy comparison to established clinical thresholds. Expert validation feedback included detailed assessments from a general surgeon and a cardiac surgeon, confirming the tool's efficiency and illustrative capabilities.

Areas for future enhancement based on user feedback include integration with hospital PACS systems for streamlined image access, addition of trend analysis for repeat scans, and customizable reporting options for different clinical contexts.

Case reports

To illustrate the enhanced diagnostic capabilities of CT-derived body composition analysis compared to traditional BMI assessment, we analyzed four distinct patient cases that demonstrate the limitations of relying solely on BMI measurements. The patient cases presented serve as illustrative examples of the interface's clinical application rather than a validation cohort. Sarcopenic status is calculated from skeletal mass index (SMI, cut off for sarcopenia: under 55 and 39 cm^2/m^2 for men and women respectively) and obesity is calculated from estimated fat mass (WBFM, cut off for obesity: over 27 and 38 % for men and women respectively). Our imaging protocol utilized two Siemens Somatom CT scanners: the Definition model for studies conducted before 2016, followed by the Somatom Drive for subsequent examinations. All scans were performed using a tri-iodinated non-ionic monomeric contrast medium (Iomeron), with ECG gating implemented for the thoracic region. To optimize image quality while minimizing radiation exposure, we employed differential slice thickness parameters, with 3 mm slices above the diaphragm and 5 mm slices below. The scanning voltage was maintained at 100 kV throughout, while the current was adjusted according to anatomical region: 284 mAs for thoracic imaging and 84 mAs for sub-diaphragmatic sections.

Case 1: Sarcopenic obesity

An 85-year-old male patient (height 170 cm, weight 90 kg, BMI 31.14 kg/m^2) who would be classified as obese by BMI standards. However, CT segmentation revealed an SMI of 31.44 cm^2/m^2, indicating significant muscle mass depletion. WBFM was 38,26%. This case represents classic sarcopenic obesity – high BMI masking underlying muscle loss (**Fig. 1**).

Case 2: Moderate sarcopenia with high BMI

An 83-year-old female patient (height 157 cm, weight 79 kg, BMI 32.05 kg/m^2) with a BMI in the obese range. The CT analysis showed an SMI of 21.78 cm^2/m^2 indicating moderate sarcopenia, that would not be apparent from BMI alone (**Fig. 2**).

Case 3: Severe sarcopenia despite high BMI

An 87-year-old male patient (height 168 cm, weight 91 kg, BMI 32.24 kg/m^2) demonstrates another critical pattern. Despite being classified as obese by BMI, CT analysis showed an SMI of 22.94 cm^2/m^2, indicating significant sarcopenia. This case highlights how BMI alone can mask serious muscle depletion in elderly patients (**Fig. 3**).

Case 4: Normal body composition with preserved muscle mass despite high BMI

An 82-year-old female patient (height 155 cm, weight 78 kg, BMI 42.47 kg/m^2). This case depicts the normal body composition despite BMI in obesity range. CT analysis shows normal muscle mass (SMI 46.92 cm^2/m^2) and normal estimated fat mass (31.86%) despite obesity classification by BMI (**Fig. 4**).

These cases highlight the significant discrepancies between BMI-based assessment and CT-derived body composition analysis. While BMI provides a rough estimate of

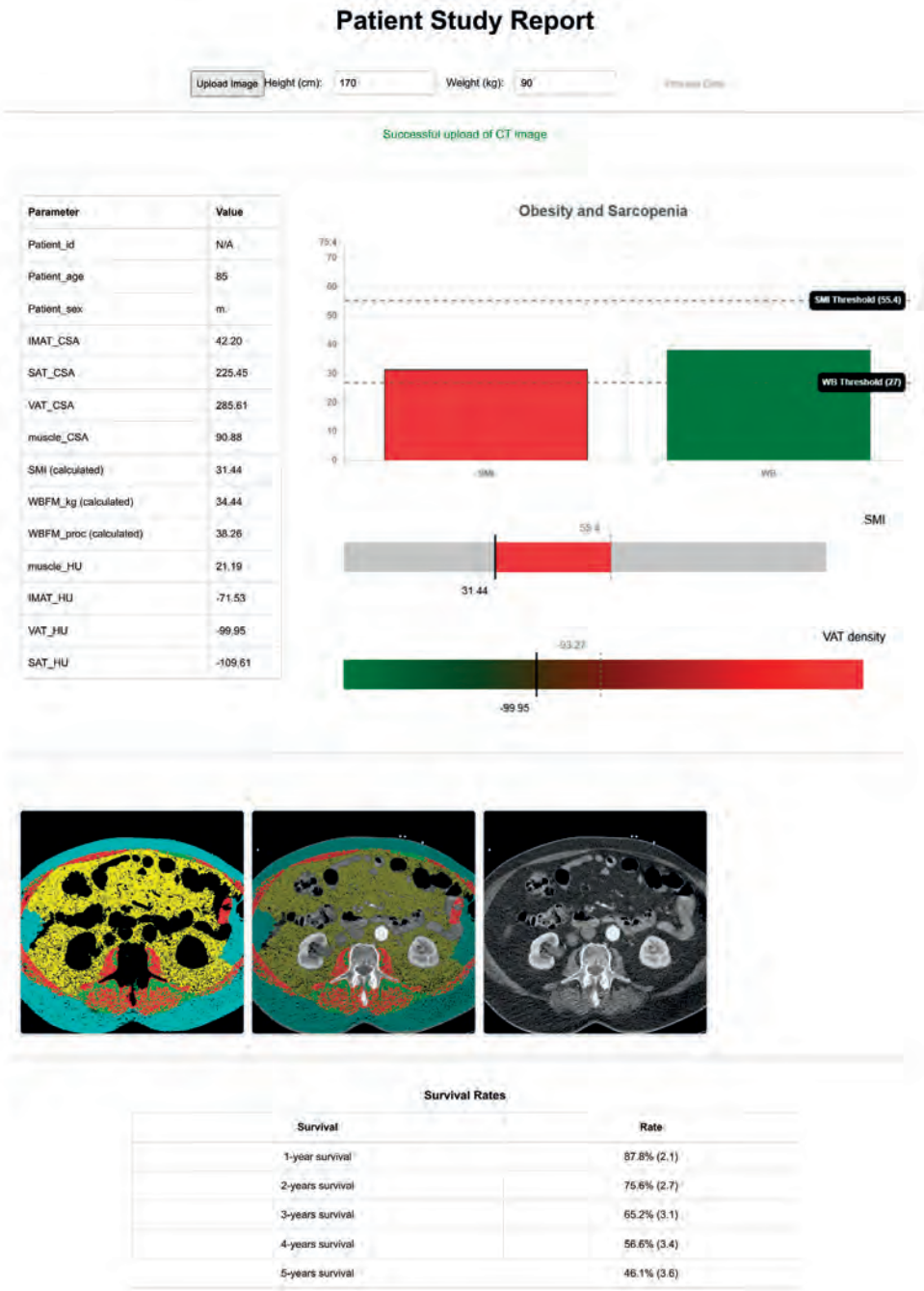


Fig. 1 – CT-based body composition analysis revealing sarcopenic obesity. Analysis of an 85-year-old male (BMI 31.14 kg/m²). The segmented CT image demonstrates low muscle mass (SMI 31.44 cm²/m²) despite high BMI, a classic pattern of sarcopenic obesity.

overall body mass relative to height, it fails to detect critical variations in muscle mass and adipose tissue distribution. The CT segmentation approach enables identification of specific body composition patterns that would be missed by BMI assessment alone: sarcopenic obesity, moderate sarcopenia, severe sarcopenia and normal body composition (despite high BMI in all four cases). Each pattern carries different clinical implications and risk factors, demonstrating the importance of tissue-specific analysis. This detailed characterization of body composition offers more precise risk stratification and could potentially guide more personalized treatment approaches for TAVI patients.

Discussion

The development of our web-based interface for CT segmentation analysis represents a significant step forward in the risk assessment of patients undergoing TAVI. To fully appreciate the value and potential limitations of this new tool, it is crucial to consider it within the broader context of existing scoring systems used in TAVI patient evaluation.

Several established scoring systems are currently used in TAVI patient evaluation, each with its own strengths and limitations. The EuroSCORE II is widely used for estimating

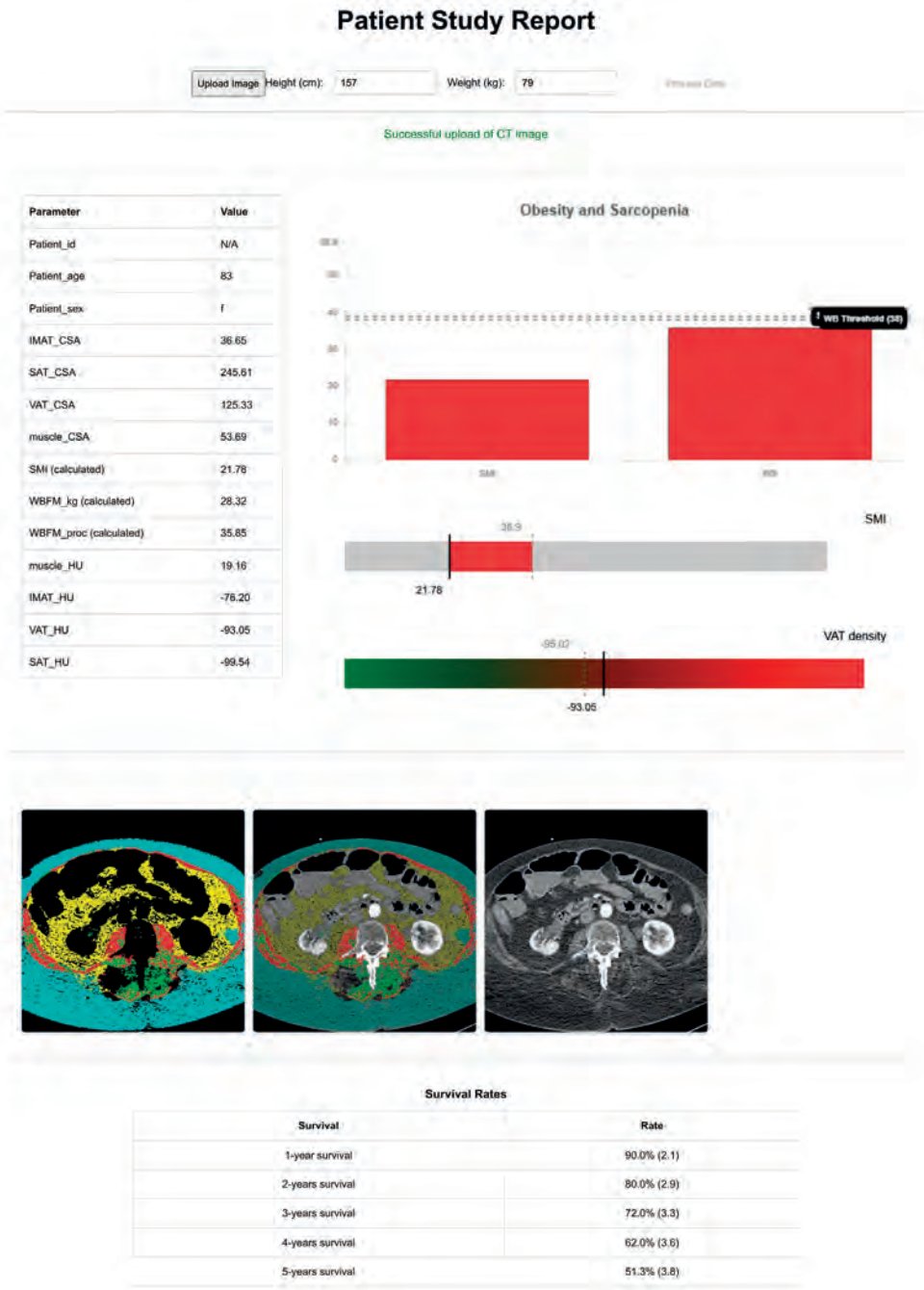


Fig. 2 – Moderate sarcopenia with high BMI. Analysis of an 83-year-old female (BMI 32.05 kg/m²). CT segmentation reveals moderate sarcopenic changes (SMI 21.78 cm²/m²) that would be missed by BMI assessment alone.

surgical mortality risk.[5] However, it does not assess long-term survival and is not specifically designed for minimally invasive or catheter-based procedures. The Clinical Frailty Scale offers a simple 9-point scale that evaluates overall health status, activity level, and dependency.[6] It is easily applicable in clinical practice and internationally validated, but it may be biased when assessed during inpatient care due to patients' typically deteriorated condition. The 6-Minute Walk Test provides data for predicting long-term mortality but is time- and space-intensive to perform.[7] The Comprehensive Geriatric Assessment is the most comprehensive test, including physical, cognitive, psychosocial, and nutritional assessments, with robust data for predicting long-term mortality. However, it is highly time- and personnel-intensive.[8] The Charlson Comorbidity Index generally provides excellent results in risk assessment and long-term mortality prediction[9] but is not primarily designed for patients undergoing minimally invasive or catheter-based procedures, potentially overestimating risk.

Our CTL3 parameters offer several advantages over these existing systems. They provide a comprehensive body composition analysis, unlike BMI, offering detailed insights into muscle mass, visceral fat, and subcutaneous fat distribution. This allows for the detection of hidden

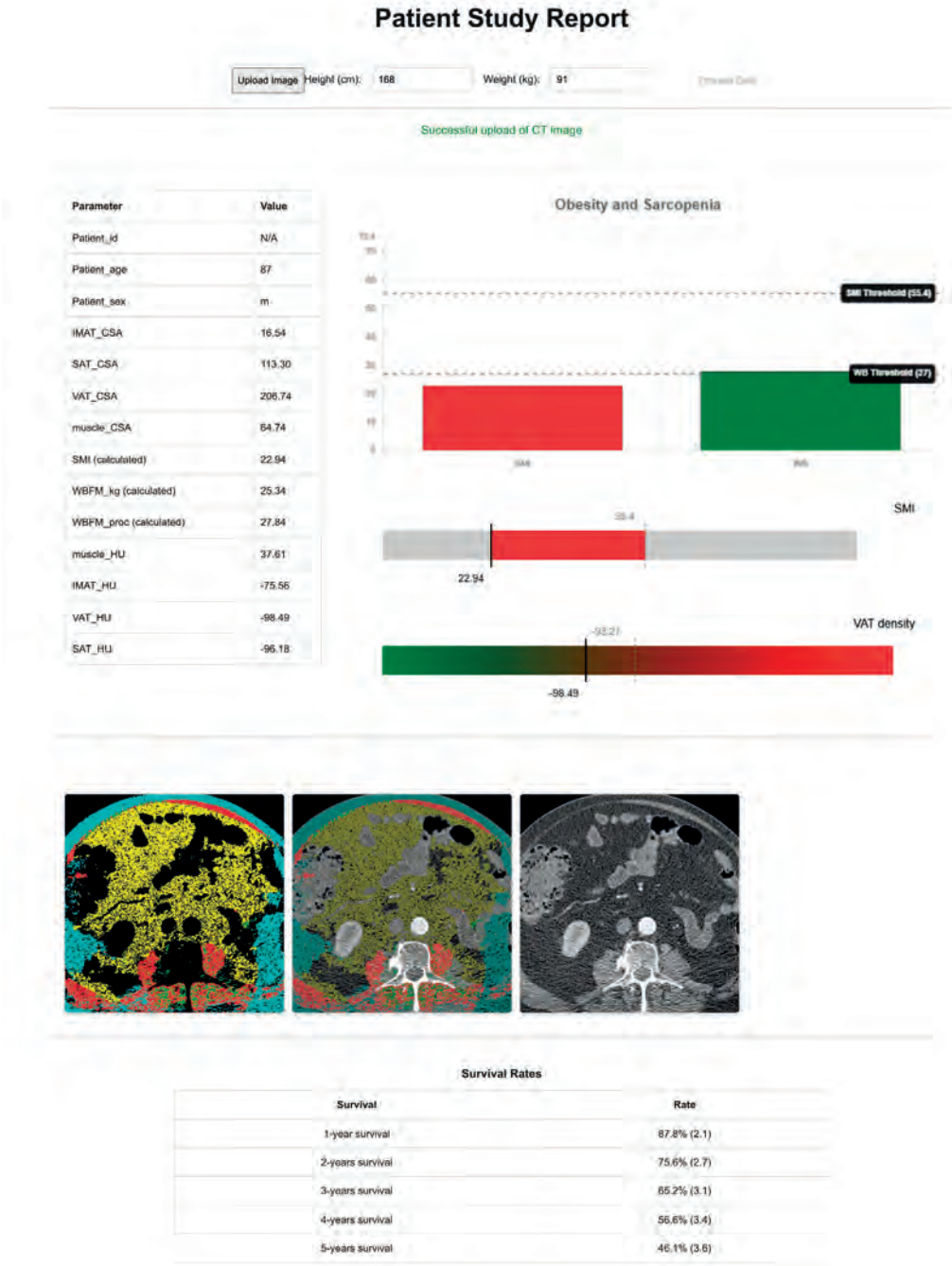


Fig. 3 – Severe sarcopenia masked by high BMI. CT analysis of an 87-year-old male (BMI 32.24 kg/m²) revealing significant muscle depletion (SMI 22.94 cm²/m²) despite obesity by BMI standards, emphasizing the importance of tissue-specific analysis.

conditions such as sarcopenia, obesity, or sarcopenic obesity that may not be apparent from external examination or traditional metrics like BMI. The CTL3 parameters offer objective quantification, providing precise measurements of tissue areas and densities, allowing for more accurate risk stratification. They also enable longitudinal comparison, allowing tracking of body composition changes over time, which could be valuable for assessing treatment efficacy or disease progression. Importantly, this analysis integrates with routine imaging, utilizing CT scans already performed as part of the TAVI workup, requiring no additional patient procedures.

However, it's important to acknowledge potential limitations of relying solely on CTL3 parameters. While providing detailed body composition data, CTL3 analysis does not capture other important factors such as cardiovascular function, frailty, or cognitive status. The predictive value of CTL3 parameters for TAVI outcomes, while promising, requires further large-scale, multicenter validation. The analysis relies on the availability of high-quality CT scans and specialized software, which may not be universally accessible. Additionally, it does not provide information about the patient's physical capabilities or daily living activities, which are crucial for comprehensive risk assessment.

Fig. 4 – Normal body composition with preserved muscle mass despite high BMI. Results from an 82-year-old female with high BMI (42.47 kg/m²). CT analysis shows normal muscle mass (SMI 46.92 cm²/m²) and normal estimated fat mass (31.86%) despite obesity classification by BMI.

Given the strengths and limitations of each scoring system, including our CTL3-based analysis, we propose a synergistic approach to TAVI patient evaluation. This approach would combine CTL3 analysis with established scoring systems like EuroSCORE II and Clinical Frailty Scale for a more comprehensive risk profile. The CTL3 parameters provide unique insights into body composition that complement, rather than replace, existing functional assessments. For instance, while the 6-minute walk test evaluates cardiorespiratory fitness and functional capacity through dynamic exercise testing, CTL3 analysis offers objective quantification of muscle mass and adipose tissue distribution that may influence exercise capacity and post-procedural outcomes. This complementary relationship is particularly valuable in cases where traditional metrics may be misleading or where functional tests may be difficult to perform. By integrating these different assessment modalities, clinicians can develop a more nuanced understanding of each patient's risk profile: CTL3 providing detailed body composition data, functional tests like the 6-minute walk test assessing physical capacity, and established risk scores evaluating broader clinical parameters. This multi-modal approach promises to enhance risk stratification accuracy and support more individualized treatment decisions in TAVI candidates.

Study limitations

Several limitations of our study should be acknowledged. First, while our interface successfully streamlines the implementation of AutoMATiCA's validated AI model, its effectiveness depends on the availability of high-quality CT scans and specific technical infrastructure requirements, which may not be universally available across all healthcare settings. Second, our current implementation requires manual file handling, as direct integration with hospital PACS systems has not yet been achieved. This may impact workflow efficiency in high-volume clinical settings. Third, while body composition analysis provides valuable prognostic information, it captures only one aspect of patient health status; it does not directly assess functional capacity, cardiovascular status, or cognitive function, which are also crucial for comprehensive TAVI risk assessment. Fourth, although our interface demonstrates excellent usability among the tested clinician group, broader validation across multiple centers and diverse healthcare settings would be beneficial to ensure generalizability. Fifth, the system's reliance on specific CT scan parameters (including slice thickness and radiation dosage) may require protocol standardization across institutions for optimal results. Finally, while our tool effectively identifies body composition patterns, longitudinal studies are needed to validate its predictive value for specific TAVI outcomes across diverse patient populations. Future development should focus on addressing these limitations through PACS integration, protocol standardization, and multi-center validation studies.

Conclusion

The development and implementation of our web-based interface for CT segmentation analysis represents a significant advancement in the risk assessment and management of patients undergoing TAVI. This study has demonstrated that our user-friendly interface has successfully bridged the gap between complex body composition analysis and clinical practicality, making advanced risk stratification tools more accessible to a broader range of clinicians. The integration of sarcopenia and obesity assessment according to CT-derived body composition and risk stratification according to adipose tissue density provides a more nuanced understanding of patient health status compared to traditional metrics such as BMI alone. While CTL3 parameter analysis offers valuable insights into body composition and potential risks for TAVI patients, it should be used as part of a comprehensive evaluation strategy. By combining the strengths of various scoring systems and assessment tools, including our new CT segmentation interface, clinicians can develop a more nuanced understanding of each patient's risk profile and tailor treatment approaches accordingly. This synergistic and individualized approach holds the promise of improving outcomes and patient care in the evolving field of TAVI.

Authors contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work. MP, MK, JB, and PB contributed to concept and design; MP, MK, and JH were responsible for acquisition, analysis, and interpretation of data; MP, MK, JB, and PB drafted the manuscript; MP, MK, LB, and JH provided critical review of the manuscript for important intellectual content; MP supervised the project.

Conflicts of interest

The authors declare no conflicts of interest.

Funding

This article has been produced with the financial support of the European Union under the LERCO project number CZ.10.03.01/00/22_003/0000003 via the Operational Programme Just Transition. The work and the contributions were supported by the project SP2024/071 "Biomedical Engineering systems XX" and Internal grant of Agel INT2023001.

Ethical statement

The four cases presented in this technical report were selected from the comprehensive TAVI Registry at Hospital AGEL Třinec-Podlesí, the Czech Republic, which contains demographic information, pre-TAVI CT scans, and clinical follow-up data collected since 2010. All data processing complied with GDPR requirements. Registry participants provided written informed consent for both the TAVI procedure and future research use of their anonymized data. The Hospital AGEL Třinec-Podlesí ethics committee approved the analysis of registry data (EK 301/22) according to the Declaration of Helsinki principles, and the primary study was registered under NCT05672160 at Clinical Trials.

Data availability statement

The data supporting this study are available from the authors upon reasonable request.

References

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597–1607.
2. Pekar M, Jiravsky O, Novak J, et al. Sarcopenia and adipose tissue evaluation by artificial intelligence predicts the overall survival after TAVI. Sci Rep 2024;14:8842.
3. Brown AD, Li B, Gabriel S, et al. Association Between Sarcopenia and Adverse Events Following Transcatheter Aortic Valve Implantation. CJC Open 2021;4:173–179.
4. Paris MT, Tandon P, Heyland DK, et al. Automated body composition analysis of clinically acquired computed tomography scans using neural networks. Clin Nutr 2020;39:3049–3055.
5. Nashef SAM, Roques F, Sharples LD, et al. EuroSCORE II. Eur J Cardiothorac Surg 2012;41:734–745.
6. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–95.
7. Chodór P, Wilczek K, Zielińska T, et al. Assessment of cardiovascular function following transcatheter aortic valve implantation based on six-minute walk test. Cardiol J 2017;24:167–175.
8. Chin K, Jones R, Lester E, et al. Comprehensive geriatric assessment, and related interventions, to improve outcomes for older patients undergoing transcatheter aortic valve implantation (TAVI): a systematic review. Eur Geriatr Med 2024;15:1615–1630.
9. Charlson ME, Carrozzino D, Guidi J, Patierno C. Charlson Comorbidity Index: A Critical Review of Clinimetric Properties. Psychother Psychosom 2022;91:8–35.

Původní sdělení | Original research article

Prevalence of Near-Death Experiences (NDE) in Patients with Refractory Cardiac Arrest Treated with Conventional and Extracorporeal Cardiopulmonary Resuscitation

Jaroslava Tereza Kovářová[a], Daniel Rob[b], František Trantina[b,c], Jan Bělohlávek[b]

[a] *Kardiologie Kovář s.r.o., Prague 12, the Czech Republic*
[b] *2nd Department of Internal Medicine, 1st Faculty of Medicine, Charles University and General University Hospital in Prague, Prague, the Czech Republic*
[c] *Ministry of Health, Prague, the Czech Republic*

ARTICLE INFO

Article history:
Submitted: 1. 12. 2024
Revised: 5. 2. 2025
Accepted: 28. 2. 2025
Available online: 6. 6. 2025

Klíčová slova:
Extrakorporální kardiopulmonální resuscitace
Extrakorporální membránová oxygenace
Kardiopulmonální resuscitace
Zážitky blízké smrti

SOUHRN

Cíl: Zážitky blízké smrti (near death experience, NDE) dosud nebyly studovány u pacientů s refrakterní srdeční zástavou léčených extrakorporální kardiopulmonální resuscitací (ECPR). Cílem tohoto pilotního projektu bylo zjistit výskyt NDE u pacientů z randomizované studie refrakterních srdečních zástav Prague OHCA a analyzovat rozdíly mezi pacienty resuscitovanými standardní kardiopulmonální resuscitací (KPR) a pacienty resuscitovanými metodou ECPR.
Metodika: Analýza NDE pomocí standardizovaného mezinárodně používaného dotazníku pacientů z randomizované studie Prague OHCA s dlouhodobým přežitím. Srovnání výskytu NDE u pacientů po srdeční zástavě léčených standardní KPR a pacientů resuscitovaných metodou ECPR.
Výsledky: Dotazník vyplnilo 44 z 60 pacientů, kteří byli dlouhodobě sledováni po studii Prague OHCA (medián věku 57,5 roku, 83 % muži, průměrná délka KPR 37,5 min), z toho 12 pacientů léčených ECPR (průměrná délka srdeční zástavy 54 min). Alespoň jeden příznak NDE prožilo celkem 15/44 pacientů (34,1 %), z toho 10/32 (31,3 %) ve skupině standardní KPR a 5/12 (41,6%) ve skupině ECPR (p = 0,52). Kritéria kompletní NDE (28 a více bodů v dotazníku NDE) splňovalo celkem 9/44 pacientů (20,5 %), z toho 6/32 (18,8 %) ve skupině standardní KPR a 3/12 (25 %) ve skupině ECPR (p = 0,65).
Závěr: Výskyt NDE v našem souboru pacientů s refrakterní srdeční zástavou odpovídá výskytu NDE v dosud publikovaných studiích, které analyzovaly pacienty léčené standardní KPR s kratší délkou srdeční zástavy. Numericky vyšší počet NDE u pacientů léčených strategií ECPR je hypotézu generující a nedosáhl statistické významnosti. Pro další závěry je nutná analýza větší kohorty pacientů.

Keywords:
Cardiopulmonary resuscitation
Extracorporeal cardiopulmonary resuscitation
Extracorporeal membrane oxygenation
Near-death experience

ABSTRACT

Objective: Near-death experiences (NDE) have not yet been studied in patients with refractory cardiac arrest treated with extracorporeal cardiopulmonary resuscitation (ECPR). The aim of this pilot project was to determine the prevalence of NDEs in patients from the randomized Prague OHCA study with refractory cardiac arrest and to analyze differences between patients resuscitated with standard cardiopulmonary resuscitation (CPR) and those resuscitated using the ECPR method.
Methods: NDEs were analyzed using a standardized and internationally validated questionnaire among long-term survivors of the randomized Prague OHCA study. The prevalence of NDEs was compared between patients treated with standard CPR and those resuscitated with the ECPR method.
Results: The questionnaire was completed by 44 out of 60 patients who were followed up long-term after the Prague OHCA study (median age: 57.5 years, 83% male, average CPR duration: 37.5 minutes), including 12 patients treated with ECPR (average cardiac arrest duration: 54 minutes). At least one symptom of NDE was experienced by 15/44 patients (34.1%), including 10/32 (31.3%) in the standard CPR group and 5/12 (41.6%) in the ECPR group (p = 0.52). Criteria for a complete NDE (score ≥28 on the NDE questionnaire) were met by 9/44 patients (20.5%), including 6/32 (18.8%) in the standard CPR group and 3/12 (25%) in the ECPR group (p = 0.65).

Address: MUDr. Jaroslava Tereza Kovářová, Kardiologie Kovář s.r.o., Soukalova 3355/3, 143 00 Prague 12, the Czech Republic, e-mail: s.l.a.v.k.a@seznam.cz
DOI: 10.33678/cor.2025.031

Please cite this article as: Kovářová JT, Rob D, Trantina F, Bělohlávek J. Prevalence of Near-Death Experiences (NDE) in Patients with Refractory Cardiac Arrest Treated with Conventional and Extracorporeal Cardiopulmonary Resuscitation. Cor Vasa 2025;67:331–335.

Conclusion: The prevalence of NDEs in our cohort of patients with refractory cardiac arrest corresponds to the prevalence reported in previous studies that analyzed patients treated with standard CPR and shorter durations of cardiac arrest. The numerically higher occurrence of NDEs in patients treated with the ECPR strategy is hypothesis-generating but did not reach statistical significance. Further conclusions require analysis in larger patient cohorts.

Introduction

Near-death experiences (NDEs) are defined as specific cognitive phenomena occurring during periods of unconsciousness in life-threatening situations, including cardiac arrest.[1]

NDEs have been a long-studied topic, and extensive multicenter studies on NDEs have been published in prominent scientific journals.[2–4] Guidelines[1] have also established a strictly scientific approach to studying this phenomenon.

In the context of care for critically ill and dying patients, NDEs can provide benefits. For these patients, NDEs may bring reconciliation with mortality, reduce fear of dying, and help manage physical and emotional pain. For relatives and caregivers, the NDE phenomenon can offer a new perspective on death as a natural part of life, improving care quality and easing the grieving process.[5,6]

Modern medicine, with new techniques, increasingly intervenes at the boundary between life and death. However, NDEs have mostly been analyzed in patients treated with standard cardiopulmonary resuscitation (CPR) with relatively short cardiac arrest durations.[2–4] In recent years, the global use of extracorporeal cardiopulmonary resuscitation (ECPR) has increased for patients with refractory cardiac arrest unresponsive to standard CPR. ECPR involves connecting the patient to venoarterial extracorporeal membrane oxygenation (VA ECMO) during resuscitation. This method allows survival in selected patients even after more than 60 minutes of unsuccessful conventional CPR.[7] However, NDEs have not yet been analyzed in this cohort.

The Prague OHCA study, published in 2022, is the largest randomized study to date focused on refractory cardiac arrest. It compares standard CPR with invasive treatment that includes early transport to a cardiac center, the use of ECPR for patients without return of circulation, and early invasive diagnosis and treatment of the cardiac arrest cause.[7]

This study aimed to determine the prevalence and characteristics of NDEs in survivors of refractory cardiac arrest treated with conventional CPR and the advanced ECPR method.

Materials and methods

We based our analysis on a cohort of patients who participated in the randomized Prague OHCA study.[7] Conducted between March 2013 and October 2020, this study was a collaboration between Prague Emergency Medical Services and the cardiac center of the General University Hospital in Prague. It compared two approaches for patients with out-of-hospital cardiac arrest: standard CPR and an invasive approach involving early transport to a cardiac center using mechanical chest compression, emergency VA ECMO (ECPR) for patients without restored circulation during transport, and early invasive diagnosis and treatment.

During long-term follow-up after cardiac arrest, patients who provided informed consent completed a standardized international NDE questionnaire. We obtained permission from the authors[8] to use the internationally recognized NDE questionnaire for Czech patients. The questionnaire was translated into Czech and validated through reverse translation into English. This made it suitable for use by Czech physicians and patients (**appendix 1**).

The NDE questionnaire, developed over decades, is based on statements from hundreds of patients. It was first published in 1983 with 16 questions.[9] Its latest version, from 2020,[8] includes 20 questions, with patients rating their experiences on a 0–4 scale corresponding to the intensity of their experience. The total score can reach a maximum of 80 points, with a score of 28 or higher indicating the presence of an NDE.

Our goal was to verify the prevalence and extent of NDEs in patients with refractory cardiac arrest treated with standard CPR compared to those treated with ECPR. Fisher's exact test was used to compare parameters between the two groups. Statistical significance was assessed at a significance level of 0.05.

Results

Survival of patients with good neurological outcomes (CPC 1–2)[9] at 180-day post-cardiac arrest was 31.5% in the invasive ECPR arm and 22% in the standard CPR arm.[7]

In the long-term follow-up cohort of patients from the Prague OHCA study, there were a total of 60 survivors at the time of our investigation (3/2022–5/2022), with an average age of 57 years, 83% male, and an average CPR duration of 37.5 minutes.

A total of 44/60 patients agreed to complete the NDE questionnaire.

At least one symptom of an NDE was reported by 15/44 patients (34.1%)–10/32 (31.3%) in the CPR arm and 5/12 (41.6%) in the ECPR arm, *p*-value 0.52.

A complete NDE score (≥28 points) was achieved by 9/44 patients (20.5%)–6/32 (18.8%) in the CPR arm and 3/12 (25%) in the ECPR arm, *p*-value 0.65.

Table 1 provides a more detailed overview of the questionnaire results for individual items.

Table 1 – NDE in CPR vs. ECPR

Pattern	Characteristics	CPR (%)	ECPR (%)	*p-value*
NDE-1	Time perception	21.88	50.00	0.135
NDE-2	Speeded thoughts	15.63	16.67	1.000
NDE-3	Voice	6.25	25.00	0.116
NDE-4	Understanding	12.50	25.00	0.116
NDE-5	Peacefulness	18.75	25.00	0.369
NDE-6	Harmony/unity	15.63	8.33	1.000
NDE-7 core	Bright light	12.50	16.67	0.658
NDE-8	Unusual sensation	28.13	33.33	0.729
NDE-9	Extrasensory perception	15.63	25.00	0.663
NDE-10	Precognition	6.25	8.33	1.000
NDE-11 core	Out of body experience	6.25	8.33	1.000
NDE-12 core	Leaving earthly world	18.75	16.67	1.000
NDE-13	Life review	9.38	8.33	1.000
NDE-14	Encounter	15.63	33.33	0.227
NDE-15	Non-existence/void/fear	15.63	25.00	0.663
NDE-16 core	Border/point of no return	9.38	8.33	1.000
NDE-17 core	Decision to come back	12.50	16.67	0.658
NDE-18 core	Dying	12.50	25.00	0.369
NDE-19 core	Gateway	9.38	16.67	0.603
NDE-20	Ineffability	12.50	41.67	0.087

Discussion

Our pilot study is the first to investigate the prevalence of near-death experiences (NDEs) in patients with refractory cardiac arrest treated not only with standard CPR but also using the ECPR method. The results showed that the prevalence of NDEs in the observed cohort aligns with previously published studies that analyzed patients treated exclusively with standard CPR with shorter cardiac arrest durations.

The numerically higher prevalence of NDEs in patients treated with the ECPR strategy may be attributed to the longer duration of cardiac arrest and the potential impact of circulatory support and reperfusion on neurocognitive processes. While this difference was not statistically significant, it may be hypothesis-generating. Mechanisms leading to NDEs may be multifactorial, involving complex interactions between hypoxia, neurocognitive activity, and the patient's subjective perception during critical conditions.

One limitation of our study is the small cohort size, which limits the statistical power and generalizability of our results. Additionally, potential selection bias should be considered, as only patients with long-term survival and good neurological outcomes (CPC 1–2) were included in the analysis. It is possible that patients with more severe neurological impairments or those who died during hospitalization may have had different experiences. Furthermore, the subjective nature of NDEs may be influenced by individual factors such as cultural, religious, or psychological background.

Nonetheless, our study represents an important step toward understanding this phenomenon in the context of advanced resuscitation care. The findings suggest that the ECPR method, which enables the survival of patients with prolonged cardiac arrest, provides a unique opportunity for further study of neurocognitive phenomena such as NDEs.

Currently, the number of publications on the NDE phenomenon is increasing.[11–23] For future research, it would be appropriate to analyze larger patient cohorts and consider a broader spectrum of variables. Longitudinal follow-up of patients and their subjective accounts would also be beneficial to better understand the long-term implications of NDEs on quality of life and psychological adaptation.

The phenomenon of NDEs in the context of modern resuscitation medicine represents not only a scientific but also an ethical and philosophical challenge that may significantly influence care for critically ill patients and the support provided to their families.

Conclusion

Our pilot study demonstrates that the prevalence of NDEs in patients with refractory cardiac arrest corresponds to existing findings from studies focused on patients treated with standard CPR with shorter cardiac arrest durations.

Although a numerically higher prevalence of NDEs was observed in our cohort of patients treated with the ECPR method, this difference was not statistically significant and primarily serves as a basis for hypothesis generation.

The findings suggest that advanced interventional strategies such as ECPR may offer new insights not only into survival and neurological recovery but also into the subjective experiences of patients near death. These experiences may have the potential to improve care and quality of life for patients and their families. However, further research is needed to confirm these findings and deepen our understanding.

Conflict of interest

The authors declare that they have no conflicts of interest. This publication has not been and will not be submitted for publication in another journal.

Funding

The research and publication were conducted independently of any influence from sponsors or other third parties that could affect the data or conclusions.

Ethical statement

The study was approved by the Institutional Review Board of the General University Hospital and the First Faculty of Medicine, Charles University, Prague. The trial complied with the Declaration of Helsinki and is registered at www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT01511666).

Informed consent

All participants were survivors of cardiac arrest who were fully conscious, clinically stable, and capable of providing informed consent at the time of questionnaire administra-

tion. Informed consent was obtained from all participants after they were provided with information about the study purpose, voluntary nature, and confidentiality measures. All data were anonymized to protect participants privacy.

Literature:

1. Parnia S, Post S, Matthew T, et al. Guidelines and Standards for the study of death and recalled experiences of death – a multidisciplinary consensus statement and proposed future directions. Ann N Y Acad Sci 2022;1511:5–21.
2. Lommel PV, Wees RV, Meyers V et al. Near-death experience in survivors of cardiac arrest: a prospective study in the Netherlands. Lancet 2001;358:2039–2045.
3. Parnia S, Spearpoint K, Fenwick PB. Near death experiences, cognitive function and psychological outcomes of surviving cardiac arrest. Resuscitation 2007;74:215–221.
4. Parnia S, Shirazi TK, Jignesh P, et al. AWAreness during REsuscitation – II: A multi-center study of consciousness and awareness in cardiac arrest. Resuscitation 2023;191:109903.
5. Greyson B. After – A Doctor Explores What Near-Death Experience Reveal About Life and Beyond. Penquin Random House UK, 2022.
6. Lommel P. Consciousness beyond life. The Science of the Near--Death Experience. HarperCollins Publishers, New York, 2010.
7. Belohlavek J, Smalcova J, Rob D, et al. Effect of Intra-arrest Transport, Extracorporeal Cardiopulmonary Resuscitation, and Immediate Invasive Assesment and Treatment on Functional Neurologic Outcome in Refractory Out-of-Hospital Cardiac Arrest: A Randomized Clinical Trial. JAMA 2022;327:737–747.
8. Martial C, Simon J, Puttaert N, et al. The Near-Death Experience Content (NDE-C) scale: Development and psychometric validation. Conscious Cogn 2020;86:103049.
9. Greyson B. The Near-Death Experience Scale – Construction, Reliability and Validity. J Nerv Ment Dis 1983;171:369–375.
10. Safar P, Bleyaert A, Nemoto EM, et al. Cerebral Resuscitation after Global Ischemia-anoxia. Crit Care Med 1978;6:215–227.
11. Martial CH, Cassol H, Laureys S, et al. Near-Death Experience as a Probe to Explore (Disconnected) Consciousness. Trends Cogn Sci 2020;24:173–183.
12. Hashemi A, Oroojan AA, Maryam R, et al. Explanation of near-death experiences: a systematic analysis of case reports and qualitative research. Front Psychol 2023;14:1048929.
13. West RL, Otto Q, Drennan IR, et al. CPR-related cognitive aktivity, consciousness, awareness and recall, and its management: A scoping review. Resusc Plus 2022:10:100241.
14. Kondziella D. The neurology of Death and the Dying Brain: A Pictorial Essay. Front Neurol 2020;11:736.
15. Vicente R, Rizzuto M, Sarica C, et al. Enhanced Interplay of Neuronal Coherence and Coupling in the Dying Human Brain. Front Aging Neurosci 2022;14:813531.
16. Long J, Woollacott M. Long-term transformational effects of near-death experiences. Explore (NY) 2024;20:103030.
17. Woollacott M. Near-death experience: memory recovery during hypnosis. Explore (NY) 2024;20:103036.
18. King RA. Suicide Folowing a Near-Death Experience. Crisis 2024;45:348–354.
19. Rousseau AF, Dams L, Massart Q, et al. Incidence of near-death experiences in patients surviving a prolonged critical illness and their long-term impact: a prospective observational study. Crit Care 2023;27:76.
20. Bicego A, Cassol H, Simon J, et al. Personality traits and pattern of beliefs of near-death(-like) experiencers. Front Hum Neurosci 2023;17:1124739.
21. Cassol H, Martial C, Annen J, et al. A systematic analysis of distressing near-death experience accounts. Memory 2019;27:1122–1129.
22. Martial CH, Gosseries O, Cassol H, et al. Studying death and near-death experiences requires neuroscientific expertise. Ann N Y Sci 2022;1517:11–14.
23. Romand R, Ehret G. Neuro-functional modeling of near-death experiences in contexts of altered states of consciousness. Front Psychol 2023;13:846159.

Appendix 1

Otázky pro pacienty po srdeční zástavě

Zažil(a) jste situaci, kdy se bojovalo o váš život a podařilo se to. Zajímaly by nás vaše zážitky.
Zkuste nám, prosím, zodpovědět následujících 20 otázek.
Odpovídejte zaškrtnutím čísla:
0 – ne, vůbec
1 – mírně
2 – středně
3 – silně (ekvivalent k jinému silnému životnímu zážitku)
4 – extrémně (víc než cokoli jiného v mém životě)
Budeme rádi, když své odpovědi rozvedete, upřesníte nebo sdělíte něco, na co jsme se zapomněli zeptat.

1. Vaše vnímání času bylo změněné?
0 1 2 3 4

2. Vaše myšlenky se zrychlily?
0 1 2 3 4

3. Slyšel(a) jste jeden nebo více hlasů, které nepatřily žádné konkrétní osobě?
0 1 2 3 4

4. Měl(a) jste pocit náhlého porozumění všemu, co se týká vás, jiných a/nebo vesmíru?
0 1 2 3 4

5. Měl(a) jste pocit míru a/nebo duševní pohody?
0 1 2 3 4

6. Cítil(a) jste pocit harmonie, jednoty, jako byste patřil(a) k většímu celku?
0 1 2 3 4

7. Viděl(a) jste nebo cítil(a) jste se obklopen(a) zářivým světlem?
0 1 2 3 4

8. Zažil(a) jste neobvyklé vjemy – zrakové, sluchové, čichové, hmatové a/nebo chuťové?
0 1 2 3 4
(zkuste je popsat, pokud to lze)

9. Uvědomoval(a) jste si věci za hranicí toho, co vaše smysly obvykle vnímají?
0 1 2 3 4

10. Získal(a) jste vhled do budoucnosti?
0 1 2 3 4

11. Měl(a) jste pocit, že jste vně nebo oddělen(a) od svého těla?
0 1 2 3 4

12. Měl(a) jste pocit opuštění pozemského světa nebo vstupu do nové dimenze a/nebo prostředí?
0 1 2 3 4

13. Viděl(a) nebo znovuprožil(a) jste události z vaší minulosti?
0 1 2 3 4
(zkuste popsat jaké, pokud chcete)

14. Setkal(a) jste se s bytostí a/nebo s nějakým subjektem – např. zemřelým?
0 1 2 3 4

15. Zažil jste pocit neexistence, pobytu v absolutním prázdnu a/nebo strach, úzkost?
0 1 2 3 4

16. Přišel/přišla jste k hranici nebo bodu odkud není návratu?
0 1 2 3 4

17. Rozhodl(a) jste se nebo jste byl(a) přinucen(a) se vrátit zpět z tohoto prožitku?
0 1 2 3 4

18. Měl(a) jste pocit že umíráte a/nebo že jste zemřel(a)?
0 1 2 3 4

19. Viděl(a) nebo vstoupil(a) jste do brány nebo tunelu nebo dveří nebo podobné?
0 1 2 3 4
(zkuste popsat, pokud chcete)

20. Máte pocit, že zážitek nemůže být adekvátně popsán slovy?
0 1 2 3 4

Questions for patients after cardiac arrest

You have experienced a situation where your life was in danger, and it was saved. We are interested in hearing about your experiences. Please try to answer the following 20 questions.
Respond by ticking the appropriate number:
0 – not at all
1 – slightly
2 – moderately
3 – strongly
4 – extremely

1. Your perception of time was altered
0 1 2 3 4

2. Your thoughts speeded up
0 1 2 3 4

3. You heard one or several voices which did not have any material incarnation
0 1 2 3 4

4. You had the feeling of suddendly understanding everything about yourself, the others and/or the universe
0 1 2 3 4

5. You had the feeling of peace and/or well-being
0 1 2 3 4

6. You felt a sense of harmony or unity, as if you belonged to a larger whole
0 1 2 3 4

7. You saw or felt surrounded by a bright light without any determined material origin
0 1 2 3 4

8. You experienced unusual sensation (sight, hearing, smell, touch and/or taste)
0 1 2 3 4

9. You were aware of things beyond what your senses can usually perceive
0 1 2 3 4

10. You gained insightful knowledge about the future
0 1 2 3 4

11. You had the impression of being outside of, or separated from your own body
0 1 2 3 4

12. You had the sensation of leaving the earthly world or of entering a new dimension and/or enviroment
0 1 2 3 4

13. You saw or relieved events from your past
0 1 2 3 4

14. You encountered a presence and/or an entity (who might be deceased)
0 1 2 3 4

15. You had a feeling of non-existence, of being in a total void, and/or of fear
0 1 2 3 4

16. You came close to a border and/or point of no return
0 1 2 3 4

17. You made the decision, or were forced, to come back from the experience
0 1 2 3 4

18.You had the feeling of dying and/or being dead
0 1 2 3 4

19. You saw or entered a gateway (for instance a tunnel or a door)
0 1 2 3 4

20. You sense that the experience cannot be described adequately in words
0 1 2 3 4

Původní sdělení | Original research article

Změny tělesného složení během ambulantního a hybridního typu kardiovaskulární rehabilitace u pacientů s ischemickou chorobou srdeční

(Changes in Body Composition During Outpatient and Hybrid Cardiovascular Rehabilitation in Patients with Coronary Artery Disease)

Marko Zváč[a], Ladislav Baťalík[a–d]

[a] *Katedra fyzioterapie a rehabilitace, Lékařská fakulta Masarykovy univerzity, Brno, Česká republika*
[b] *Rehabilitační klinika, Fakultní nemocnice Brno, Brno, Česká republika*
[c] *Rehabilitační klinika, Lékařská fakulta Masarykovy univerzity, Brno, Česká republika*
[d] *Ústav veřejného zdraví, Lékařská fakulta Masarykovy univerzity, Brno, Česká republika*

INFORMACE O ČLÁNKU

Historie článku:
Vložen do systému: 2. 1. 2025
Přijat: 10. 2. 2025
Dostupný online: 28. 5. 2025

Klíčová slova:
Hybridní rehabilitace
Ischemická choroba srdeční
Kardiovaskulární rehabilitace
Kardiovaskulární rizikové faktory
Tělesné složení

SOUHRN

Cíl: Zhodnotit efektivitu tradičního ambulantního programu a hybridního programu kardiovaskulární rehabilitace (KR) při zlepšení tělesného složení a kardiovaskulárních rizikových faktorů u pacientů s ischemickou chorobou srdeční (ICHS).
Soubor a metodika: Dvanáctitýdenní program KR dokončilo 136/169 (76 %) pacientů s ICHS, kteří absolvovali buď tradiční ambulantní (n = 91), nebo hybridní (n = 45) KR. Tělesné složení bylo hodnoceno pomocí bioelektrické impedanční analýzy. Účinnost KR byla posuzována na základě změn tělesného složení (hmotnost, svalová hmota, útrobní tuk) a kardiovaskulárních parametrů (krevní tlak, LDL cholesterol, aerobní kapacita) před programem a po programu.
Výsledky: Obě skupiny prokázaly významná zlepšení v tělesném složení, kardiovaskulárních parametrech a aerobní kapacitě (+18 W vs. +19 W, obě $p < 0,05$). Ambulantní skupina vykázala významně vyšší nárůst svalové hmoty (+0,65 %, $p < 0,05$) a výraznější redukci útrobního tuku oproti hybridní skupině. Hybridní skupina měla významnější pokles systolického krevního tlaku. U žádného pacienta nebyly zaznamenány závažné nežádoucí příhody spojené s KR.
Závěr: Tradiční i hybridní modely KR představují účinné přístupy ke zlepšení tělesného složení a kardiovaskulárních rizikových faktorů u pacientů s ICHS. Hybridní model navíc nabízí vyšší flexibilitu a srovnatelný bezpečnostní profil, což z něj činí atraktivní alternativu pro širší spektrum pacientů.

Keywords:
Body composition
Cardiac rehabilitation
Cardiovascular risk factors
Coronary artery disease
Hybrid rehabilitation

ABSTRACT

Objective: To evaluate the effectiveness of traditional outpatient and hybrid cardiac rehabilitation (CR) programs in improving body composition and cardiovascular risk factors in patients with coronary artery disease (CAD).
Methods: A total of 136 out of 169 CAD patients completed a 12-week CR program (outpatient: n = 91, hybrid: n = 45). Body composition was assessed using bioelectrical impedance analysis, while cardiovascular parameters were measured before and after the program.
Results: Both groups showed significant improvements in body composition, cardiovascular parameters, and aerobic capacity (+18 W vs +19 W; $p < 0.05$). The outpatient group exhibited a higher increase in muscle mass (+0.65%, $p < 0.05$) and visceral fat reduction, while the hybrid group showed a greater decrease in systolic blood pressure. No serious adverse events were reported.
Conclusion: Both CR models are effective in improving body composition and cardiovascular risk factors. The hybrid model offers comparable safety and flexibility, making it an attractive alternative for a broader patient population.

Adresa: Doc. Mgr. Ladislav Baťalík, Ph.D., CRFC, Rahabilitační klinika, Fakultní nemocnice Brno, Jihlavská 20, 625 00 Brno, Česká republika,
e-mail: batalik.ladislav@fnbrno.cz
DOI: 10.33678/cor.2025.026

Tento článek prosím citujte takto: Zváč M, Baťalík L. Změny tělesného složení během ambulantního a hybridního typu kardiovaskulární rehabilitace u pacientů s ischemickou chorobou srdeční. Cor Vasa 2025;67:336–343.

Úvod

Kardiovaskulární onemocnění (KVO) zahrnují celou řadu poruch postihujících srdce a cévy a jsou celosvětově nejčastější příčinou úmrtí, kdy v roce 2021 na ně zemřelo přibližně 20,5 milionu lidí.[1] Mezi nejvýznamnější typy patří ischemická choroba srdeční (ICHS), což je nejčastější onemocnění srdce, při kterém dochází k postupnému zúžení nebo úplnému uzávěru věnčitých tepen v důsledku aterosklerózy a které je charakterizováno ukládáním aterosklerotických plátů. Tento proces může vést k omezení průtoku krve a následně k srdečním infarktům.[2,3] Podle odhadů činí ekonomická zátěž KVO v Evropské unii přibližně 282 miliard eur ročně, přičemž zdravotní a dlouhodobá péče představuje přibližně 155 miliard eur z této částky, což představuje 55 % celkových nákladů a 11 % celkových výdajů EU na zdravotnictví.[4] Kromě optimální medikamentózní léčby a revaskularizace se v případě potřeby v léčebných doporučeních důrazně doporučuje kardiovaskulární rehabilitace (KR), která se zaměřuje na pomoc pacientům při zavádění rutinního zdravého životního stylu.[5] KR je komplexní program určený ke zlepšení kardiovaskulárního zdraví osob, které se zotavují z problémů souvisejících s onemocněním srdce. Tento program pod lékařským a fyzioterapeutickým dohledem se zaměřuje na tři hlavní složky: cvičební trénink, vzdělávání pro zdravý životní styl u osob se srdečním onemocněním a poradenství pro snížení stresu.[6] Mezi hlavní benefity programu KR patří zlepšení kardiovaskulárního zdraví, snížení rizika další příhody a optimalizace krevního tlaku, cholesterolu a glykemie.[7] Taktéž se snižuje riziko hospitalizací, infarktu myokardu a úmrtí.[8] Program KR také významně podporuje zvýšení fyzické kondice, což zahrnuje nejen zlepšení svalové síly a vytrvalosti, ale také zvýšení aerobní kapacity, která je klíčová pro efektivní fungování srdce a cév během fyzické aktivity.[9] Důležitým přínosem KR je zlepšení psychického zdraví díky snížení úzkosti a deprese a podpoře kvality života.[10] Rehabilitace rovněž zlepšuje adherenci k léčbě, podporuje zdravý životní styl a pomáhá pacientům lépe zvládat farmakoterapii.[11] Dalším benefitem je redukce nákladů na zdravotní péči díky snížení potřeby hospitalizací a prevence komplikací. Individuální přístup a vzdělávání pacientů umožňují lepší porozumění rizikům a jejich zvládání, přičemž skupinové aktivity poskytují sociální a komunitní podporu.[12,13] Navzdory jednoznačným přínosům KR zůstává adherence pacientů nízká, což představuje zásadní problém v sekundární prevenci KVO.[14,15] Proto je nezbytné hledat způsoby, jak zlepšit dostupnost a přístup k programům KR, aby mohly být využity širší populací pacientů. Alternativní modely rehabilitace, jako je domácí KR nebo hybridní KR (kombinace domácího a ambulantního přístupu), se ukázaly být stejně účinné jako tradiční centrálně řízený model KR.[16–18] Komplexní programy KR, které jsou v současné době poskytovány pacientům s KVO a mají dostatek kompetencí zdůraznit fyzické cvičení a zdravou výživu pro optimalizaci tělesného složení.[19] Účelem této studie bylo zhodnotit změny v tělesném složení v tradičním ambulantním programu KR ve srovnání s alternativním hybridním programem KR v jednom nemocničním centru.

Metody

Charakter studie a populace

Do studie byli zařazeni pacienti s ICHS, kteří v období od 3. 10. 2019 do 30. 9. 2024 absolvovali tradiční nebo hybridní program KR ve Fakultní nemocnici Brno. Do studie byli zařazeni pouze pacienti s ICHS, kteří měli diagnózu stanovenou přibližně před třemi měsíci (s tolerancí ± osm týdnů), jež zahrnovala následující diagnózy: koronární bypass, koronární stent nebo angioplastiku, anginu pectoris nebo infarkt myokardu. U pacientů s implantovaným stimulátorem srdce nebo defibrilátorem bylo zařazení kontraindikováno. Zahrnuty byly výsledky kardiovaskulárního zdraví a tělesného složení před 12týdenním programem KR a po něm. Pacienti vstupující do programu KR měli možnost volby modelu KR podle vlastních preferencí. Pacienti, kteří absolvovali méně než 60 % předepsaných lekcí, byli ze studie vyloučeni.

Měření tělesného složení

Tělesné složení bylo hodnoceno pomocí přístroje InBody 370S (Soul, Jižní Korea) měřením s využitím multifrekvenčních analyzátorů. V souladu s pokyny výrobce zůstal každý pacient v kontaktu s elektrodami váhy na rukou a nohou, zatímco rukama, nohama a trupem pacienta procházelo několik různých frekvencí elektrického proudu (5 kHz, 50 kHz a 250 kHz). Tyto frekvence jsou aplikovány na pět segmentů těla (pravá paže, levá paže, trup, pravá noha, levá noha), což umožňuje provést 15 měření impedance. Celé vyšetření trvalo přibližně 45 sekund a bylo vyhodnoceno několik ukazatelů tělesného složení, včetně hmotnosti tělesného tuku, útrobního tuku, hmotnosti kosterního svalstva a indexu tělesné hmotnosti (BMI).

Validační studie bioelektrické impedanční analýzy InBody při hodnocení tělesného složení prokázaly silné korelace s výpočetní tomografií, což naznačuje její užitečnost jako alternativy pro měření oblasti viscerálního tuku a hmoty kosterního svalstva.[20,21]

Srdeční hemodynamika, zátěžová kapacita a laboratorní parametry

Měření klidových a zátěžových parametrů srdeční hemodynamiky bylo provedeno na základě doporučení Evropské kardiologické společnosti (ESC) a American Heart Association (AHA).[22] Vyšetření zahrnovalo jak klidová měření krevního tlaku (TK) a srdeční frekvence (SF), tak i zatížení pomocí kardiopulmonálního zátěžového testu (CPET). CPET byl proveden na bicyklovém ergometru Ergoselect 100 (Ergoline, Bitz, Německo) s progresivním zvyšováním zátěže až do dosažení symptom-limitujícího maxima. Během testu byly kontinuálně monitorovány následující parametry: maximální srdeční frekvence (HR_{max}), která byla stanovena při dosažení limitu subjektivní námahy nebo symptomů, klidová a maximální hodnota krevního tlaku (TK), měřená manuálně tonometrem CA-MI (CAMI Group, Parma, Itálie) každé dvě minuty, ventilační parametry a plynová analýza, stanovené pomocí přímé spirometrické analýzy (např. Cortex Metalyzer 3B), a elektrokardiografické změny, hodnocené standardním 12svodovým EKG. Test byl prováděn pod dohledem léka-

ře, který sledoval bezpečnost pacienta a zaznamenával případné nežádoucí příhody.

Laboratorní parametry

Z laboratorních vyšetření byl analyzován lipidový profil se zaměřením na LDL cholesterol (LDL-C). Odběr byl proveden nalačno v ranních hodinách (7.00–9.00) ve standardní klinické laboratoři. Koncentrace LDL-C byla stanovena enzymatickou kolorimetrickou metodou pomocí automatického analyzátoru (Cobas, Roche Diagnostics, Německo).

Programy kardiovaskulární rehabilitace

Tradiční program KR ve Fakultní nemocnici Brno trvá 8–12 týdnů a zahrnuje tři tréninkové jednotky týdně. Každá jednotka se skládá ze zahřívací fáze, aerobně-odporového tréninku a relaxační fáze s celkovou délkou 45–60 minut. Individuální cvičební režim je přizpůsoben specifickému zdravotnímu stavu a potřebám každého pacienta. Před zahájením KR pacient podstoupí vyšetření kardiologem včetně CPET, jehož cílem je stanovit bezpečné limity fyzické aktivity.

Tréninkové parametry jsou nastavovány fyzioterapeutem každému pacientovi striktně individuálně, a to s přihlédnutím k aktuálnímu kardiálnímu i pohybovému stavu, doplněnému o měření SF. Intenzita cvičení je individualizována a nastavena na 65–80 % HR_{max}.

Pacienti jsou během obou modelů KR edukováni o sekundární prevenci a zdravém životním stylu, včetně významu pravidelné fyzické aktivity, vyvážené stravy a kontroly tělesné hmotnosti. Důraz je kladen také na omezení kouření a alkoholu, zvládání stresu a pravidelné sledování rizikových faktorů, jako jsou krevní tlak, cholesterol a koncentrace cukru v krvi.

Hybridní program KR představoval kombinaci tradičního programu KR a domácího cvičení ve stejném předpisu frekvence, intenzity a trvání. Pacienti absolvovali jedno ambulantní sezení týdně a dvě sezení týdně v domácím prostředí po dobu 8–12 týdnů. Domácí část zahrnovala zahřívací fázi, aerobní trénink a relaxaci, avšak bez odporového posilování. Domácí cvičení bylo zaměřeno výhradně na aerobní aktivity, jako je chůze, jízda na kole či nordic walking v exteriéru, nebo využití aerobních trenažérů (rotoped, ergometr, chodecký pás) v domácím prostředí dle preferencí a možností pacienta. Intenzita a trvání tréninkových jednotek v domácím prostředí odpovídaly hodnotám předepsaným během ambulantního sezení.

Statistické metody

Porovnání vstupních charakteristik ambulantních pacientů s účastníky hybridního programu KR bylo provedeno pomocí chí-kvadrát testu, Mannova–Whitneyho U-testu a t-testů pro nezávislé vzorky podle potřeby. Změny v rámci skupiny během KR byly hodnoceny pomocí párových t-testů, zatímco změny mezi dvěma skupinami rehabilitace byly hodnoceny pomocí t-testů pro nezávislé vzorky. Také byly vypočteny procentuální změny několika ukazatelů tělesného složení, a to vydělením průměrné změny před KR průměrnou hodnotou po rehabilitaci. Všechny analýzy byly provedeny pomocí programu IBM SPSS Statistics, verze 25.

Výsledky

Během sledovaného období bylo celkově zařazeno do studie 169 pacientů. Celkem 136 pacientů (75,7 %) absolvovalo tradiční nebo hybridní model. Důvody pro vyřazení ze studie byly: návrat do práce (n = 17; 10,1 %), bez udání důvodu (n = 10; 5,9 %), kardiovaskulární klinický problém (n = 3; 1,8 %) nebo jiný klinický problém (n = 3; 1,8 %).

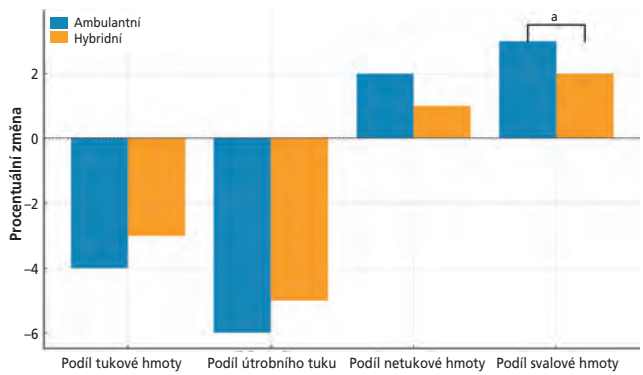
Z celkového počtu účastníků studie absolvovalo 91 pacientů (66,9 %) tradiční ambulantní program KR, zatímco zbývajících 45 pacientů (33,1 %) dokončilo hybridní program KR. Základní demografické a klinické charakteristiky obou skupin jsou uvedeny v **tabulce 1**. Ve sledovaných ukazatelích nebyly mezi pacienty v ambulantním a hybridním programu KR zjištěny významné rozdíly. Během programu KR u žádného pacienta nedošlo k závažným nežádoucím příhodám.

Změna KV rizikového profilu během KR

Účastníci obou programů KR (ambulantního a hybridního) prokázali významná zlepšení ve vybraných ukazatelích kardiovaskulárního rizika a tělesného složení (**tabulka 2**). Klidová SF zůstala podobná bez významné změny, zatímco systolický i diastolický TK mírně poklesly, přičemž nejvýraznější zlepšení bylo pozorováno u hybridního programu. Významný nárůst byl zaznamenán u aerobní kapacity, měřené hodnotou výkonu, který se zvýšil o 19 W (14 %) u ambulantní a o 18 W (12 %) u hybridní skupiny (obě skupiny $p < 0,05$).

Významné zlepšení bylo rovněž zaznamenáno u kardiologických biomarkerů, především u koncentrace LDL cholesterolu, která se snížila jak v ambulantním programu (o 0,36 mmol/l, $p < 0,05$), tak v hybridním programu (o 0,23 mmol/l, $p < 0,05$). Tyto změny svědčí o pozitivním vlivu KR na metabolický profil účastníků.

Pokud jde o tělesné složení, byl zaznamenán významný pokles tělesné hmotnosti, relativního podílu tukové hmoty a útrobního tuku. Současně byl zaznamenán významný rozdíl podílu svalové hmoty mezi skupinami (ambulantní: o 0,65 %, $p < 0,05$; **obr. 1**).



Obr. 1 – Obrázek zobrazuje procentuální změny v tělesném složení u ambulantních a hybridních pacientských skupin. Kategorie zahrnují podíl tukové hmoty, útrobního tuku, netukové hmoty a svalové hmoty. a = $p < 0,05$.

Tabulka 1 – Charakteristiky účastníků na začátku kardiovaskulární rehabilitace[a]				
Charakteristika	**Všichni účastníci (n = 136)**	**Ambulantní (n = 91)**	**Hybridní (n = 45)**	**Hodnota *p*[b]**
Věk, medián (rozsah)	56 (21–84)	56 (21–80)	56 (21–84)	0,552
Ženské pohlaví (%)	37 (27)	25 (28)	12 (27)	0,916
Kardiovaskulární rizikové faktory				
Anamnéza kouření (%)	46 (34)	29 (32)	17 (38)	0,622
Diabetes mellitus (%)	27 (20)	17 (19)	10 (22)	0,796
Hypertenze (%)	88 (65)	55 (60)	33 (73)	0,197
Srdeční hemodynamika a zátěžová kapacita				
Klidová TF (tep/min)	73.62 ± 10,62	73,88 ± 10,71	73,1 ± 10,44	0,686
Systolický TK (mm Hg)	125 ± 17	123 ± 17	130 ± 16	0,052
Diastolický TK (mm Hg)	76 ± 11	76 ± 11	75 ± 9	0,685
Výkon (W)	138,06 ± 34,29	134,35 ± 33,65	145,34 ± 36,15	**0,039**
Nižší (≤ 40%) EF LK	12 (9)	10 (11)	2 (4)	0,306
Kardiologické biomarkery				
LDL cholesterol (mmol/l)	2,46 ± 0,46	2,47 ± 0,4	2,45 ± 0,59	0,687
Tělesné složení				
Hmotnost (kg)	87,03 ± 16,69	86,9 ± 16,85	87,32 ± 16,54	0,890
Index tělesné hmotnosti (kg/m^2)	28,58 ± 4,03	28,66 ± 4,08	28,42 ± 3,99	0,740
Podíl netukové hmoty (%)	58,75 ± 11,89	58,99 ± 11,92	58,26 ± 11,91	0,631
Podíl svalové hmoty (%)	35 ± 7,6	35,12 ± 7,62	34,72 ± 7,63	0,681
Podíl tukové hmoty (%)	25,85 ± 9,18	26,1 ± 9,36	25,34 ± 8,88	0,637
Úroveň útrobního tuku (1–20)	11,5 ± 4,67	11,43 ± 4,62	11,6 ± 4,82	0,887

LDL cholesterol – cholesterol v lipoproteinech o nízké hustotě; TF – tepová frekvence, TK – krevní tlak.
[a] Data jsou vyjádřena jako průměr ± směrodatná odchylka (SD) nebo n (%).
[b] Hodnota *p* představuje rozdíly před rehabilitací mezi ambulantním a hybridním programem kardiovaskulární rehabilitace.

Tabulka 2 – Kardiovaskulární rizikové faktory a změny tělesného složení					
Charakteristika	**Ambulantní: před KR**	**Ambulantní: po KR**	**Hybridní: před KR**	**Hybridní: po KR**	**Hodnota *p***
Srdeční hemodynamika a zátěžová kapacita					
Klidová TF (tep/min)	73,88 ± 10,71	72,81 ± 9,60	73,1 ± 10,44	73,73 ± 8,88	0,207
Systolický TK (mm Hg)	123 ± 17	122 ± 13,74	130 ± 16	124,78 ± 16,31	0,281
Diastolický TK (mm Hg)	76 ± 11	74,57 ± 9,86	75 ± 9	72,8 ± 7	0,587
Výkon (W)	134,35 ± 33,65	**153,38 ± 34,97*** **	145,34 ± 36,15	**163,71 ± 40,75*** **	0,923
Relativní výkonnost (W/kg)	1,6 ± 0,5	**1,85** ± 0,5***	1,7 ± 0,5	**1,94** ± 0,5***	0,782
Kardiologické biomarkery					
LDL cholesterol (mmol/l)	2,47 ± 0,4	**2,11 ± 0,67*** **	2,45 ± 0,59	**2,22 ± 0,81*** **	0,161
Tělesné složení					
Hmotnost (kg)	86,9 ± 16,85	**86,05 ± 17,30*** **	87,32 ± 16,54	**86,51 ± 16,30*** **	0,922
Index tělesné hmotnosti (kg/m^2)	28,66 ± 4,08	**28,40 ± 4,18*** **	28,42 ± 3,99	28,29 ± 3,92	0,388
Podíl netukové hmoty (%)	58,99 ± 11,92	**59,61 ± 11,88*** **	58,26 ± 11,91	58,40 ± 11,81	0,052
Podíl svalové hmoty (%)	35,12 ± 7,62	**35,77 ± 7,49*** **	34,72 ± 7,63	34,93 ± 7,44	**0,038**
Podíl tukové hmoty (%)	26,1 ± 9,36	**25,21 ± 8,86*** **	25,34 ± 8,88	**24,50 ± 8,52*** **	0,910
Úroveň útrobního tuku (1–20)	11,43 ± 4,62	**10,99 ± 4,61*** **	11,6 ± 4,82	**11,22 ± 4,47*** **	0,760

LDL cholesterol – cholesterol v lipoproteinech o nízké hustotě; TF – tepová frekvence, TK – krevní tlak.
Data jsou vyjádřena jako průměr ± směrodatná odchylka (SD).
Hodnota *p* průměrných změn pozorovaných mezi těmito dvěma skupinami.
*** $p < 0,05$ pro průměrnou změnu v rámci skupiny.

Tabulka 3 – Kardiovaskulární rizikové faktory a změny tělesného složení u mužů, ambulantní (n = 66) a hybridní (n = 33)

Charakteristika	Ambulantní: před KR	Ambulantní: po KR	Hybridní: před KR	Hybridní: po KR	Hodnota *p*
Srdeční hemodynamika a zátěžová kapacita					
Klidová TF (tep/min)	74,3 ± 11,0	73,4 ± 9,4	74,7 ± 11,3	74,7 ± 9,2	0,721
Systolický TK (mm Hg)	123,5 ± 16,5	122,0 ± 13,2	129,9 ± 16,1	127,0 ± 17,7	0,629
Diastolický TK (mm Hg)	76,0 ± 11,6	74,2 ± 9,5	74,6 ± 9,2	72,9 ± 7,6	0,852
Výkon (W)	136,2 ± 30,5	**156,7 ± 30,6*** **	153,2 ± 34,1	**168,5 ± 39,5*** **	0,085
Kardiologické biomarkery					
LDL cholesterol (mmol/l)	2,5 ± 0,4	**2,1 ± 0,7*** **	2,3 ± 0,6	**2,2 ± 0,8*** **	0,094
Tělesné složení					
Hmotnost (kg)	85,1 ± 16,8	**84,3 ± 17,3*** **	90,3 ± 17,3	**89,4 ± 17,2*** **	0,914
Index tělesné hmotnosti (kg/m²)	28,5 ± 4,3	**28,2 ± 4,4*** **	29,0 ± 4,1	28,9 ± 4,0	0,690
Podíl netukové hmoty (%)	57,8 ± 12,0	**58,5 ± 11,9*** **	60,6 ± 12,2	60,6 ± 12,1	0,062
Podíl svalové hmoty (%)	34,4 ± 7,7	**35,0 ± 7,6*** **	36,3 ± 7,7	36,4 ± 7,5	0,067
Podíl tukové hmoty (%)	25,7 ± 9,0	**24,6 ± 8,6*** **	26,3 ± 9,0	**25,4 ± 8,8*** **	0,806
Úroveň útrobního tuku (1–20)	11,5 ± 4,8	**11,0 ± 4,9*** **	12,0 ± 5,0	**11,5 ± 4,6*** **	0,904

LDL cholesterol – cholesterol v lipoproteinech o nízké hustotě; TF – tepová frekvence; TK – krevní tlak.
Data jsou vyjádřena jako průměr ± směrodatná odchylka (SD).
Hodnota *p* průměrných změn pozorovaných mezi těmito dvěma skupinami.
*** $p < 0,05$ pro průměrnou změnu v rámci skupiny.

Tabulka 4 – Kardiovaskulární rizikové faktory a změny tělesného složení u žen, ambulantní (n = 25) a hybridní (n = 12)

Charakteristika	Ambulantní: před KR	Ambulantní: po KR	Hybridní: před KR	Hybridní: po KR
Srdeční hemodynamika a zátěžová kapacita				
Klidová TF (tep/min)	72,9 ± 10,3	71,2 ± 10,1	68,6 ± 6,6	71,0 ± 7,6
Systolický TK (mm Hg)	123,2 ± 20,0	122,1 ± 15,4	128,4 ± 17,7	118,7 ± 10,0
Diastolický TK (mm Hg)	76,8 ± 12,5	75,5 ± 10,8	75,0 ± 8,5	72,6 ± 5,3
Výkon (W)	129,1 ± 39,4	**142,9 ± 38,2*** **	123,8 ± 33,9	150,6 ± 43,0***
Kardiologické biomarkery				
LDL cholesterol (mmol/l)	2,4 ± 0,5	**2,0 ± 0,7*** **	2,7 ± 0,6	2,4 ± 0,8
Tělesné složení				
Hmotnost (kg)	91,7 ± 16,4	**90,7 ± 16,0*** **	79,1 ± 10,9	78,5 ± 10,9
Index tělesné hmotnosti (kg/m²)	29,2 ± 3,5	28,8 ± 3,5	26,8 ± 3,3	26,7 ± 3,2
Podíl netukové hmoty (%)	62,1 ± 11,3	**62,7 ± 11,5*** **	51,8 ± 8,6	**52,3 ± 8,8*** **
Podíl svalové hmoty (%)	37,2 ± 7,1	**37,8 ± 7,1*** **	30,5 ± 5,5	**30,8 ± 5,6*** **
Podíl tukové hmoty (%)	27,2 ± 10,2	26,7 ± 9,5	22,8 ± 8,4	22,1 ± 7,7
Úroveň útrobního tuku (1–20)	11,3 ± 4,1	11,0 ± 3,6	10,6 ± 4,2	10,5 ± 4,4

LDL cholesterol – cholesterol v lipoproteinech o nízké hustotě; TF – tepová frekvence; TK – krevní tlak.
Data jsou vyjádřena jako průměr ± směrodatná odchylka (SD).
*** $p < 0,05$ pro průměrnou změnu v rámci skupiny

Při analýze výsledků podle pohlaví bylo zaznamenáno signifikantní zlepšení vybraných ukazatelů kardiovaskulárního rizika a tělesného složení u mužů i žen (**tabulky 3 a 4**). U mužů byly změny mezi ambulantním a hybridním programem srovnatelné. Naopak u žen se vyskytly statisticky významné rozdíly ve vstupních charakteristikách mezi rehabilitačními skupinami, zejména v tělesné hmotnosti a složení, což neumožnilo přímé porovnání těchto podskupin (**tabulka 4**).

Diskuse

Naše výsledky potvrdily efektivitu obou typů KR – ambulantní i hybridní ve zlepšení klíčových KV rizikových faktorů a tělesného složení u pacientů s ICHS. Snížení koncentrace LDL cholesterolu, nárůst fyzické kapacity a pokles tělesné hmotnosti po absolvování programů KR odpovídají závěrům předchozích studií, které prokázaly, že strukturovaná KR vede ke zlepšení lipidového profilu a zvýšení

aerobní kapacity.[23–25] Význam KR potvrzuje i snížení hospitalizací a mortality spojené s ICHS při účasti v hybridních programech KR.[26]

Rozdíly ve změnách tělesného složení mezi ambulantní a hybridní rehabilitací

V rámci této studie byly pozorovány výraznější změny tělesného složení mezi skupinami v nárůstu svalové hmoty. Tento nález může být způsoben vyšší frekvencí a intenzitou odporové složky cvičení v kontrolovaném prostředí ambulantního programu, která je k dispozici na rozdíl od domácího prostředí, kde pacienti často nemají k dispozici odpovídající vybavení, což vede k dominantnímu zaměření na aerobní složku tréninku. Tento trend je v souladu s výsledky studie autorů Lavie a spol., která ukázala, že hybridní program KR, který částečně probíhá v domácím prostředí, nemusí postrádat takovou míru kontroly a zpětné vazby, což může vysvětlovat menší rozsah změn ve složení těla.[27]

Průměrná hodnota BMI ve sledované populaci byla relativně nízká, což mohlo ovlivnit rozsah změn tělesného složení. Nižší BMI je spojeno s menším potenciálem pro redukci tukové hmoty, což může částečně vysvětlovat méně výrazné změny v tomto parametru v obou skupinách. Tento faktor je důležitý zejména při interpretaci výsledků v kontextu studií, které zahrnovaly populaci s vyššími hodnotami BMI a zaznamenaly větší redukci tělesné hmotnosti a tuku v reakci na programy KR. To zdůrazňuje význam sledování nejen BMI, ale také relativních změn ve svalové hmotě, tělesném složení a celkové fyzické kapacitě (např. relativní výkonnosti W/kg), které mohou být klinicky relevantnějšími ukazateli efektivity KR.

Celkově lze konstatovat, že KR vedla ke zlepšení zdravotních ukazatelů v obou skupinách, přičemž ambulantní skupina dosáhla mírně lepších výsledků v některých ukazatelích tělesného složení, zejména v redukci útrobního tuku a podílu svalové hmoty. Je však důležité upozornit, že tyto výsledky se nemusejí nutně vztahovat na všechny pacienty a rozdíly mezi jednotlivými skupinami mohou být ovlivněny specifickými faktory, jako jsou motivace pacienta a jeho přístup k domácímu cvičení.

Vliv prostředí rehabilitace na hemodynamické parametry

Naše studie zjistila významnější pokles systolického krevního tlaku v hybridní skupině. Tento výsledek by mohl naznačovat, že domácí cvičení poskytuje pacientům vyšší míru autonomie a komfortu, což může vést ke snížení stresu a následnému poklesu krevního tlaku.[28] Domácí prostředí může některým pacientům umožnit začlenit cvičení do každodenního života snadněji než v případě pevného rozvrhu ambulantní KR.[29,30] Nicméně tyto výsledky je třeba interpretovat s opatrností, protože domácí prostředí zároveň může snižovat míru kontroly nad správností a intenzitou cvičení.

Bezpečnost a efektivita hybridních přístupů

Studie iATTEND rovněž zdůrazňuje bezpečnost hybridní KR, protože u žádného pacienta nedošlo k závažným nežádoucím příhodám nebo pádům během rehabilitace nebo po rehabilitaci. Tyto výsledky podporují názor, že hybridní modely KR mohou být stejně efektivní jako tradiční modely a nabízejí pacientům větší flexibilitu při zachování bezpečnosti a efektivity.[31,32] Podobné závěry přináší i studie HYCARET, která prokázala non-inferioritu hybridního modelu ve srovnání se standardní rehabilitací u pacientů s ischemickou chorobou srdeční v prostředí s omezenými zdroji. Zaznamenala dokonce nižší výskyt kardiovaskulárních příhod ve skupině hybridní KR, což naznačuje, že tento model může být bezpečnou a účinnou alternativou.[33] Významným faktorem byla vyšší adherence pacientů k řízeným cvičebním jednotkám ve srovnání se standardní KR, což může pozitivně ovlivnit dlouhodobou efektivitu rehabilitace. Tyto výsledky dále podporují využití hybridních přístupů jako přizpůsobitelné alternativy tradiční rehabilitace s ohledem na individuální preference pacientů a dostupné zdroje.

Telemedicína v kardiovaskulární rehabilitaci

Telemedicína představuje inovativní strategii pro zvýšení dostupnosti a efektivity KR.[34–37] Programy hybridní KR s využitím digitální medicíny umožňují pacientům s KVO dostávat rehabilitační služby na dálku při zachování blízkého monitorování zdravotnickými profesionály.[38,39] Tyto programy kombinují fyzický trénink, vzdělávání o rizikových faktorech a psychologickou podporu prostřednictvím telekomunikačních technologií, což umožňuje pacientům sledovat své vitální funkce pomocí nositelných zařízení během cvičení.[40] Vzhledem k pandemii covidu-19 se vzdáleně vedené programy staly důležitou alternativou tradiční KR, která minimalizuje riziko infekcí spojených s návštěvami zdravotnických zařízení.[41,42] Studie ukazují, že vzdáleně vedená KR je stejně efektivní jako tradiční rehabilitační péče při zlepšování kvality života pacientů s KVO a snižování míry hospitalizací.[43,44] Navíc využití digitálních technologií, jako jsou mobilní aplikace a synchronní audiovizuální komunikace, podporuje personalizaci péče a poskytuje okamžitou zpětnou vazbu, což přispívá ke zlepšení adherence a dlouhodobých výsledků.[45,46]

Omezení studie a návrhy na budoucí výzkum

Tato studie má několik omezení, která je třeba vzít v úvahu. Především se jedná o relativně malý počet pacientů v hybridní skupině, což omezuje schopnost detekovat jemnější rozdíly v některých sledovaných parametrech. Dále chybí podrobnější analýza dlouhodobého vlivu KR na udržení dosažených zlepšení. Také je zde subjektivní prvek spojený s hodnocením kvality a intenzity domácího cvičení, což může ovlivnit přesnost výsledků hybridní KR.[47] Budoucí studie by měly zahrnovat větší vzorky pacientů a využít pokročilé monitorovací technologie, jako jsou nositelná zařízení pro měření srdeční frekvence pohybové aktivity a adherence, aby byla zajištěna vyšší objektivita a přesnost dat.[48,49] Kromě toho může být přínosné uplatnění nástrojů, které umožňují identifikaci překážek a potřeb pacientů v hybridním doručování programů KR.[50–52] Další výzkumnou perspektivou by mohlo být hlubší zapojení facilitátorů do domácích cvičebních programů KR u pacientů s ICHS. Jak bylo uvedeno jinde,[53–57] význam podpory sociální interakce, personalizované zpětné vazby a technologických inovací, jako jsou jednoduché uživatelské rozhraní a flexibilní časování, může vést k vyšší míře zapojení pacientů.

Závěr

Naše studie potvrzuje efektivitu jak ambulantního, tak hybridního modelu KR při zlepšování kardiovaskulárního zdraví a tělesného složení u pacientů s ICHS. Hybridní modely KR se ukazují jako bezpečná a flexibilní alternativa, přičemž budoucí výzkum by se měl zaměřit na optimalizaci dlouhodobých výsledků a identifikaci klíčových bariér účasti, které lze překonat pomocí pokročilých technologií a personalizovaných přístupů.

Poděkování
Autoři děkují multidisciplinárnímu týmu Fakultní nemocnice Brno za odborný dohled a realizaci standardizovaných postupů druhé fáze KR. Rovněž děkují všem pacientům, kteří se zúčastnili studie, za jejich čas a spolupráci.

Prohlášení autorů o možném střetu zájmů
Žádný střet zájmů.

Financování
Realizace výzkumu byla podpořena Ministerstvem zdravotnictví České republiky – koncepční rozvoj výzkumné organizace (FNBr, 65269705) projekt PIG 07/19 a projektem specifického výzkumu č.j. MUNI/A/1619/2024 z programu podpory studentských projektů Masarykovy univerzity v Brně.

Prohlášení autorů o etických aspektech publikace
Studie byla schválena Etickou komisí Fakultní nemocnice Brno pod jednacím číslem 12-170419/EK.

Informovaný souhlas
Všichni pacienti byli před zahájením studie řádně poučeni o jejím průběhu, cílech a možných rizicích. Následně dobrovolně udělili informovaný souhlas s účastí ve výzkumu. Veškerá data byla sbírána a zpracována anonymně, v souladu s platnými etickými a právními předpisy a Helsinskou deklarací.

Literatura

1. Di Cesare M, Perel P, Taylor S, et al. The Heart of the World. Glob Heart 2024;19:11.
2. Flora GD, Nayak MK. A Brief Review of Cardiovascular Diseases, Associated Risk Factors and Current Treatment Regimes. Curr Pharm Des 2019;25:4063–4084.
3. Libby P, Theroux P. Pathophysiology of coronary artery disease. Circulation 2005;111:3481–3488.
4. Roth GA, Mensah GA, Johnson CO, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol 2020;76:2982–3021.
5. European Association of Cardiovascular Prevention and Rehabilitation Committee for Science Guidelines; EACPR; Corrà U, Piepoli MF, Carré F, et al. Secondary prevention through cardiac rehabilitation: physical activity counselling and exercise training: key components of the position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. Eur Heart J 2010;31:1967–1974.
6. Chaloupka V, Siegelová J, Špinarová L, et al. Rehabilitace u nemocných s kardiovaskulárním onemocněním. Cor Vasa 2006;48:7–8.
7. Winnige P, Vysoky R, Dosbaba F, Batalik L. Cardiac rehabilitation and its essential role in the secondary prevention of cardiovascular diseases. World J Clin Cases 2021;9:1761–1784.
8. Candelaria D, Randall S, Ladak L, Gallagher R. Health-related quality of life and exercise-based cardiac rehabilitation in contemporary acute coronary syndrome patients: a systematic review and meta-analysis. Qual Life Res 2020;29:579–592.
9. Franklin BA, Eijsvogels TMH, Pandey A, et al. Physical activity, cardiorespiratory fitness, and cardiovascular health: A clinical practice statement of the American Society for Preventive Cardiology Part II: Physical activity, cardiorespiratory fitness, minimum and goal intensities for exercise training, prescriptive methods, and special patient populations. Am J Prev Cardiol 2022;12:100425.
10. Taylor RS, Dalal HM, McDonagh STJ. The role of cardiac rehabilitation in improving cardiovascular outcomes. Nat Rev Cardiol 2022;19:180–194.
11. Ciuca-Pană M-A, Boulmpou A, Ileri C, et al. Chronic Heart Failure and Coronary Artery Disease: Pharmacological Treatment and Cardiac Rehabilitation. Medicina 2025;61:211.
12. Dibben GO, Faulkner J, Oldridge N, et al. Exercise-based cardiac rehabilitation for coronary heart disease: a meta--analysis. Eur Heart J 2023;44:452–469.
13. Batalik L, Filakova K, Sladeckova M, et al. The cost--effectiveness of exercise-based cardiac telerehabilitation intervention: a systematic review. Eur J Phys Rehabil Med 2023;59:248–258.
14. Grace SL, Kotseva K, Whooley MA. Cardiac Rehabilitation: Under-Utilized Globally. Curr Cardiol Rep 2021;23:118.
15. Winnige P, Filakova K, Hnatiak J, et al. Validity and Reliability of the Cardiac Rehabilitation Barriers Scale in the Czech Republic (CRBS-CZE): Determination of Key Barriers in East--Central Europe. Int J Environ Res Public Health 2021;18:13113.
16. McDonagh ST, Dalal H, Moore S, et al. Home-based versus centre-based cardiac rehabilitation. Cochrane Database Syst Rev 2023;10:CD007130.
17. Stefanakis M, Batalik L, Antoniou V, Pepera G. Safety of home--based cardiac rehabilitation: A systematic review. Heart Lung 2022;55:117–126.
18. Keteyian SJ, Ades PA, Beatty AL, et al. A Review of the Design and Implementation of a Hybrid Cardiac Rehabilitation Program: AN EXPANDING OPPORTUNITY FOR OPTIMIZING CARDIOVASCULAR CARE. J Cardiopulm Rehabil Prev 2022;42:1–9.
19. Brown TM, Pack QR, Aberegg E, et al. Core Components of Cardiac Rehabilitation Programs: 2024 Update: A Scientific Statement From the American Heart Association and the American Association of Cardiovascular and Pulmonary Rehabilitation. Circulation 2024;150:e328–e347.
20. Ogawa H, Fujitani K, Tsujinaka T, et al. InBody 720 as a new method of evaluating visceral obesity. Hepatogastroenterology 2011;58:42–44.
21. Kim EY, Kim SR, Won DD, et al. Multifrequency Bioelectrical Impedance Analysis Compared With Computed Tomography for Assessment of Skeletal Muscle Mass in Primary Colorectal Malignancy: A Predictor of Short-Term Outcome After Surgery. Nutr Clin Pract 2020;35:664–674.
22. Guazzi M, Adams V, Conraads V. EACPR/AHA Scientific Statement. Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. Circulation 2012;126:2261–2274.
23. Batalik L, Pepera G, Su JJ. Cardiac telerehabilitation improves lipid profile in the long term: Insights and implications. Int J Cardiol 2022;367:117–118.
24. Mirman AM, Nardoni NR, Chen AY, Horwich TB. Body Composition Changes During Traditional Versus Intensive Cardiac Rehabilitation in Coronary Artery Disease. J Cardiopulm Rehabil Prev 2020;40:388–393.
25. Racodon M, Vanhove P, Bolpaire R, et al. Is hybrid cardiac rehabilitation superior to traditional cardiac rehabilitation? Acta Cardiol 2023;78:773–777.
26. Heindl B, Ramirez L, Joseph L, et al. Hybrid cardiac rehabilitation – The state of the science and the way forward. Prog Cardiovasc Dis 2022;70:175–182.

27. Lavie CJ, Arena R, Swift DL, et al. Exercise and the cardiovascular system: clinical science and cardiovascular outcomes. Circ Res 2015;117:207–219.
28. Farinatti P, Monteiro WD, Oliveira RB. Long Term Home-Based Exercise is Effective to Reduce Blood Pressure in Low Income Brazilian Hypertensive Patients: A Controlled Trial. High Blood Press Cardiovasc Prev 2016;23:395–404.
29. Baťalík L. (Cardiovascular telerehabilitation: remotely monitored physical exercise). Cor Vasa 2021;63:79–85. [In Czech]
30. Scherrenberg M, Wilhelm M, Hansen D, et al. The future is now: a call for action for cardiac telerehabilitation in the COVID-19 pandemic from the secondary prevention and rehabilitation section of the European Association of Preventive Cardiology. Eur J Prev Cardiol 2021;28:524–540.
31. Keteyian SJ, Grimshaw C, Brawner CA, et al. A Comparison of Exercise Intensity in Hybrid Versus Standard Phase Two Cardiac Rehabilitation. J Cardiopulm Rehabil Prev 2021;41:19–22.
32. Keteyian SJ, Grimshaw C, Ehrman JK, et al. The iATTEND Trial: A Trial Comparing Hybrid Versus Standard Cardiac Rehabilitation. Am J Cardiol 2024;221:94–101.
33. Seron P, Oliveros MJ, Marzuca-Nassr GN, et al. Hybrid Cardiac Rehabilitation Program in a Low-Resource Setting: A Randomized Clinical Trial. JAMA Netw Open. 2024;7:e2350301.
34. Blioumpa C, Karanasiou E, Antoniou V, et al. Efficacy of supervised home-based, real time, videoconferencing telerehabilitation in patients with type 2 diabetes: a single--blind randomized controlled trial. Eur J Phys Rehabil Med 2023;59:628–639.
35. Su JJ, Yu DSF, Paguio JT. Effect of eHealth cardiac rehabilitation on health outcomes of coronary heart disease patients: A systematic review and meta-analysis. J Adv Nurs 2020;76:754–772.
36. Antoniou V, Davos CH, Kapreli E, et al. Effectiveness of Home--Based Cardiac Rehabilitation, Using Wearable Sensors, as a Multicomponent, Cutting-Edge Intervention: A Systematic Review and Meta-Analysis. J Clin Med 2022;11:3772.
37. Su JJ, Yu DS. Effects of a nurse-led eHealth cardiac rehabilitation programme on health outcomes of patients with coronary heart disease: A randomised controlled trial. Int J Nurs Stud 2021;122:104040.
38. Su JJ, Wong AKC, He XF, et al. Feasibility and effectiveness of cardiac telerehabilitation for older adults with coronary heart disease: A pilot randomized controlled trial. Contemp Clin Trials Commun 2024;42:101365.
39. Su JJ, Wong AKC, Zhang LP, et al. Technology-assisted cardiac rehabilitation for coronary heart disease patients with central obesity: a randomized controlled trial. Eur J Phys Rehabil Med 2024;60:95–103.
40. Yang Z, Jia X, Li J, et al. Efficacy and Safety of Hybrid Comprehensive Telerehabilitation (HCTR) for Cardiac Rehabilitation in Patients with Cardiovascular Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Occup Ther Int 2023;2023:5147805.
41. Stefanakis M, Batalik L, Papathanasiou J, et al. Exercise-based cardiac rehabilitation programs in the era of COVID-19: a critical review. Rev Cardiovasc Med 2021;22:1143–1155.
42. Batalik L, Konecny V, Dosbaba F, et al. Cardiac Rehabilitation Based on the Walking Test and Telerehabilitation Improved Cardiorespiratory Fitness in People Diagnosed with Coronary Heart Disease during the COVID-19 Pandemic. Int J Environ Res Public Health 2021;18:2241.
43. Rawstorn JC, Gant N, Direito A, et al. Telehealth exercise-based cardiac rehabilitation: a systematic review and meta-analysis. Heart 2016;102:1183–1192.
44. Brouwers RWM, van Exel HJ, van Hal JMC, et al. Cardiac telerehabilitation as an alternative to centre-based cardiac rehabilitation. Neth Heart J 2020;28:443–451.
45. Antoniou V, Kapreli E, Davos CH, et al. Safety and long--term outcomes of remote cardiac rehabilitation in coronary heart disease patients: A systematic review. Digit Health 2024;10:20552076241237661.
46. Pepera G, Antoniou V, Su JJ, et al. Comprehensive and personalized approach is a critical area for developing remote cardiac rehabilitation programs. World J Clin Cases 2024;12:2009–2015.
47. Su JJ. Exploring the Relationship Between Usage and Outcomes of an eHealth Cardiac Rehabilitation Intervention: Subanalysis of a Randomized Controlled Trial. Comput Inform Nurs 2023;41:578–585.
48. Etiwy M, Akras Z, Gillinov L, et al. Erratum to accuracy of wearable heart rate monitors in cardiac rehabilitation. Cardiovasc Diagn Ther 2020;10:644–645.
49. Arena R, Williams M, Forman DE, et al. Increasing referral and participation rates to outpatient cardiac rehabilitation: the valuable role of healthcare professionals in the inpatient and home health settings: a science advisory from the American Heart Association. Circulation 2012;125:1321–1329.
50. Grace SL, Ghanbari M, Cruz MMMAD, et al. Psychometric validation of the Cardiac Rehabilitation Barriers Scale Revised (CRBS-R) for hybrid delivery. BMJ Open 2024;14(10):e090261.
51. Ghisi GLM, da Cruz MMA, Vanderlei LCM, et al. Psychometric validation of the short version of the Information Needs in Cardiac Rehabilitation scale through a first global assessment. Eur J Prev Cardiol 2024;31:1927–1936.
52. Ferrel-Yui D, Candelaria D, Pettersen TR, et al. Uptake and implementation of cardiac telerehabilitation: A systematic review of provider and system barriers and enablers. Int J Med Inform 2024;184:105346.
53. Bomtempo APD, Main E, Ghisi GLM. Remote Exercise Engagement Among Individuals With Cardiovascular Disease: A Systematic Review of Barriers and Facilitators. J Cardiopulm Rehabil Prev 2025;45:8–19.
54. Su JJ, Paguio JT, Wang W, Batalik L. Designing a Nurse--Led eHealth Cardiac Rehabilitation Program: Insights From Participant Experiences and Qualitative Feedback. Public Health Nurs 2025;42:144–153.
55. Su JJ, Paguio J, Baratedi WM, et al. Experience of coronary heart disease patients with a nurse-led eHealth cardiac rehabilitation: Qualitative process evaluation of a randomized controlled trial. Heart Lung 2023;57:214–221.
56. Echefu G, Batalik L, Lukan A, et al. The Digital Revolution in Medicine: Applications in Cardio-Oncology. Curr Treat Options Cardiovasc Med 2025;27:2.
57. Su JJ, Bayuo J, Abu-Odah H, et al. Perception of eHealth Programs for Cardiovascular Health: Qualitative Systematic Review and Meta-synthesis. J Cardiovasc Nurs 2024;39:E140–E149.

Původní sdělení | Original research article

Comparison of EuroSCORE II, STS Score, and ACEF II Score as Predictors of Mortality in CABG Patients at Tertiary Referral Hospital in East Indonesia

Yan Efrata Sembiring[a], Ali Mustofa[b], Andrianto[c], Heroe Soebroto[a]

[a] *Department of Thoracic Cardiac and Vascular Surgery, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[b] *Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[3]*Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*

ARTICLE INFO

Article history:
Submitted: 25. 2. 2024
Revised: 5. 1. 2025
Accepted: 5. 1. 2025
Available online: 16. 6. 2025

Klíčová slova:
Aortokoronární bypass
EuroSCORE II
Model stratifikace rizika
Skóre ACEF II
Skóre STS

SOUHRN

Kontext: Součástí přípravy na operaci je stanovení optimálního chirurgického postupu a léčby pacienta. Ve snaze pomoci při hodnocení faktorů souvisejících s výsledkem operace byly vypracovány různé modely stratifikace rizika jako EuroSCORE II, skóre STS a skóre ACEF II. Tyto skórovací systémy se dnes používají při stratifikaci rizika pacientů podstupujících aortokoronární bypass (coronary artery bypass graft, CABG). Dosud však není jasné, který z těchto modelů je vhodnější pro pacienty v Indonésii. Cílem této studie bylo porovnat systémy EuroSCORE II, skóre STS a skóre ACEF II u indonéských pacientů po CABG.
Metody: V období od ledna 2021 do března 2023 byla provedena průřezová studie s použitím sekundárních údajů ze zdravotnických záznamů všech pacientů podstupujících CABG. Byly vytvořeny křivky operační charakteristiky přijímače (receiver operating characteristic, ROC) a následně vypočtena plocha pod těmito křivkami (area under the ROC curve, AUC) pro výpočet diskriminační síly každého modelu.
Výsledky: Do studie bylo zařazeno celkem 131 pacientů. Mortalita celé skupiny činila 5 % (sedm jedinců). Predikovaná mortalita podle modelu EuroSCORE II byla 1,58 ± 2,08, při použití skóre STS to bylo 1,14 ± 1,58, a podle skóre ACEF II činila hodnota 1,60 ± 0,97. Diskriminační síla operační mortality podle plochy pod křivkou při použití systémů EuroSCORE II, skóre STS a skóre ACEF II činila 0,94 (95% CI 0,86–0,99; $p < 0,0001$), resp. 0,93 (95% CI 0,81–0,99; $p < 0,0001$) a 0,76 (95% CI 0,55–0,97; $p < 0,05$).
Závěr: Z výsledků vyplývá, že systémy EuroSCORE II, skóre STS a skóre ACEF II mají uspokojivou diskriminační sílu. Nicméně všechny uvedené modely stratifikace rizika mají své slabiny a limitace použití a je nutno je používat uvážlivě.

Keywords:
ACEF II score
CABG
EuroSCORE II
Risk Stratification Model
STS score

ABSTRACT

Background: Identifying the optimal surgical approach and therapy for a patient is an important step in the preoperative preparation process. Risk stratification models such as EuroSCORE II, STS score, and ACEF II score were created to assist in evaluating factors associated with surgical outcomes. This scoring models are now utilized to risk stratify patients having coronary artery bypass graft (CABG) surgery. However, it has not been determined which model is better for Indonesian patients. The purpose of this study was to compare EuroSCORE II, STS score, and ACEF II score in CABG patients from Indonesia.
Methods: A cross-sectional study was conducted from January 2021 to March 2023 by utilizing secondary data collected from medical records of all patients undergoing CABG. Receiver operating characteristic (ROC) curves were created, and the area under the ROC curve (AUC) was calculated to measure the discriminative power of each score.
Results: A total of 131 patients were included in the study. The overall observed mortality on the entire group was 7 (5%). The EuroSCORE II-predicted mortality was 1.58 ± 2.08, the STS score-predicted mortality was 1.14 ± 1.58, and the ACEF II score-predicted mortality was 1.60 ± 0.97. The discriminative ability for operative mortality by area under the curve for EuroSCORE II, STS Score, and ACEF II score was 0.94 (95% CI 0.86–0.99; $p < 0.0001$), 0.93 (95% CI 0.81–0.99; $p < 0.0001$), and 0.76 (95% CI 0.55–0.97; $p < 0.05$), respectively.
Conclusion: This result suggests that EuroSCORE II, STS score, and ACEF II score have satisfactory discriminatory power. However, all three risk stratification models have their own strengths and limitation in their application and should be used wisely.

Address: Ali Mustofa, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, e-mail: alimustofa210203@gmail.com
DOI: 10.33678/cor.2025.005

Please cite this article as: Sembiring YE, Mustofa A, Andrianto, Soebroto H. Comparison of EuroSCORE II, STS Score, and ACEF II Score as Predictors of Mortality in CABG Patients at Tertiary Referral Hospital in East Indonesia. Cor Vasa 2025;67:344–349.

Background

Coronary artery bypass graft, known as CABG, is a surgical procedure used to recover blood flow in heart that has a blocked artery, thus restoring cardiac vascularization. This open-heart surgery procedure involves grafting a part of a blood vessel to bypass obstructions in coronary arteries and improve the flow of blood to the heart.[1] In the context of cardiac surgery, in-hospital mortality or mortality due to the procedure serves as a key indication of healthcare quality.[2] Failure to achieve the ideal level of heart function during cardiac surgery often results in mortality, leading to early health complications and adverse long-term effects. It is essential to take consideration of the risk factors related to patients undergoing surgery carefully in order to improve healthcare services.

Determining the best surgical strategy and therapy for patient is an important step in the preparation process prior to surgery.[3] Risk stratification models have been developed to help in assessing risk factors that are correlated with surgical outcomes. These risk stratification models assist in predicting surgical outcomes and enhancing patient care quality. Another reason for the utilization of risk stratification models is the process of decision-making. Risk stratification model can play a crucial role in aiding physicians and hospitals in managing patients with high-risk profiles. Furthermore, risk stratification models are essential for enhancing surgical success rates, conducting quality analyses, and accomplishing significant outcomes.[3]

Risk stratification model such as STS score (Society of Thoracic Surgeons), EuroSCORE (European System for Cardiac Operative Risk Evaluation) and ACEF (Age, Creatinine, and Ejection Fraction) can be used to assess the degree of risk involved in cardiac surgical procedures. EuroSCORE is among the risk stratification models utilized to evaluate the quality of cardiac surgery. EuroSCORE I wass established in 1999 and was once considered as a gold standard in risk stratification models.[3,4] EuroSCORE II represents an update and improvement of EuroSCORE I, aimed at preserving and optimizing its utility in predicting cardiac surgeries. This development and update were a response of the previous EuroSCORE's tendency to overestimate risk and outcomes.[5,6] STS score stands out as one of the most frequently utilized risk stratification models. The essentials data for its development are derived from the Society of Thoracic Surgeons National Cardiac Database (STS NCD), which was established in 1989 and represents the largest clinical database of its kind.[3,7] ACEF (Age, Creatinine, and Ejection Fraction) is one of the risk stratification models in cardiac surgery that has been developed in recent years. It involves the patient's age, serum creatinine and ejection fraction to calculate the risk and outcome.[8,9] ACEF II incorporates five risk factors in determining the patient's risk level, with the formula being age (in years) / ejection fraction (%). Additional points are assigned for specific conditions such as serum creatinine >2 mg/dl (2 points), emergency status of the surgery (3 points), and anemia (hematocrit/HCT <36%, 0.2 points for each HCT point below 36%).[10] Furthermore, the ACEF score can also be utilized to predict risk in patients undergoing percutaneous coronary interventions, in addition to elective cardiac surgeries.[8,11]

Many surgeons and medical institutions tend to use this risk stratification model for risk assessment since there has not been a risk stratification model designed specifically utilizing local patient data. However, it's crucial to remember that the patient data used to construct these risk assessment model came from patients in Europe and America. Considering the fact that these models weren't initially designed for Indonesia patients in mind, there are still concerns about how effectively it may predict the risk for these individuals.

To this day, limited information is available regarding risk stratification models in Indonesian patients. In research carried out in Indonesia, only EuroSCORE II has shown good validity.[12] But another study suggests that EuroSCORE II was unsuitable for risk prediction of in-hospital mortality.[13,14] Furthermore, there is a shortage of data related to ACEF score and limited research on ACEF II score in Indonesia. However, limited data is available on STS score and ACEF II score. The lack of comparable evaluations of the discriminatory and calibration capacities of these risk stratification models is another area of concern. Hence, this study aims to assess the performance of STS score, EuroSCORE II, and ACEF II score in Indonesian patients undergoing CABG surgery.

Methods

All patients undergoing CABG procedures between January 2021 and February 2023 were included in this study. Data was collected in the Department of Thoracic, Cardiac and Vascular Surgery database and was analyzed retrospectively. The inclusion criteria were patients undergoing coronary artery bypass graft above the age of 18 years. This study also enrolled patients undergoing CABG with other procedures like CABG with mitral valve repair (MVR) or CABG with aorta valve repair (AVR). All patients undergoing CABG were included whether they had an elective, urgent, emergency, or other circumstances and condition on the patients as long as the risk probability can be calculated by the risk stratification models. Mortality in this study is defined as in-hospital mortality. Exclusion criteria of this study were lack of perioperative data that hinder the calculation of the risk stratification model and the analyses of the study.

The outcome of this study was the comparison of risk stratification model between EuroSCORE II, STS score, and ACEF II score in predicting mortality in patients undergoing CABG procedures. This was assessed by calculating their discriminatory power in predicting mortality and calibration of the models. Another outcome of the study is assessed with the correlation between this three risk stratification models and evaluated with the predicted probability for operative mortality.

The calibration of the models was assessed using the Hosmer–Lemeshow test. Essentially, it measures the model's capacity to predict survival across different levels of patient risk.[15] The discriminatory ability was assessed by calculating the receiver operating characteristic (ROC) curve. From this, the area under the curve (AUC) can be

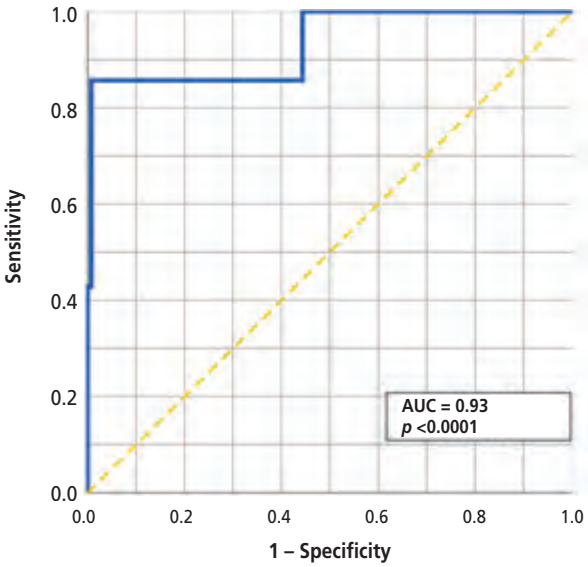


Fig. 1 – ROC curve of STS score.

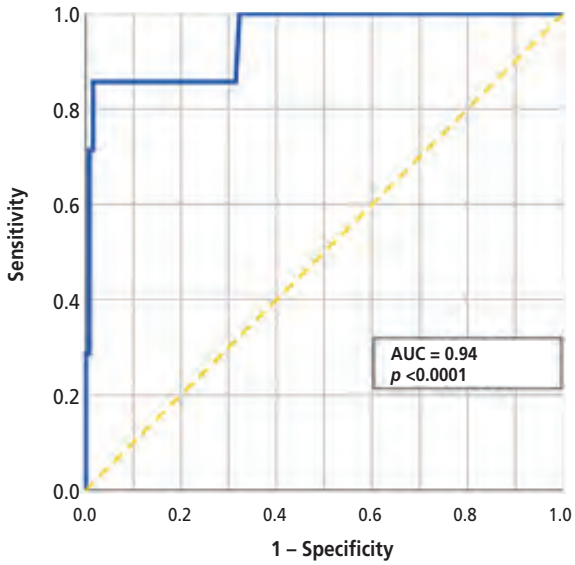


Fig. 2 – ROC curve of EuroSCORE II.

found for each model. AUC is defined as the measure of how often a patient who survives is predicted using the models to have a greater likelihood of survival compared to a patient who passes away during their hospital stay.[5,15] The discriminatory ability of STS score, EuroSCORE II, and ACEF II score were compared using these analyses. The correlation between the risk stratification models was assessed using Spearman correlations. A positive correlation between them indicates the agreement of the models. The higher the score, the higher the agreement between the models. This study also conducted univariate logistic regression analyses to evaluate the predicted probability for operative mortality.

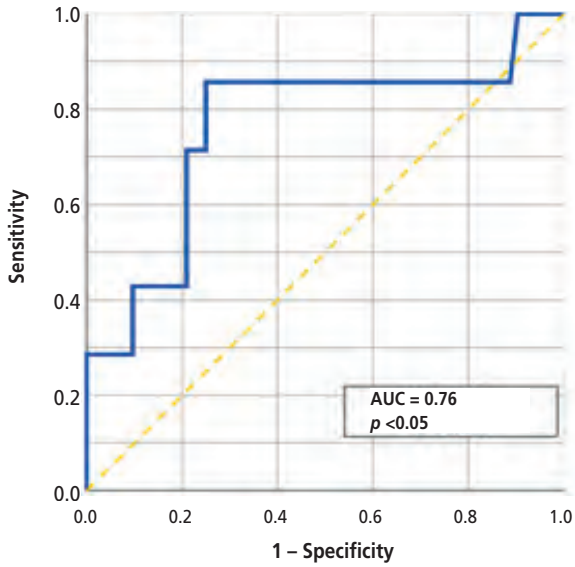


Fig. 3 – ROC curve of ACEF II score.

Results

There were 131 patients undergoing CABG procedures during the study period. Those consisted of 16 (12%) women. In this study, there were 58 (44%) patients with diabetes and 77 (59%) with hypertension comorbidity. According to the urgency of operation, elective surgery was the highest type of surgery. Patient characteristics and detailed demographics are described in **Table 1**.

The overall mortality in the entire group was 7 (5%). Risk stratification model using EuroSCORE II found a predicted mortality of 1.58 ± 2.08, STS score-predicted mortality was 1.14 ± 1.58, and ACEF II score-predicted mortality was 1.60 ± 0.97. Hosmer–Lemeshow test for STS has a *p*-value of 0.230. For EuroSCORE II and ACEF II score, the Hosmer–Lemeshow test showed a *p*-value with $p = 0.731$ and $p = 0.80$, respectively. These results indicated good model fit for all risk stratification models ($p > 0.05$). The discriminative ability for operative mortality of the STS score was 0.93 (95% CI 0.81–0.99; $p < 0.0001$]). The discriminative ability of the EuroSCORE II, as measured by the AUC, was 0.94 (95% CI 0.86–0.99; $p < 0.0001$). On the other hand, discriminative ability for ACEF II score showed the value 0.76 (95% CI 0.55–0.97; $p < 0.05$). These analyses indicate that all three risk scores have good discriminative ability, but EuroSCORE II and STS score is more superior than ACEF II score. There is a very subtle difference in the discriminative power between EuroSCORE II and STS score.

The correlation analyses showed that all three risk stratification models were well correlated with each other. The STS score was highly correlated with EuroSCORE II ($r = 0.75$, $p < 0.0001$). ACEF score II was moderately correlated with EuroSCORE II ($r = 0.56$, $p < 0.0001$) and the STS score ($r = 0.52$, $p < 0.0001$). These results indicate that three risk stratification models are in agreement between each other.

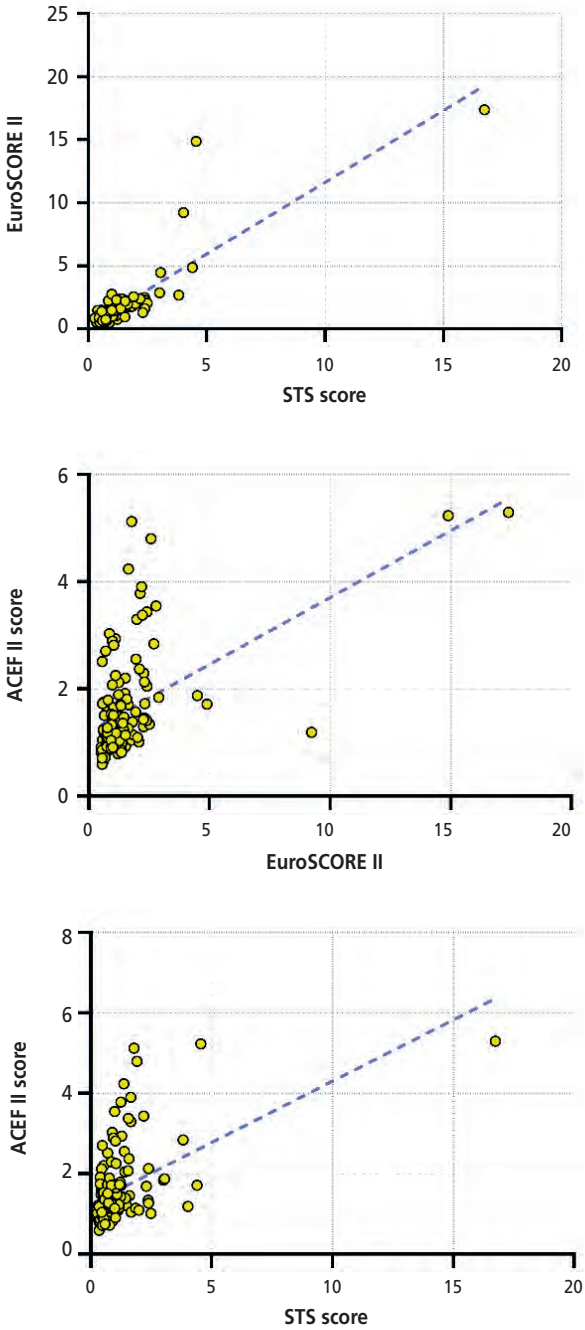


Fig. 4 – Scatterplots demonstrating the correlation between STS score, EuroSCORE II, and ACEF II score.

Univariate logistic regression found that age, smoking status, STS score-predicted mortality, EuroSCORE II-predicted mortality, and ACEF II score-predicted mortality have significant results. Patients with higher age tend to be more susceptible to mortality than the younger age group (OR 1.24; 95% CI 1.09–1.43; p <0.05). For each year increase in patient age, there is 1.24-times increase in the likelihood of patient mortality. Patients with current smoker status are 7-times more susceptible to mortality than patients that have never smoked (OR 7.10; 95% CI 1.09–46.27; p <0.05).

Table 1 – Patient characteristics (n = 131)	
Age (mean ± SD)	59.5 ± 8.75
Gender (female)	16 (12%)
Diabetes	58 (44%)
Hypertension	77 (59%)
Ejection fraction (%)	51.6 ± 14.0
Creatinine (mg/dL)	1.14 ± 0.41
Heart valve disease	73 (56%)
Aorta regurgitation	20 (15%)
Mitral regurgitation	62 (47%)
Tricuspid regurgitation	34 (26%)
Urgency of operation	
Elective	99 (76%)
Urgent	31 (24%)
Emergency	1 (1%)
Mortality	7 (5%)
STS mortality risk (%)	1.14 ± 1.58
EuroSCORE II mortality risk (%)	1.58 ± 2.08
ACEF II mortality risk (%)	1.60 ± 0.97

Values are mean ± SD or n (%). EuroSCORE – European System for Cardiac Operative Risk Evaluation; STS – the Society of Thoracic Surgeons.

Discussion

Mortality rate among patients undergoing CABG procedures was 5% out of 131 in this study. This figure aligns with the previous research that 8.9% patients experienced mortality from 292 patients who underwent adult cardiac surgery between January 2016 and December 2018.[16] According to the Society of Thoracic Surgeons' National Cardiac Database, there were 205,778 patients who underwent CABG between 1984 and 1993, with a mortality rate of 2.9% during that period.[17] Another study in the United States reported a 2.4% mortality rate for CABG surgery during the period 1997–2011.[18] In the UK, a study covering the years 2002–2016 revealed a mortality rate of 1.73% among patients undergoing CABG.[19] Similarly, a study in India showed a mortality rate of 1.5% for CABG surgeries conducted from 2015 to 2020.[15] In China, during the period from 2000 to 2018, there was a mortality rate of 2.21% among patients undergoing CABG surgery.[20]

Compared to other countries, mortality rate among patients undergoing CABG surgery in Indonesia is higher, surpassing countries where mortality rates fall below 3%. Several factors may contribute including lack of public awareness regarding healthcare in Indonesia. Additionally, the geographical distance from healthcare centers and the economics condition, particularly of the lower-middle class people, may contribute to this issue. Another problem in Indonesia are insufficient cardiovascular diseases services in primary healthcare and disease monitoring in

the population, and low patient compliance both in the prevention and treatment of diseases.[21]

Male gender dominates the gender demographic among those undergoing CABG procedures with 115 (88%) of the total 131 patients. Previous research also indicates a higher prevalence of males in adult cardiac surgery, with 164 (77%) male patients.[16] Studies in India reported that 86.5% of CABG surgery cases were among males.[15] Similarly, research in China revealed that males constituted the majority, accounting for 75.78% of total CABG patients.[20] This aligns with previous studies on cardiovascular diseases, indicating a higher prevalence among males.[22,23] The elevated prevalence of cardiovascular diseases in males can be attributed to their susceptibility to these diseases at a younger age. Hormonal factors in females tend to provide some protection against cardiovascular diseases before menopause, after which the risk significantly increases.[24] Other risk factors such as smoking, diabetes, and dyslipidemia contribute to the higher incidence of cardiovascular diseases in males.[23] However, it's essential to note that females are not exempt from cardiovascular diseases. Various risk factors, including age, hypertension, and cholesterol levels, pose significant challenges for women. Other factors such as endocrine disorders and pregnancy-related complications make women vulnerable to cardiovascular diseases.[23,25]

This study calculated discriminative ability of the risk stratification models for each patient undergoing CABG procedures. The results indicate that STS score, EuroSCORE II, and ACEF II score have discrimination abilities of 0.93, 0.94, and 0.76, respectively. In a previous study, EuroSCORE II demonstrated good discriminatory capability, with an AUC value of 0.85 on the ROC curve.[16] However, another research suggests that EuroSCORE II may be unsuitable for predicting mortality risk in Indonesia.[13,14] On the other hand, there is still limited information regarding STS score and ACEF II score in Indonesia.

STS score, EuroSCORE II, and ACEF II score demonstrate good capabilities in predicting mortality. However, several studies in the United States indicate that STS score outperforms EuroSCORE II in predicting mortality among adult cardiac surgery.[26] In contrast, European studies suggest that EuroSCORE II is superior to STS score in predicting mortality in adult cardiac surgery patients.[27–29] Another research indicates that EuroSCORE II is superior to ACEF II score.[30] Studies in Asia also show that these risk stratification models perform equally well and do not favor one scoring system over the other despite limitations in information regarding ACEF II score.[15,20,31]

Based on other factors, EuroSCORE II and ACEF II score are more versatile in their application across various types of cardiac surgery procedures compared to STS score. EuroSCORE II and ACEF score II can be applied to almost all cardiac surgery procedures, whole STS score is limited to 7 types of cardiac surgical procedures. Moreover, EuroSCORE II and ACEF II score require only 17 and 5 variables, respectively, in contrast to STS score that need 67 variables. This makes EuroSCORE II and ACEF II score faster in assessing the prediction of patient mortality. However, STS score has an ability to predict postoperative patient morbidity, such as renal failure, stroke, prolonged ventilation, deep sternal wound infection, reoperation, short length of stay, and long length of stay.

All three risk stratification models exhibit good capabilities and applicable in hospital settings. However, they have their own strengths and limitations in their application. Risk stratification models should not be used alone when predicting patient mortality. Other consideration, such as discussion among doctors and healthcare professionals, patient's condition, and patient's own decisions, also play a crucial role in predicting and performing CABG procedures. Furthermore, risk stratification models do not incorporate variables related to the skill and proficiency of the surgeon, as well as the quality of service before and after the operation. Therefore, these factors need to be considered when estimating optimal management for patients. Another consideration in performing CABG surgery is the patient's mental state and motivation. According to previous research, optimism is associated with better outcomes in the recovery process after CABG surgery.[32] Other factors, such as the economic and social conditions of the patient, also need to be taken into account.

Conclusion

ACEF II score, EuroSCORE II, and STS score predict the outcome fairly accurate in Indonesian population and should be used. Based on our study, EuroSCORE II and STS score is superior to ACEF II score. However, all three risk stratification models have their own strengths and limitation in their application. Physician, surgeon, or healthcare professional should use them wisely. Risk stratification models should also not be used alone when predicting patient mortality and consider another role such as discussion among professional, patient's condition and decisions, skill and proficiency of the surgeon, and service's quality.

Limitation

This study was conducted as a single-center study and become the important limitation. Small number of patients in this study has also become the limitation in our study. This condition may not be representative of real-life practices in the surgical association among Indonesian's professional despite the large sample size. For more accurate validation risk stratification models, it is important to involve several centers with geographical and healthcare infrastructure difference as well as the impact of economic and social variations on results.

Acknowledgement
The author would like to thank to Pandit Bagus Tri Saputra from Faculty of Medicine, Universitas Airlangga for his substantial feedback.

Conflict of interest
The authors declare that there is no known conflict for this work.

Funding
None.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
This research has been approved by the Health Research Ethics Committee of Dr. Soetomo Hospital with number 1098/LOE/301.4.2/X/2022.

Consent for publication
Not applicable

Authors' contribution
Conceptualization YES, AM; data curation AM, YES; formal analysis YES, AM, A; investigation YES, AM, A; methodology YES, AM, A; project administration YES, AM, A; software YES, AM; supervision YES, A, HS; validation YES, AM, A, HS; visualization AM writing original draft YES, AM; writing review and editing by all author. Approval of final manuscript by all authors.

References

1. Diodato M, Chedrawy EG. Coronary artery bypass graft surgery: the past, present, and future of myocardial revascularisation. Surg Res Pract 2014;2014:1–6.
2. Coulson TG, Mullany DV, Reid CM, et al. Measuring the quality of perioperative care in cardiac surgery. Eur Heart J Qual Care Clin Outcomes 2017;3:11–19.
3. Prins C, Jonker IDV, Botes L, Smit FE. Cardiac surgery risk-stratification models. Cardiovasc J Afr 2012;23:160.
4. Nashef SAM, Roques F, Michel P, et al. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothor Surg 1999;16:9–13.
5. Ad N, Holmes SD, Patel J, et al. Comparison of EuroSCORE II, Original EuroSCORE, and The Society of Thoracic Surgeons Risk Score in Cardiac Surgery Patients. Ann Thorac Surg 2016;102:573–579.
6. Nashef SAM, Roques F, Sharples LD, et al. Euroscore II. Eur J Cardiothor Surg 2012;41:734–745.
7. O'Brien SM, Feng L, He X, et al. The Society of Thoracic Surgeons 2018 Adult Cardiac Surgery Risk Models: Part 2-Statistical Methods and Results. Ann Thorac Surg 2018;105:1419–1428.
8. Ranucci M, Castelvecchio S, Menicanti L, et al. Risk of assessing mortality risk in elective cardiac operations: age, creatinine, ejection fraction, and the law of parsimony. Circulation 2009;119:3053–3061.
9. Borracci RA, Rubio M, Baldi J, et al. Validation of ACEF score in cardiac surgery 297 validation of age, creatinine and ejection fraction (ACEF) and Cockcroft-Gault ACEF scores in elective cardiac surgery. Medicina (Buenos Aires) 2017;77:297–303.
10. Ranucci M, Pistuddi V, Scolletta S, et al. The ACEF II Risk Score for cardiac surgery: updated but still parsimonious. Eur Heart J 2018;39:2183–2189.
11. Wykrzykowska JJ, Garg S, Onuma Y, et al. Value of age, creatinine, and ejection fraction (ACEF score) in assessing risk in patients undergoing percutaneous coronary interventions in the "All-Comers" LEADERS Trial. Circ Cardiovasc Interv 2011;4:47–56.
12. Sembiring YE, Ginting A, Puruhito, Budiono. Validation of EuroSCORE II to predict mortality in post-cardiac surgery patients in East Java tertiary hospital. Med J Indones 2021;30:54–59.
13. Widyastuti Y, Boom CE, Parmana IMA, et al. Validation in Indonesia of Two Published Scores for Mortality Prediction after Cardiac Surgery. Ann Card Anaesth 2023;26:23.
14. Kurniawaty J, Setianto BY, Widyastuti Y, et al. Validation for EuroSCORE II in the Indonesian cardiac surgical population: a retrospective, multicenter study. Expert Rev Cardiovasc Ther 2022;20:491–496.
15. Shales S, Uma Maheswara Rao S, Khapli S, et al. Comparison of European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgeons(STS) score for risk prediction in Indian patients undergoing coronary artery bypass grafting. Indian J Thorac Cardiovasc Surg 2021;37:623–630.
16. Sembiring YE, Ginting A, Puruhito, Budiono. Validation of EuroSCORE II to predict mortality in post-cardiac surgery patients in East Java tertiary hospital. Med J Indones 2021;30:54–59.
17. Clark RE, Edwards FH, Schwartz M. Profile of preoperative characteristics of patients having CABG over the past decade. Ann Thorac Surg 1994;58:1863–1865.
18. Cornwell LD, Omer S, Rosengart T, et al. Changes over time in risk profiles of patients who undergo coronary artery bypass graft surgery: the Veterans Affairs Surgical Quality Improvement Program (VASQIP). JAMA Surg 2015;150:308–315.
19. Ohri SK, Benedetto U, Luthra S, et al. Coronary artery bypass surgery in the UK, trends in activity and outcomes from a 15-year complete national series. Eur J Cardiothorac Surg 2022;61:449–456.
20. Gao F, Shan L, Wang C, et al. Predictive Ability of European Heart Surgery Risk Assessment System II (EuroSCORE II) and the Society of Thoracic Surgeons (STS) Score for in-Hospital and Medium-Term Mortality of Patients Undergoing Coronary Artery Bypass Grafting. Int J Gen Med 2021;14:8509–8519.
21. Qanitha A, Qalby N, Amir M, et al. Clinical Cardiology in South East Asia: Indonesian Lessons from the Present towards Improvement. Glob Heart 2022;17:66.
22. Bots SH, Peters SAE, Woodward M. Sex differences in coronary heart disease and stroke mortality: a global assessment of the effect of ageing between 1980 and 2010. BMJ Glob Health 2017;2:e000298.
23. Gao Z, Chen Z, Sun A, Deng X. Gender differences in cardiovascular disease. Med Nov Technol Devices 2019;4:100025.
24. Rodgers JL, Jones J, Bolleddu SI, et al. Cardiovascular Risks Associated with Gender and Aging. J Cardiovasc Dev Dis 2019;6:19.
25. Maas AHEM, Appelman YEA. Gender differences in coronary heart disease. Neth Heart J 2010;18:598.
26. Osnabrugge RL, Speir AM, Head SJ, et al. Performance of EuroSCORE II in a large US database: implications for transcatheter aortic valve implantation. Eur J Cardiothorac Surg 2014;46:400–408.
27. Kunt AG, Kurtcephe M, Hidiroglu M, et al. Comparison of original EuroSCORE, EuroSCORE II and STS risk models in a Turkish cardiac surgical cohort. Interact Cardiovasc Thorac Surg 2013;16:625–629.
28. Luc JGY, Graham MM, Norris CM, et al. Predicting operative mortality in octogenarians for isolated coronary artery bypass grafting surgery: a retrospective study. BMC Cardiovasc Disord 2017;17:275.
29. Kirmani BH, Mazhar K, Fabri BM, Pullan DM. Comparison of the EuroSCORE II and Society of Thoracic Surgeons 2008 risk tools. Eur J Cardiothorac Surg 2013;44:999–1005.
30. Santarpino G, Nasso G, Peivandi AD, et al. Comparison between the age, creatinine and ejection fraction II score and the European System for Cardiac Operative Risk Evaluation II: which score for which patient? Eur J Cardiothorac Surg 2022;61:1118–1122.
31. Luo HD, Teoh LKK, Gaudino MF, et al. The Asian system for cardiac operative risk evaluation for predicting mortality after isolated coronary artery bypass graft surgery (ASCORE-C). J Card Surg 2020;35:2574–2582.
32. Arsyi DH, Permana PBD, Karim RI, Abdurachman. The role of optimism in manifesting recovery outcomes after coronary artery bypass graft surgery: A systematic review. J Psychosom Res 2022;162:111044.

Původní sdělení | Original research article

Value of peri-procedural lung ultrasound in predicting heart failure or left ventricular systolic dysfunction within 3 months in STEMI patients undergoing primary PCI

Ahmed Talaat, Mohamed Abou El Ezz, Mohamed Mahmoud Abd El Ghany, Mohamed Abdel Meguid Mahdy, Kareem Mahmoud

Department of Cardiovascular Medicine, Faculty of Medicine Cairo University, Cairo, Egypt

ARTICLE INFO

Article history:
Submitted: 25. 2. 2024
Revised: 5. 1. 2025
Accepted: 5. 1. 2025

Klíčová slova:
Infarkt myokardu
Infarkt myokardu s elevacemi úseku ST
Srdeční selhání
Ultrazvukové vyšetření plic

SOUHRN

Cíl: Zjistit, zda by detekce subklinického městnání ultrazvukovým vyšetření plic (lung ultrasound, LUS) pacientů se STEMI mohla pomoci předpovědět rozvoj srdečního selhání a systolické, nebo diastolické dysfunkce levé komory.
Metody: Do studie bylo zařazeno 150 pacientů. U všech byla provedena úspěšná revaskularizace a při příjmu u nich nebylo z klinického hlediska přítomno srdeční selhání. Během prvních 24 hodin od příjmu u nich bylo provedeno LUS s 28 plicními body a byly spočítány B-linie. Pacienti byli rozděleni do dvou skupin: 64 pacientů do skupiny LUS pozitivní (se 6 nebo více B-liniemi) a 86 jedinců do skupiny LUS negativní; po tříměsíčním sledování byli vyšetřeni na přítomnost srdečního selhání stupně II nebo vyššího podle klasifikace NYHA, ejekční frakci (EF) ≤40%, a celková longitudinální deformace myokardu (global longitudinal strain, GLS) ≤–16 %.
Výsledky: K rozvoji klinického srdečního selhání došlo u většího počtu pacientů ve skupině LUS pozitivní (17 vs. 2 ve skupině LUS negativní; $p < 0,01$); totéž platilo pro EF ≤ 40 % (34 vs. 3; $p < 0,01$) i GLS ≤ –16 % (60 vs. 58; $p < 0,01$). Křivky operační charakteristiky přijímače (receiver-operating characteristic, ROC) prokázaly, že optimální mezní hodnota počtu B-linií pro predikci rozvoje klinického srdečního selhání i poruchy systolické funkce je 6 nebo více (senzitivita = 89,47 %, specificita = 64,62 %, resp. senzitivita = 91,89 %, specificita = 74,11 %). Analýza podskupin podle počáteční diagnózy prokázala, že predikční hodnota LUS byla statisticky významná pouze v případě STEMI přední stěny.
Závěry: Ultrazvukové vyšetření plic u pacientů se STEMI, provedené do 24 hodin od příjmu, dokáže předpovědět rozvoj klinického srdečního selhání nebo systolické dysfunkce do tří měsíců, zvláště v případě infarktu přední stěny.

ABSTRACT

Aim: To see if the detection of subclinical congestion in STEMI patients by lung ultrasound (LUS) could be helpful in predicting the development of future heart failure, systolic dysfunction or diastolic dysfunction.
Methods: 150 patients were included. All patients were successfully revascularized and were not suffering from clinical heart failure on admission. The patients had a 28-point LUS study within the first 24 hours of admission, and B-lines were counted. Patients were divided into two groups: 64 patients into the LUS positive group (with 6 or more B-lines) and 86 into the LUS negative group. They were followed-up after 3 months, looking for heart failure NYHA II or greater, ejection fraction (EF) ≤40%, and global longitudinal strain (GLS) ≤–16%.
Results: More patients from the LUS positive group developed clinical heart failure (17 vs 2 in the LUS negative group, $p < 0.01$), EF ≤40% (34 vs 3, $p < 0.01$), GLS ≤–16% (60 vs 58, $p < 0.01$). Optimal cutoff derived from ROC curves revealed that the best B-line number cutoff to predict clinical heart failure as well as impaired systolic function was 6 or greater (sensitivity = 89.47%, specificity = 64.62% and sensitivity = 91.89%, specificity = 74.11%, respectively). Subgroup analysis by initial diagnosis revealed that the predictive power of LUS was significant only in anterior STEMI.
Conclusions: LUS in STEMI patients, performed within 24 hours of admission, is able to predict the occurrence of clinical heart failure or systolic dysfunction at 3 months, especially in anterior infarctions.

Keywords:
Heart failure
Lung ultrasound
Myocardial infarction
ST-segment elevation myocardial infarction

Address: Mohamed Abou El Ezz, MD, Department of Cardiovascular Medicine, Faculty of Medicine Cairo University, Cairo, Egypt,
e-mail: mohamed.abouelezz@kasralainy.edu.eg
DOI: 10.33678/cor.2025.006

Please cite this article as: Talaat A, El Ezz MA, Abd El Ghany MM, et al. Value of peri-procedural lung ultrasound in predicting heart failure or left ventricular systolic dysfunction within 3 months in STEMI patients undergoing primary PCI. Cor Vasa 2025;67:350–359.

Introduction

Heart failure is the most common complication of STEMI, and ischemic heart disease is the most prominent cause of heart failure.[1] The development of heart failure or asymptomatic systolic dysfunction after STEMI is associated with poorer in-hospital and long-term prognosis.[2–8]

In many cases, systolic dysfunction occurs after STEMI without necessarily becoming symptomatic. Lung ultrasound has been a very useful diagnostic tool in heart failure even in the pre-symptomatic phase, by detecting lung congestion at an early stage.[9,10] It also provides prognostic value and is useful in following-up treatment response.[11]

We investigated the value of early lung ultrasound, conducted within 24 hours of the development of STEMI, in predicting the occurrence of clinical heart failure and systolic dysfunction within the next 3 months.

Materials and methods

This is a single-center, prospective cohort, non-consecutive study conducted in Cairo University Hospitals from March 2021 to February 2023. A total of 240 patients aged 18 years or older with ST-segment elevation myocardial infarction who have undergone successful primary PCI to the culprit lesion (defined as TIMI flow III at the end of the procedure in the infarct-related artery) were screened for inclusion, of which 150 made the final cut. Most of the rest of the patients were either lost in a follow-up or did not meet the inclusion criteria. Written informed consent was obtained from all participants.

We excluded patients younger than 18 years of age at enrollment, patients with heart failure Killip class II or greater on admission, patients with pre-existing left ventricular systolic dysfunction (LVEF ≤40% or GLS ≤16%, by history or previous documents if applicable), patients with history of CKD KDOQI ≥ stage 3 and patients with interstitial lung disease that may confound the LUS findings. We also excluded patients who developed a non-transient confounding event that could precipitate heart failure or hemodynamic instability on its own and confound the results (e.g. failed primary PCI, stent thrombosis, mechanical complications such as ventricular septal rupture, acute kidney injury, or resuscitated cardiac arrest). Transient events such as promptly cardioverted ventricular tachycardia were not counted as exclusion criteria.

All participants were managed according to the standard ACS protocol in Cairo University hospitals, while upholding the ethical standards of human experimentation in our institution.

On admission, the following data was collected:

1. Patient history: Age, significant risk factors of atherosclerotic cardiovascular disease.
2. Examination: Anthropometry, vital signs, signs of heart failure including jugular venous pressure, lung rales, lower limb edema and oxygen saturation on room air and signs of peripheral perfusion.
3. ECG on presentation.
4. Procedural details: Infarct-related artery, presence of disease in other vessels, and the intervention done.

During hospital stay, the following was performed:

1. Lung ultrasound

A 28-point lung ultrasound was performed within 24 hours of the primary PCI procedure, often shortly after returning to the CCU. The device used was a Philips EPIQ 7 ultrasound system and an X5 probe (1–5 MHz). The protocol used was the 28-point protocol, with scanning done in the 2nd, 3rd and 4th spaces bilaterally, and the 5th space on the right side only, in the parasternal, midclavicular, anterior axillary and mid-axillary lines as per the current consensus recommendations. B-lines, defined as vertical hyperechoic lines extending from the pleura to the bottom of the screen, moving with lung sliding, will be counted and totaled in all 28 zones (**Fig. 1**).

When B-lines are too many to the point where they coalesce together, the arc of the intercostal space that is in white relative to the width of the whole space is divided by 10 to obtain the number of B-lines (e.g. if 70% of the space is white, the number of B-lines is considered to be 7) (**Fig. 2**).

Other lung ultrasound findings such as the presence of pleural effusion were recorded as well, but were not specifically looked for beyond the scope of the 28-point study. All images will be digitally stored for offline analysis. The minimum number of B-lines considered significant was ≥5.

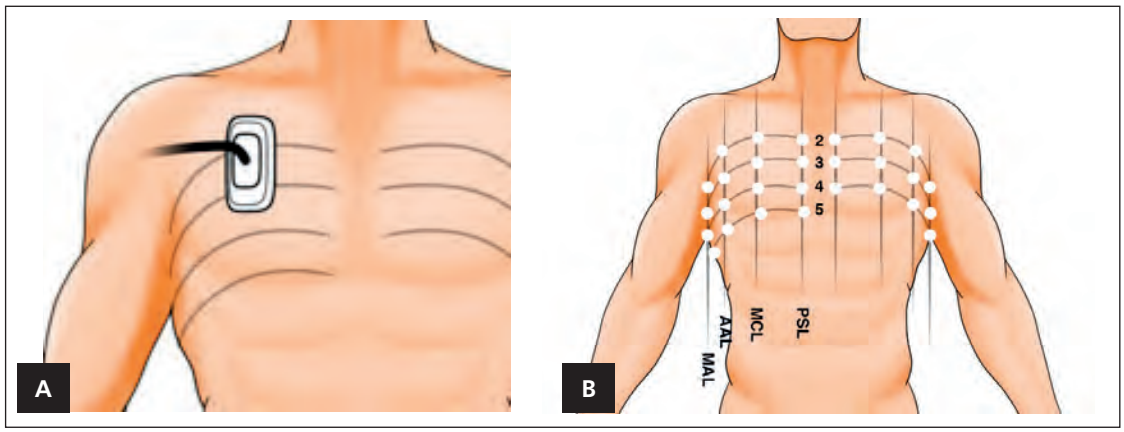


Fig. 1 – (A) Probe position relative to the ribs. (B) Sites that were scanned.

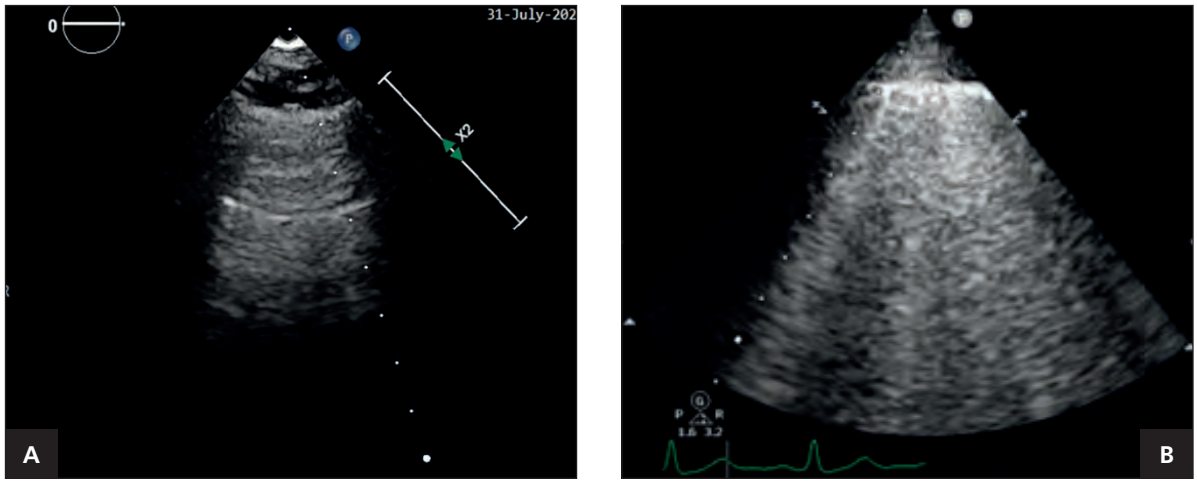


Fig. 2 – (A) Normal scan showing transverse A-lines. (B) Scan showing multiple vertical B-lines.

2. Transthoracic echocardiography
Transthoracic echocardiography was performed in all subjects using a commercially available Philips EPIQ 7 ultrasound system and X5 probe. Important echocardiographic data required for management of the patient were recorded, including LV dimensions in the parasternal long axis view, systolic function using apical biplane Simpson's method whenever the image quality was sufficient and eyeballing whenever image quality was very poor, diastolic function using E and E′ velocities, E/A and E/E′ ratio, segmental wall motion abnormalities, left atrial volume using the biplane Simpson's method, valvular regurgitation, the presence of mechanical complications and right ventricular dimensions and TAPSE. All measurements were done as per ASE/EACVI guidance.

During the follow-up visit 3 months later, the following data was collected:
1. Clinical follow-up
This includes any cardiac symptoms, any new comorbidities, vital signs, JVP, lung rales and lower limb edema. Adherence to medications was also inquired about (defined as intake of appropriate doses of the prescribed drug in over 80% of the elapsed duration).

2. Transthoracic echocardiography
Was performed again using the same devices. The data recorded in follow up included the same parameters recorded in the in-hospital echocardiogram, in addition to global longitudinal strain and left atrial volume using the apical biplane Simpson's method in end-systole. Imaging acquisition was done and offline analysis was performed using Philips Q-lab v10.0.

The primary outcome was determining the prognostic value of number of B-lines in LUS peri-primary PCI in predicting the development of systolic left ventricular dysfunction (defined as EF ≤40% or GLS ≥–16%) within the 3-month follow up period.

Secondary outcomes were the development of clinical heart failure (as per the ESC definition mentioned previously), diastolic left ventricular dysfunction (grade II or above), and cardiovascular mortality within the same period.

Statistical analysis
Based on the study conducted by Xiao-Jun Ye et al.[12] and assuming that the number of B-lines in lung ultrasound could predict the occurrence of in-hospital as well as short-term left ventricular systolic dysfunction, with an intermediate effect size (0.15) and a probability significance of 0.05 and a power of 0.8, and using an online sample size calculator, the estimated minimum sample size is 84 patients. 150 patients were ultimately included in this study.

Analysis was done in the IBM Statistical Package for Social Sciences program (SPSS) version 24.0. Continuous data is displayed as mean ± standard deviation if the data is normally distributed, and as a median and interquartile range if not, while categorical data is displayed as an absolute number and a percentage. Comparison between continuous data was done using Student's unpaired t-test, while comparison between categorical data was done using a chi-square test.

When testing for correlation between two sets of continuous data, a scatter plot with a line of best fit was constructed when applicable, and the Pearson's product-moment correlation coefficient was calculated. For correlation between continuous data and categorical data, a one-way analysis-of-variance test was used. For correlation between two sets of categorical data, a chi-square test was used.

To determine the optimum sensitivity and specificity, ROC curves (sensitivity plotted against 1-specificity) were plotted using SPSS for each of the outcomes being examined. The uppermost, leftmost point corresponded to the cutoff with best sensitivity and specificity. To calculate positive predictive value and negative predictive value at a particular cutoff as well as their confidence intervals, an online calculator was used. For regression analysis, stepwise multiple linear regression analysis was performed when the dependent variable was continuous in nature, while logistical regression analysis was performed when the dependent variable was categorical in nature.

Findings with a two-tailed *p*-value of <0.05 were considered statistically significant.

Results

Out of the included 150 patients, 64 had 6 or more total B-lines on presentation on LUS "LUS positive", while the remaining 86 did not "LUS negative". The cutoff was selected in concordance with the HFA position paper on diuretics released in 2019. The baseline characteristics of the included patients, as well as patients in each group are presented in **Table 1**.

Five patients in the study had history of previous acute coronary syndrome; 3 in the LUS positive group and 2 in the LUS negative group. Five patients had previous CCS (by history or tests), 2 in the LUS positive group, and 3 in the other group (one of which had an old coronary bypass surgery). All of these patients who had history of previous coronary artery disease had normal EF before their presentation to our center in older echocardiograms (**Table 2**).

There was a statistically significant difference in initial presentation between LUS positive and LUS negative groups, with the majority of the patients in the former group presenting with anterior or anterolateral STEMI, while the majority of the patients in the latter group presented with inferior, inferolateral, posterior or lateral STEMI. Mirroring the skew in diagnosis seen between both groups, over 85% of the patients in the LUS positive group had PCI to the LAD or LM vessels. On the other hand, over half of the patients in the LUS negative group had PCI to the LCx or RCA.

Table 1 – Baseline characteristics of the included patients

	Total	LUS positive (n = 64)	LUS negative (n = 86)	*p*-value
Patient characteristics				
Age mean ± SD	53.32 ± 11.24 y	51.93 ± 12.04 y	54.36 ± 10.56 y	0.201
Male	120 (80%)	50 (78%)	70 (81%)	0.620
Diabetes mellitus	60 (40%)	23 (36%)	37 (43%)	0.381
Hypertension	48 (32%)	17 (27%)	31 (36%)	0.218
Cigarette smoking	83 (55%)	31 (49%)	52 (63%)	0.143
FH of premature ASCVD	8 (5%)	5 (8%)	3 (4%)	0.243
Obesity (BMI ≥30)	24 (16%)	13 (20%)	11 (13%)	0.214

ASCVD – atherosclerotic cardiovascular disease; BMI – body mass index; FH – family history; LUS – lung ultrasound; y – years.

Table 2 – Findings on initial presentation in the included patients

	LUS positive (n = 64)	LUS negative (n = 86)	*p*-value
Initial diagnosis			
Anterior STEMI	32 (50%)	26 (31%)	**0.014**
Anterolateral STEMI	25 (40%)	3 (3%)	**<0.01**
Inferior STEMI	5 (6%)	32 (37%)	**<0.01**
Inferoposterior STEMI	1 (2%)	11 (13%)	**0.012**
Isolated posterior STEMI	0	5 (6%)	0.050
Lateral STEMI	0	9 (10%)	**<0.01**
LM equivalent	1 (2%)	0	0.245
Chest pain duration mean ± SD	15.18 ± 16.32 hours	7.76 ± 8.29 hours	**0.013**
Clinical data			
SBP mean ± SD	139.32 ± 67.70 mmHg	142.39 ± 73.00 mmHg	0.252
DBP mean ± SD	88.86 ± 42.95 mmHg	89.35 ± 45.31 mmHg	0.446
Pulse mean ± SD	104.02 ± 50.56 bpm	90.00 ± 45.87 bpm	**<0.01**
Procedural details: Culprit vessel PCI			
LM or LM-LAD	4 (6%)	0	**0.019**
LAD or branches	52 (81%)	29 (34%)	**<0.01**
LCx or branches	4 (6%)	32 (37%)	**<0.01**
RCA or branches	4 (6%)	25 (29%)	**<0.01**

DBP – diastolic blood pressure; LUS – lung ultrasound; PCI – percutaneous coronary intervention; SBP – systolic blood pressure; STEMI – ST-segment elevation myocardial infarction.

Table 3 – In-hospital events in each group

	LUS positive (n = 64)	LUS negative (n = 86)	*p*-value
In-hospital heart failure	6 (10%)	0	**<0.01**
Clinical lung congestion requiring the use of intravenous diuretics	4 (6%)	0	**0.019**
Cardiogenic shock	2 (3%)	0	0.094
Arrhythmias			
Complete heart block	1 (2%)	0	0.245
Ventricular tachycardia	1 (2%)	3 (3%)	0.469
Atrial fibrillation	0	1 (1%)	0.386
In-hospital mortality	1 (2%)	0	0.245
In-hospital echocardiogram			
Ejection fraction mean ± SD	44.90 ± 7.04%	53.40 ± 8.20%	**<0.01**
Grade II diastolic dysfunction or more	20 (31%)	33 (38%)	0.465
Mural thrombus	5 (8%)	3 (4%)	0.244

LUS – lung ultrasound.

Table 4 – Summary of the follow-up visit findings in each group

	LUS positive (n = 63)	LUS negative (n = 86)	*p*-value
Clinical heart failure	19 (30%)	2 (2%)	**<0.01**
NYHA II	17 (27%)	2 (2%)	**<0.01**
NYHA class III+	2 (3%)	0	0.346
Patient compliance	35 (56%)	51 (59%)	0.690
Echocardiographic data: Systolic function			
Ejection fraction ≤40%	34 (55%)	3 (4%)	**<0.01**
	41.08 ± 4.74%	55.22 ± 8.26%	
Global longitudinal strain ≤–16%	60 (96%)	58 (67%)	**<0.01**
	–12.31 ± 1.24%	–15.24 ± 1.91%	
Echocardiographic data: Diastolic function			
Grade II diastolic dysfunction or more	25	28	0.469
Left atrial volume index	36.41 ± 15.94 ml/m^2	29.38 ± 11.88 ml/m^2	**<0.01**
Average E/E'	13.24 ± 7.16	9.06 ± 4.25	**<0.01**

LUS – lung ultrasound; NYHA – New York Heart Association.

In-hospital events

More patients in the LUS positive group ultimately developed in-hospital acute heart failure (6 patients versus none in the LUS negative group, *p*-value = 0.003), mostly lung congestion requiring eventual in-hospital IV diuretic use (**Table 3**).

However, this statistical significance could not be demonstrated in cardiogenic shock specifically due to the low event count.

There was a statistically significant difference in the mean ejection fraction during hospitalization between both groups, with the LUS positive group being lower. However, there was no statistically significant difference between both groups in terms of number of patients with grade II diastolic dysfunction or more in-hospital.

Follow-up visit

Nineteen patients from the LUS positive group developed exertional dyspnea at 3 months, as opposed to only two in the LUS negative group (**Table 4**). Most of the patients had dyspnea NYHA class II. Only two patients developed dyspnea NYHA III; both were in the LUS positive group.

ROC curves were plotted to identify the best B-line cutoff that provided the highest sensitivity and specificity for impaired ejection fraction. The best cutoff to predict an impaired ejection fraction was ≥6 lines (which was what we used in this study) with an area under the ROC curve of 0.92. The sensitivity and specificity of ≥6 lines is displayed in **Table 5, Figure 3**.

Using the follow-up data, an evaluation of LUS as a diagnostic test was done by calculating the sensitivity,

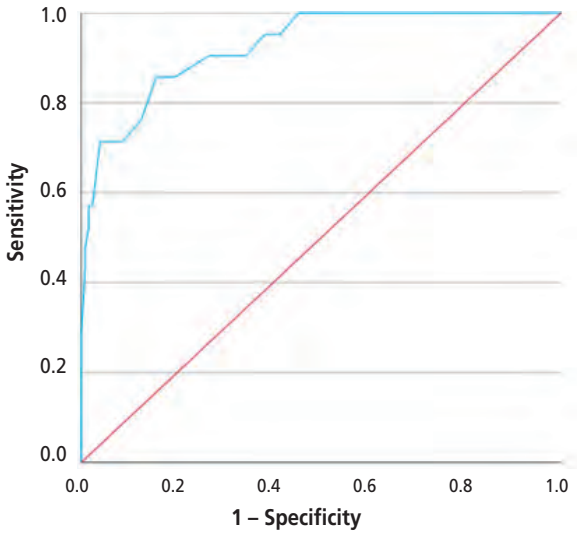


Fig. 3 – ROC curve for number of B-lines sensitivity and specificity in predicting clinical heart failure.

specificity, PPV and NPV to detect clinical heart failure or systolic dysfunction by ejection fraction or global longitudinal strain. LUS demonstrated a high sensitivity and high negative predictive value in predicting the occurrence of clinical heart failure or an ejection fraction ≤40%. For global longitudinal strain, LUS demonstrated a low sensitivity but high specificity in detection of impaired GLS in this subset of patients (**Table 5**).

Subgroup analysis according to the initial presentation

After performing subgroup analysis on follow-up data, the statistical significance of the difference between the LUS positive and LUS negative groups in clinical heart failure, ejection fraction ≤40 and global longitudinal strain ≥–16% at 3 months was carried over for anterior infarctions (including anterior, anterolateral, and anteroinferior infarctions), and lost for inferior infarctions (including inferior, inferolateral, and inferoposterior infarctions) (**Table 6**).

Correlation analysis

Pearson correlation analysis between the number of B-lines and ejection fraction ≤ 40%, global longitudinal strain ≥ –16%, left atrial volume index and average E/E' ratio was done. The number of B-lines was strongly negatively correlated with the ejection fraction (r = –0.619, p <0.01), and strongly positively correlated with the global longitudinal strain (r = 0.521, p <0.01). It was also moderately positively correlated with the average E/E' ratio (r = 0.389, p <0.01).

Table 5 – Sensitivity, specificity, positive predictive value, and negative predictive value of 6 or more B-lines in LUS in predicting various endpoints

	Sensitivity	Specificity	PPV	NPV
Follow-up data				
Clinical HF	89.47% 95% CI: 66.8–98.7%	64.62% 95% CI: 55.7–72.8%	26.98% 95% CI: 21.8–32.8%	97.67% 95% CI: 59.7–75.2%
EF ≤40%	91.89% 95% CI: 78.1–98.3%	74.11% 95% CI: 65.0–81.9%	53.97% 95% CI: 45.8–61.9%	96.51% 95% CI: 90.3–98.8%
GLS ≤–16%	50.85% 95% CI: 41.5–60.2%	90.32% 95% CI: 74.3–98.0%	95.24% 95% CI: 87.1–98.4%	32.56% 95% CI: 28.0–37.5%

CI – confidence interval; EF – ejection fraction; GLS – global longitudinal strain; HF – heart failure; NPV – negative predictive value; PPV – positive predictive value.

Table 6 – Subgroup analysis of the groups according to the initial diagnosis

LUS positive – LUS negative	LUS positive	LUS negative	*p*-value
Anterior STEMI	n = 57	n = 29	
Clinical heart failure	18 (32%)	2 (7%)	**0.022**
Ejection fraction ≤40%	32 (56%)	2 (7%)	**<0.01**
Global longitudinal strain ≥–16%	57 (100%)	25 (86%)	**0.020**
Grade II diastolic dysfunction or more	20 (35%)	7 (24%)	0.430
Inferior STEMI	n = 6	n = 43	
Clinical heart failure	1 (17%)	0	0.245
Ejection fraction ≤40%	1 (17%)	0	0.245
Global longitudinal strain ≥–16%	5 (83%)	22 (52%)	0.296
Grade II diastolic dysfunction or more	4 (67%)	18 (42%)	0.480

LUS – lung ultrasound; STEMI – ST-segment elevation myocardial infarction.

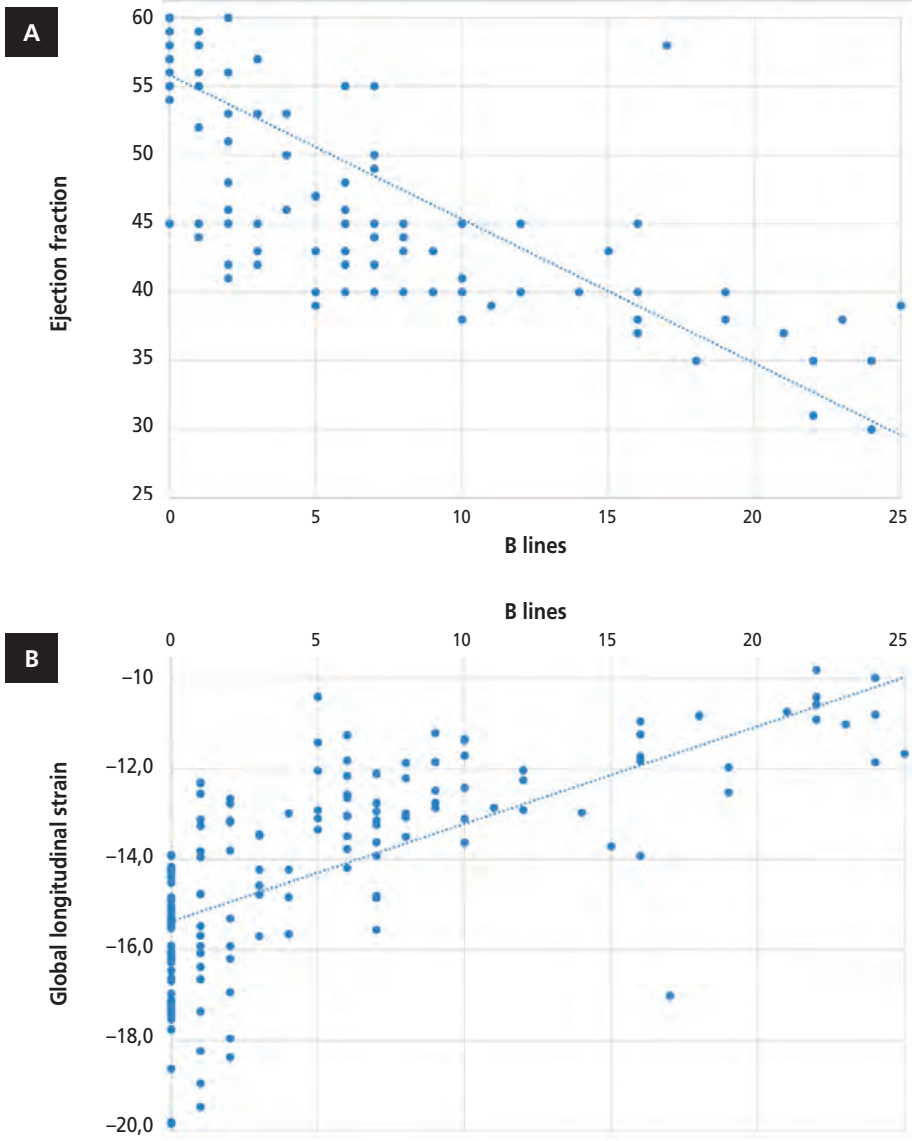


Fig. 4 – Scatter plots of number of B-lines against the ejection fraction (A) and global longitudinal strain (B).

Table 7 – Linear regression analysis results

	Unstandardized coefficients		Standardized coefficients	
	B	**Standard error**	**Beta**	***p*-value**
Ejection fraction at 3 month follow-up visit R = 0.845, R square = 0.714, adjusted R square = 0.691				
Presentation HR	–0.105	0.035	–0.186	**<0.01**
In-hospital EF%	0.380	0.083	0.349	**<0.01**
Number of B-lines	–0.617	0.095	–0.483	**<0.01**
Global longitudinal strain at 3 month follow-up visit R = 0.796, R square = 0.634, adjusted R square = 0.604				
Hypertension	-0.743	0.325	–0.164	**0.025**
Presentation HR	0.022	0.009	0.172	**0.017**
In-hospital EF%	–0.097	0.017	–0.244	**<0.01**
Number of B-lines	0.051	0.018	0.514	**<0.01**

EF – ejection fraction; HR – heart rate; STEMI – ST-segment elevation myocardial infarction.

However, no statistically significant correlation could be seen between the number of B-lines above 5 and the left atrial volume index (r = 0.217, p = 0.114) (**Fig. 4**).

Regression analysis

Stepwise multiple linear regression analysis was done to demonstrate the independent predictive ability of the number of B-lines in LUS. Out of age, diabetes, hypertension, smoking, heart rate on presentation, ejection fraction on presentation and B-lines on presentation, only the latter three demonstrated a statistically significant ability to independently predict the ejection fraction and global longitudinal strain at 3 months in our study. Hypertension was able to predict an impaired global longitudinal strain at 3 months, but not ejection fraction at 3 months (**Table 7**).

Discussion

In our study, there was an obvious, statistically significant association between a positive in-hospital LUS and the eventual development of in-hospital heart failure. Since B-lines are themselves markers of subclinical congestion, this conclusion is hardly surprising.

Aside from that, there was a common theme immediately apparent in the LUS positive group of patients even before they came in for their follow-up visit. Their chest pain to revascularization time was longer, they were more tachycardic, more often had anterior infarctions, and subsequently often had an LAD culprit. Their baseline systolic function measured in-hospital was also often worse. All of these characteristics are themselves established predictors of heart failure in STEMI patients.[13]

The differences in terms of the primary and secondary outcomes between the two groups in the follow-up visits could not be more discordant. Patients who had a positive LUS were much more likely to develop clinical heart failure and systolic dysfunction on follow-up. To take it a step further, there was evidence of a strong linear correlation between the number of B-lines above 5 in-hospital and the ejection fraction and global longitudinal strain in the follow-up visit.

It seems however that this predictive ability only holds true for patients with anterior infarctions, and the difference between the two groups when examining other non-anterior infarctions was not statistically significant in our study.

The results were also less conclusive in terms of diastolic function. There was no statistically significant difference in the number of patients having grade 2 or higher diastolic dysfunction (diagnosed according to the ASE algorithm) between both groups. In terms of the individual components of the algorithm however, there was a statistically significant difference in the mean left atrial volume index and the mean average E/E' ratio between the two groups.

Regression analysis reinforced the predictive power of LUS in systolic dysfunction independent of other factors.

Previous studies

The studies examining the role of LUS in STEMI patients are relatively scarce, are mostly on a limited number of patients, and most of those focus on immediate outcomes (either in-hospital or within the first 30 days after discharge).

The largest study conducted on the matter was by Araiza et al in 2022, on 226 patients.[14] The investigative team performed a 4-point LUS during the first 24 hours of hospitalization. On 30-day follow-up, there was a statistically significant increase in the incidence of heart failure in the LUS positive group, similar to our findings. It has to be noted, however, that this study did not exclude patients with renal impairment or higher Killip classes.

The study with the longest follow-up was done by Xiao-Jun Ye et al in 2019.[12] It enrolled a total of 102 STEMI patients. Interestingly, they were anterior STEMI patients; the exact subgroup where the results of our study were particularly relevant to. The investigators performed a 28-point LUS within 5 hours of admission, then monitored them for in-hospital heart failure. After discharge, rehospitalization for heart failure within two years was documented, unlike our study which monitored patients for a much shorter duration and for general (even mild) heart failure symptoms as opposed to only hospitalizations or cardiovascular events.

Ye et al. found that a positive LUS study significantly predicted heart failure rehospitalization and all-cause mortality, although the cutoff for that was 18 B-lines. The investigators also found out that the predictive power of LUS could be improved further by adding E/E' measurements and NT-proBNP. We did not use biomarkers in our study.

In a study by He et al. published in 2022 that included 63 patients with acute myocardial infarction (as opposed to just STEMI patients), an 8-point LUS conducted during the first 24 hours was able to predict not only worsening heart failure as we had found out in our study, they also found out that it predicted rehospitalization and all-cause mortality at 30 days.[15]

To the best of our knowledge, there are no published studies on the ability of LUS to predict systolic or diastolic dysfunction after a myocardial infarction.

The STEMI event itself represents the brunt of the hit on the myocardium, when transient factors such as myocardial stunning are present and not enough time is available for compensatory mechanisms to cope with the cardiac dysfunction that has happened.

The appearance of subclinical congestion early on could be interpreted as a marker that the cardiac dysfunction (whether systolic or diastolic) is significant enough to overwhelm the rest of the myocardium and elevate the left ventricular end diastolic pressure, and consequently lower the likelihood of the myocardium functioning as adequately in the future.[16]

One peculiar finding in our study is that congestion in LUS is more predictive of systolic dysfunction at 3 months (as defined before) than the ejection fraction on presentation. This is probably because as mentioned before, B-lines are a surrogate for left ventricular end diastolic pressure, which is influenced by systolic and diastolic

myocardial performance rather than just systolic. Since STEMI is a disease that affects systolic and diastolic function, not all future heart failure events can be accounted for by the admission ejection fraction alone, and LUS will be superior to it in that regard.

The biggest takeaway from this study is that LUS provides beneficial prognostic data at no extra cost, effort or time. It is performed at the end of the routine echocardiographic study that is done for all STEMI patients. It can help planning of investigations, medications and the frequency of follow-up visits.

Study limitations

The NYHA classification is entirely subjective and is subject to many confounding causes of dyspnea. The use of the Kansas City Cardiomyopathy Questionnaire or a 6-minute walk test may have been more accurate.

In many patients, a physical previous echocardiogram document was not always available and history alone may be very misleading.

Global longitudinal strain is highly influenced by the quality of the patient's echocardiographic windows.

The study was not blinded; the operator knew the results of the LUS during the follow-up visits of the patients.

The study was conducted in a single center and patients were selected non-consecutively. The sample size was limited; a larger study on a bigger sample size would be more suitably powered to detect statistically significant differences between the two arms in in-hospital cardiogenic shock, non-anterior STEMI patients, and diastolic dysfunction.

The exclusion criteria were quite exhaustive and excluded a large subset of STEMI patients, such as those with comorbidities or unsuccessful revascularization. These specific patients are the ones who may gain extra benefit from further risk assessment over stable, straightforward cases.

The study did not include the use of cardiac biomarkers such as NT-pro BNP.

Conclusion

LUS in STEMI patients, performed within 24 hours of admission, is able to predict the occurrence of clinical heart failure or systolic dysfunction at 3 months according to our study, especially in anterior infarctions.

Acknowledgements
The authors acknowledge Prof Dr Yasser Boghdady and Prof Dr Mohamed Seleem for their valuable comments and suggestions. We also acknowledge Prof Dr Magdy Abd El Hamid for his support throughout the research.

Funding
The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Ethical statement
This is an observational study. The Cairo University Faculty of Medicine ethics committee has approved this research on 19-08-2021 (Code: MD-220-2021). The work conforms to the standards currently applied to research methodology in Egypt.

Consent to participate
Informed written consent to participate in the research was obtained from all individual participants included in the study.

Consent to publish
Informed written consent to publish research results was obtained from all individual participants included in the study.

Availability of the data and material
The data is available upon reasonable request.

Author contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Mohamed Abou El Ezz. The first draft of the manuscript was written by Mohamed Abou El Ezz, and Ahmed Talaat commented on the previous versions of the manuscript. All authors read and approved the final manuscript.

References

1. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2021;42:3599–3726.
2. Khot UN, Jia G, Moliterno DJ, et al. Prognostic importance of physical examination for heart failure in non-ST-elevation acute coronary syndromes: the enduring value of Killip classification. JAMA 2003;290:2174–2181.
3. DeGeare VS, Boura JA, Grines LL, et al. Predictive value of the Killip classification in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol 2001;87:1035–1038.
4. Nešković AN, Otašević P, Bojić M, et al. Association of Killip class on admission and left ventricular dilatation after myocardial infarction: a closer look into an old clinical classification. Am Heart J 1999;137:361–367.
5. Desta L, Jernberg T, Löfman I, et al. Incidence, temporal trends, and prognostic impact of heart failure complicating acute myocardial infarction: the SWEDEHEART Registry (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies): a study of 199,851 patients admitted with index acute myocardial infarctions, 1996 to 2008. JACC: Heart Failure 2015;3:234–242.
6. Sutton NR, Li S, Thomas L, et al. The association of left ventricular ejection fraction with clinical outcomes after myocardial infarction: Findings from the Acute Coronary Treatment and Intervention Outcomes Network (ACTION) Registry–Get With the Guidelines (GWTG) Medicare-linked database. Am Heart J 2016;178:65–73.
7. Ng VG, Lansky AJ, Meller S, et al. The prognostic importance of left ventricular function in patients with ST-segment elevation myocardial infarction: the HORIZONS-AMI trial. Eur Heart J Acute Cardiovasc Care 2014;3:67–77.
8. Ersbøll M, Valeur N, Mogensen UM, et al. Prediction of all-cause mortality and heart failure admissions from global left ventricular longitudinal strain in patients with acute

myocardial infarction and preserved left ventricular ejection fraction. J Am Coll Cardiol 2013;61:2365–2373.
9. Marini TJ, Rubens DJ, Zhao YT, et al. Lung ultrasound: the essentials. Radiol Cardiothor Imaging 2021;3:e200564.
10. Mullens W, Damman K, Harjola VP, et al. The use of diuretics in heart failure with congestion – a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail 2019;21:137–155.
11. Platz E, Merz AA, Jhund PS, et al. Dynamic changes and prognostic value of pulmonary congestion by lung ultrasound in acute and chronic heart failure: a systematic review. Eur J Heart Fail 2017;19:1154–1163.
12. Ye XJ, Li N, Li JH, et al. B lines by lung ultrasound predict heart failure in hospitalized patients with acute anterior wall STEMI. Echocardiography 2019;36:1253–1262.
13. Jenča D, Melenovský V, Stehlik J, et al. Heart failure after myocardial infarction: incidence and predictors. ESC Heart Fail 2021;8:222–237.
14. Araiza-Garaygordobil D, Baeza-Herrera LA, Gopar-Nieto R, et al. Pulmonary Congestion Assessed by Lung Ultrasound and Cardiovascular Outcomes in Patients With ST-Elevation Myocardial Infarction. Front Physiol 2022;13:881626.
15. He J, Yi S, Zhou Y, et al. B-lines by lung ultrasound can predict worsening heart failure in acute myocardial infarction during hospitalization and short-term follow-up. Front Cardiovasc Med 2022;9:895133.
16. Gargani L. Lung ultrasound: a new tool for the cardiologist. Cardiovasc Ultrasound 2011;9:1–9.

Původní sdělení | Original research article

Correlation of *ITGB3* Gene rs5918T>C and *APOA1* Gene rs1799837C>T Variants with Serum Lipid Profiles in Turkish Cypriot Patients with Coronary Artery Disease

Cenk Conkbayir[a], Mahmut Cerkez Ergoren[b,c], Havva Cobanogullari[b,c], Ozlem Balcioglu[d], Irem Abras[e], Tengul Eminsel[e], Didem Melis Oztas[f], Burak Onal[g], Murat Ugurlucan[f], Sehime Gulsun Temel[h,i]

[a] *Department of Cardiology, Faculty of Medicine, Near East University, Nicosia, Cyprus*
[b] *Department of Medical Biology, Faculty of Medicine, Near East University, Nicosia, Cyprus*
[c] *DESAM Institute, Near East University, Nicosia, Cyprus*
[d] *Department of Cardiovascular Surgery, Faculty of Medicine, Near East University, Nicosia, Cyprus*
[e] *Department of Biological Sciences, Eastern Mediterranean University, Famagusta, Cyprus*
[f] *Department of Cardiovascular Surgery Clinic, Biruni University Faculty of Medicine, Istanbul, Turkey*
[g] *Department of Medical Pharmacology, Biruni University Faculty of Medicine, Istanbul, Turkey*
[h] *Department of Medical Genetics, Faculty of Medicine, Uludag University, Bursa, Turkey*
[i] *Department of Histology and Embryology, Faculty of Medicine, Uludag University, Bursa, Turkey*

ARTICLE INFO

Article history:
Submitted: 30. 10. 2024
Revised: 18. 12. 2024
Accepted: 4. 1. 2025
Available online: 17. 6. 2025

Klíčová slova:
APO-A1
HDL-C
Ischemická choroba srdeční
ITGB3
Kyperský Turek
LDL-C
Polymorfismus

SOUHRN

Cíl: Vztah mezi hypercholesterolemií, zvláště zvýšenými hodnotami cholesterolu v lipoproteinech o nízké hustotě (LDL-C) a ischemickou chorobou srdeční (ICHS), je potvrzen důkazy z předchozích epidemiologických studií. Důležité bylo popsání souvislosti mezi genetickým polymorfismem a hodnotami lipidů v plazmě. Cílem této studie bylo zkoumat vztah mezi variantami rs5918 T>C genu pro ITGB3 a variantou rs1799837 C>T genu pro APO-A1 na jedné straně a metabolismem lipidů v séru na straně druhé.
Pacienti a metody: Do této studie bylo zařazeno celkem 100 jedinců s ICHS a 250 zdravých jedinců. U každého účastníka bylo provedeno základní biochemické vyšetření včetně stanovení koncentrace glukózy v séru, celkového cholesterolu (total cholesterol, TC) v séru, hodnot HDL-C, LDL-C a triglyceridů. Pro genotypizaci polymorfismů genů pro ITGB3 a APO-A1 byla použita polymerázová řetězová reakce s následnou analýzou polymorfismu délky restrikčních fragmentů (restriction fragment length polymorphism, RFLP).
Výsledky: Pokud se týče genotypu a distribuce alel polymorfismu rs5918 T>C genu pro ITGB3, vyskytovala se alela C častěji ve skupině s ICHS než v kontrolní skupině (p = 0,001). Ve skupině s ICHS byla navíc pozorována statisticky významná souvislost mezi genotypem rs5918 ITGB3 a hodnotami celkového cholesterolu v genotypu CC na jedné straně a TC v séru a cholesterolu v lipoproteinech o vysoké hustotě (HDL-C) (p = 0,0006, resp. p = 0,016). Nicméně ani v kontrolní skupině, ani ve skupině s ICHS nebyla nalezena statisticky významná spojitost mezi polymorfismem rs1799837 C>T genu pro APO-A1 a biochemickými parametry.
Závěr: Výsledky prokázaly, že varianta rs5918 T>C genu pro ITGB3 by mohla být z klinického hlediska významná jako genetický marker zvýšené vnímavosti k rozvoji ICHS. Alelu C varianty rs5918 genu pro ITGB3 by tak bylo možno navrhnout pro screening potenciálního rozvoje ICHS u populace kyperských Turků, kteří se dostaví na kontrolu k lékaři.

Keywords:
APO-A1
Coronary artery disease
HDL-C
ITGB3
LDL-C
Polymorphism
Turkish Cypriot

ABSTRACT

Aim: The relationship between hypercholesterolemia, particularly elevated low density lipoprotein-cholesterol (LDL-C) levels and coronary artery disease is recognized by the evidence from previous epidemiologic studies. Importantly, genetic polymorphisms on different genes have been reported to be associated with plasma lipid levels. In this particular study, we aimed to investigate the relationship between the *ITGB3* gene rs5918 T>C and *APO-A1* gene rs1799837 C>T markers and serum lipid metabolism.

Address: Cenk Conkbayir, MD, Department of Medical Biology, Near East University, Faculty of Medicine, 99138 Nicosia, Cyprus, e-mail: cenkconk@hotmail.com
DOI: 10.33678/cor.2025.004

Please cite this article as: Conkbayir C, Ergoren MC, Cobanogullari H, et al. Correlation of *ITGB3* Gene rs5918T>C and *APOA1* Gene rs1799837C>T Variants with Serum Lipid Profiles in Turkish Cypriot Patients with Coronary Artery Disease. Cor Vasa 2025;67:360–366.

Patients and methods: A total of 100 subjects with CAD and 250 healthy subjects were involved in the current study. A basic biochemical analysis, including serum glucose, total serum cholesterol, HDL-C, LDL-C and triglycerides, was performed for each participant. Genotyping for the *ITGB3* gene and *APO-A1* gene polymorphisms was performed by polymerase chain reaction followed by restriction fragment length polymorphism (RFLP) analysis.

Results: With respect to the genotype and allele distributions of *ITGB3* rs5918 T>C polymorphism, the frequency of the C allele was higher in the coronary artery disease (CAD) group compared to the control group (p = 0.001). Moreover, there was a statistically significant association detected between *ITGB3* rs5918 CC genotype and serum total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) (p = 0.0006, p = 0.016, respectively) in CAD group. However there was no statistically significant association was identified between the *APOA1* rs1799837 C>T polymorphism and biochemical parameters in control and CAD group.

Conclusion: The results demonstrated that rs5918 T>C variant within the *ITGB3* gene might have a clinical importance as a genetic marker which increases the susceptibility to CAD. Therefore, the *ITGB3* gene rs5918 C allele may be offered as a screening option for CAD in Turkish Cypriot population who come in for medical check-up.

Introduction

Among the group of cardiovascular disorders, coronary artery disease (CAD) is the most commonly reported all around the world.[1,2] Among the modifiable risk factors, abnormal lipid metabolism plays a critical role in the pathogenesis of CAD.[2] According to the World Health Organization (WHO) statistics, 17.9 million people die each year from CVDs, which accounts for nearly 31% of all global deaths.[1]

Over more than a decade, it has been shown that serum concentrations of blood lipids are associated with increased risk of developing cardiovascular diseases.[3] Genetic variants on several genes are believed as one of the most significant determinants of the concentration of serum lipids and CAD.[4] The product of the *ITGB3* gene (OMIM 173470) which is located on chromosome 17 long (q) arm at 21.32 position is a protein known as integrin beta III, which is also noted as platelet glycoprotein IIIa, GP3A, GPIIIa or antigen CDG1, is a surface protein found in various tissues, and has an active role in cell surface mediated signaling and adhesion. A single base change at position 1565 in exon 2 of *ITGB3* gene (T to C) (rs5918T>C) results substitution of leucine (PlA1) amino acid for proline amino acid (PlA2) at a residue 33 of the β3 subunit of the platelet glycoprotein IIIa.[5] This polymorphism causes different spatial orientation and conformational change of protein in fibrinogen binding region.[1,6] Several mechanisms have been documented about the role of the fibrinogen in CVD, essentially when it binds to activated platelets via glycoprotein IIb/IIIa, it contributes to platelet aggregation.[6,7]

According to Shabana et al.[1] the *ITGB3* gene rs5918T>C polymorphism has a significant role in the progression of coronary artery disease and coronary thrombosis due to a key event in acute coronary syndrome. Additionally, it has been demonstrated that there is a strong association of *ITGB3* with triglycerides in non-Hispanic blacks.[3] In earlier studies, it has been shown that PlA2 variant was associated with an increased risk of coronary heart disease. Importantly, some reports suggest that PlA1/A2 heterozygotes are more prone to develop thrombotic diseases, while, PlA1/A1 homozygotes may be prone to develop early atherosclerosis.[6] A study which was undertaken by Khatami et al.,[6] showed that (PIA1/PIA2*)* polymorphism in the *ITGB3* gene is associated with CAD in the Iranian population.

Apolipoprotein A-1 *(APOA1)* gene (OMIM 107680) which is located on chromosome 11 long (q) arm at 23.3 position.[4] Also it is a crucial apolipoprotein component of HDL-C which is essential for normal HDL-C synthesis (F. Wang et al., 2019; Rosales et al., 2019). It has been indicated that inter-individual variants in plasma *APOA1* and HDL are mostly affected by a common polymorphism of a cytosine (C) to thymine (T) substitution (C/T) at -75 bp (rs1799837) in the promoter region.[4]

Genetic variants and mutations in the *APOA1* gene may reduce HDL-C levels therefore the risk of developing premature CAD may be increased.[8] In light of the evidence from previous studies, the association of "T" allele (minor/mutant allele) carriers have undoubtedly higher TG levels while other studies showed there is no association between "T" allele carriers and TG.[4] Interestingly, various studies have shown that the rs1799837 SNP is associated with higher plasma HDL-C levels in carriers of the TT genotype.[9]

Despite many genetic markers have been studied previously, *APOA5* (rs662799 T>C), *APOA5* (rs2075291 G<T), *APOA5* (rs3135507 G>A).[10] *NOS3* c.894G>T and 27-bp VNTR polymorphisms.[11] *CDKN2B-AS1* (rs4977574 A>G), *CDKN2B-AS1* (rs1333040 C>T).[12] ACE INDEL polymorphism.[13] FV Leiden (G1691A), Factor V R2 mutation (FVR2) (H1299R), *PTH* (G20210A), *FXIII* (V34L), β-fibrinogen (–455 G>A), *PAI-1* (4G/5G), *HPA1* (a/b), *MTHFR* [C677T] and [A1298C], *ACE* (I/D), *Apo B* (R3500Q), and *Apo E* (14) rs5918T>C and rs1799837C>T have not been previously investigated in the Turkish Cypriot population. Therefore, this study is the first study which aimed to investigate the association of the *ITGB3* gene rs5918T>C and the *APO-A1* gene rs1799837C>T markers with serum lipid metabolism in cardiovascular patients in the population of Turkish Cypriots.

Material and methods

Study design and participants

The study protocol was approved by the Near East University Ethics Review Board (NEU/2016/36/382) and informed

consent was obtained from all patients and control individuals. Each subject was provided with a detailed questionnaire form to collect information about their personal characteristics, including age, ethnicity, socio-economic background and health status. The current study included 438 Turkish Cypriot individuals. The participant who has history of smoking, hypertension, obesity (BMI >30), diabetes, dislipidemia, and family background were exluded from this study. The Turkish Cypriot race was identified as living on the island as well as being born to parents who have been living at least past three generations. However, participants were selected from among whole island according to their or parents residence before 1974. Furthermore, due to the small size of island population and large numbers of kinship in the Northern Cyprus, the subjects which are relatively related were eliminated from the study. Three hundred forty-five healthy subjects, having no clinical evidence of family/history of stroke or transient ischemic attacks constituted the control group and 93 patients with angiography confirmed CAD who were diagnosed by a cardiologist comprised the CAD group. The controls and CAD groups were matched according to their sex, age, and socio-economic background. Blood samples were collected from all participants and biochemical analysis was performed for total cholesterol, glucose, LDL-cholesterol, HDL-cholesterol, and triglycerides. Additionally, blood pressure measurements were also performed. Basic biochemical analysis protocol has been applied for each individual. Antecubital venous blood was collected from each individual and samples were centrifuged within 2 h of collection. Total serum cholesterol, HDL-C (high density lipoprotein cholesterol), LDL--C (low density lipoprotein cholesterol), triglycerides (TG) and serum glucose were analyzed at the Near East University Hospital Biochemistry Laboratory. Moreover, the subjects who are under any medication that might alter the serum level parameters were eliminated from the study group.

Genotyping

Blood samples were collected in tubes containing ethylenediaminetetraacetic acid (EDTA) from 350 individuals fromm the Turkish Cypriot population. QIAamp DNA Blood Mini Kit (Qiagen Inc.,Valencia, CA, USA) was used for DNA extraction. Genotypes for *ITGB3* gene (rs5918T>C) and *APOA1* gene (rs1799837C>T) polymorphisms were determined by polymerase chain reaction (PCR) followed by restriction fragment length polymorphism (RFLP) following the same primers and conditions in earlier studies.[15,16] Polymerase chain reaction (PCR) was performed in a total reaction volume of 25 µl in 200 µl tubes on an Applied Biosystems Veriti Thermal Cycler. The reaction mixture included PCR Master Mix (2X) (Thermo Scientific Waltham, CA, USA), 10nM of forward and reverse primers (Thermo Scientific Waltham, CA, USA) and 10 ng of the genomic DNA. Fragments obtained from PCR-RFLP were separated in 3% agarose gels. Then gels were visualized by ethidium bromide staining. By using UV-treated solutions, designated pipettes, and pipette tips, a class II laminar hood and DNA/DNAse free plasticware and reagents, the risk of contamination was decreased to minimum. Genotypes were determined according to presence or absence of restriction sites and alleles were designated with respect to actual base change according to the dbSNP (https://www.ncbi.nlm.nih.gov/SNP) and Ensembl (http://www.ensembl.org/) websites.

Statistical analysis

The commercial software program (Graphpad Software, Inc. California, USA) was used for statistical analysis. The data were expressed as mean ± standard deviation (SD) for normally distributed continuous variables. Intergroup differences in continuous variables were determined by the Student's unpaired *t* test, where a *p*-value (two-tailed) of less than 0.05 was considered as statistically significant. Genotype distributions and allele frequencies were measured by the gene-counting method and the Pearson's goodness of fit Chi square (χ^2) method was applied to check their compliance to the Hardy-Weinberg equilibrium. The association between the case–control status and each polymorphism was assessed by the odds ratio (OR) and its corresponding 95% confidence interval (CI), where a *P* value of < 0.05 was considered to be statistically significant. For each polymorphism, one-way ANOVA (analysis of variance) was used to evaluate the impact of the designated genotypes on biochemical parameters.

Results

Demographic, clinical and laboratory characteristics of the studied subjects

The personal characteristics and biochemical parameters of the subjects, from whom blood samples were obtained are shown in **Table 1**. The subjects composed of 350 Turkish Cypriot individuals including 100 patients with CAD and 250 Turkish Cypriots as the control group. The CAD group showed no statistically significant difference from the control group with respect to age, gender and low--density lipoproteins-cholesterol (LDL-C) (*p* >0.05), whereas, fasting plasma glucose levels, serum concentration

Table 1 – General characteristics of all studied subjects

parameters	Control	CAD	Two-tailed *p*-value
	n = 250	n = 100	0.052
Age (years)	57.5 ± 15.5	62.0 ± 12.0	
Sex	37.6% F	45% F	0.201
	62.4% M	55% M	
Glucose (mg/dl)	94.7 ± 16.2	128.0 ± 47.1	<0.0001
Cholestrol (mg/dl)	178.2 ± 39.0	204.5 ± 44.9	0.001
HDL-C (mg/dl)	52.7 ± 12.4	43.9 ± 16.3	<0.0001
LDL-C (mg/dl)	122.5 ± 39.1	135.7 ± 34.7	0.053
Triglyceride (mg/dl)	117.3 ± 76.1	160.7 ± 82.3	0.003

CAD – coronary artery disease; n – number of subjects; F – female; M – male; HDL-C – high-density lipoprotein-cholesterol; LDL-C – low density lipoprotein-cholesterol; TG – triglyceride. Data are represented as mean ± standard deviation (SD).

Table 2 – Genotype distributions and allele frequencies for the *ITGB3* rs5918 T>C and *APOA1* rs1799837 C>T among the studied groups

Genotype	Groups		Genotype	Groups	
	Control	CAD		Control	CAD
ITGB3 rs5918 T>C	(N: 250)	(N: 100)	APOA1 rs1799837 C>T	(N: 250)	(N:100)
TT	190	64	**CC**	150	63
TC	52	25	**CT**	91	29
CC	8	11	**TT**	9	8
X2	3.3	9.2	**X2**	1.14	
***p*-value**	0.69	0.002	***p*-value**	0.285	
T allele	432	153	**C allele**	391	155
C allele	68	47	**T allele**	109	45
T allele frequency	0.86	0.76	**C allele frequency**	0.78	0.78
C allele frequency	0.14	0.24	**T allele frequency**	0.22	0.22
***p* value**	0.001		***p* value**	0.839	
OR	1.951		**OR**	1.041	
95% CI	1.288-2.955		**95% CI**	0.702-1.544	

CAD – coronary artery disease; CI – confidence interval; N – number of subjects; OR – odds ratio; χ^2– Chi square; p <0.05, reaches statistical significance.

Table 3 – Comparisons of ITGB3 rs5918 T>C and APOA1 rs1799837 C>T polymorphisms with clinical parameters within both studied groups

Clinical parameters	rs5918			ANOVA *p*-value	rs1799837			ANOVA *p*-value
Control	TT	TC	CC		CC	CT	TT	
Glucose (mg/dL)	89.1 ± 5.8	96.1 ± 25.0	99.1 ± 17.8	0.664	93.9 ± 57.0	98.3 ± 33.3	88.1 ± 50.2	0.479
Cholestrol (mg/dL)	199.0 ± 36.6	202.7 ± 46.3	207.8 ± 42.3	0.878	194.7 ± 47.5	203.4 ± 45.0	213.6 ± 32.5	0.465
HDL-C (mg/dL)	55.6 ± 11.0	53.1 ± 12.8	49.0 ± 9.6	0.339	39.9 ± 13.3	49.6 ± 21.0	42.0 ± 6.5	0.295
LDL-C (mg/dL)	120.0 ± 29.3	131.6 ± 31.9	132.3 ± 37.1	0.719	125.2 ± 42.1	125.3 ± 40.2	102 ± 38.0	0.648
Triglyceride (mg/dL)	101.3 ± 37.0	125.5 ± 100.0	153.1 ± 155.5	0.503	173.6 ± 87.0	155.1 ± 78.8	149.0 ± 102.5	0.780
Clinical parameters				**ANOVA *p*-value**				**ANOVA *p*-value**
CAD	TT	TC	CC		CC	CT	TT	
Glucose (mg/dL)	124.7 ± 38.4	164.4 ± 87.1	103.3 ± 29.7	0.138	128.8 ± 57.0	120.9 ± 33.3	135.3 ± 50.2	0.844
Cholestrol (mg/dL)	165.0 ± 15.2	190.4 ± 44.6	267.6 ± 66.1	**0.0006**	188.0 ± 43.6	196.7 ± 47.5	153.6 ± 51.0	0.344
HDL-C (mg/dL)	38.5 ± 11.7	42.9 ± 16.8	66.5 ± 9.9	**0.016**	53.9 ± 13.7	51.6 ± 12.4	55.3 ± 12.1	0.607
LDL-C (mg/dL)	123.2 ± 40.7	105.2 ± 14.1	154.6 ± 53.0	0.184	124.1 ± 37.9	131.8 ± 36.6	145.0 ± 32.2	0.314
Triglyceride (mg/dL)	150.0 ± 85.5	166.0 ± 85.0	175.5 ± 30.4	0.887	106.3 ± 43.7	149.2 ± 164.1	81.7 ± 22.3	0.098

CAD – coronary artery disease; HDL-C – high-density lipoprotein-cholesterol;; LDL-C – low-density lipoprotein-cholesterol. Values are represented as mean ± standard deviation. *p <0.05, reaches to statistical significance.

of total cholesterol (TC), and the serum concentration of triglycerides (TG) were significantly higher in the CAD group compared to those in the control group (p <0.001, p = 0.001, p = 0.003, respectively). Additionally, the serum concentrations of high-density lipoprotein-cholesterol (HDL-C) was significantly lower in the CAD group compared to those in the control group (p <0.001).

Genotype and allele distributions of the ITGB3 *and* APOA1 *gene polymorphisms in the studied groups*

The allele and genotype frequency distributions of *ITGB3* rs5918 T>C and *APOA1* rs1799837 C>T gene polymorphisms among the control and CAD group are demonstrated in **Table 2**. Regarding the genotype and allele distributi-

ons of *ITGB3* rs5918 T>C, the results showed statistically significant in the CAD patients ($\chi^2 = 9.2$, $p = 0.002$) and not significant ($\chi^2 = 3.3$, $p = 0.69$) in the control group. Therefore, determining CAD risk factors, C allele was more frequent in CAD group compared to the control group ($p = 0.001$, odd ratio [OR] = 1,951, 95% CI = 1.288–2.955). However, in *APOA1* rs1799837 C>T, the allele frequency was equal for C allele and G allele in control group and CAD group ($p = 0.839$, OR = 1,041, 95%CI 0.702–1.544).

Comparison of ITGB3 *and* APOA1 *gene polymorphisms with clinical parameters within both studied groups*

The distribution of all biochemical parameters according to the *ITGB3* and *APOA1* genotypes among the control group and CAD group are shown in **Table 3**.

ANOVA standard weighted-means analysis for independent samples (df:2) was performed to determine the association between *ITGB3* rs5918 T>C and *APOA1* rs1799837 C>T polymorphisms and biochemical parameters. Data are expressed as mean ± standard deviation (SD). According to the analysis, *ITGB3* rs5918 T>C variant showed significant association in serum total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) values in CAD group. Importantly, the statistically significant association has been observed between *ITGB3* rs5918 CC genotype and serum total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) ($p = 0.0006$, $p = 0.016$, respectively). On the other hand, no statistically significant association was found between the *APOA1* rs1799837 C>T SNP and biochemical parameters in control and CAD group.

Discussion

Among the group of cardiovascular diseases, coronary artery disease (CAD) is the most commonly observed cardiovascular disease all around the World.[17] While gender, age, family history, diabetes mellitus, sedentary lifestyle, hypertension, stress, obesity, smoking, and dyslipidemia are known as some of the important risk factors for CAD,[1,6] the most common etiological factor of coronary artery disease is atherosclerosis.[18] In addition to these, a number of polymorphisms on several genes have been previously shown to play a critical role in serum lipid concentrations.[19] This particular study was focused on evaluating the association of the *ITGB3* rs5918 T>C and the *APOA1* rs1799837 C>T gene polymorphisms with serum lipid metabolism in cardiovascular patients in Turkish Cypriot population. To our knowledge, this is the first study investigating the effect of *ITGB3* rs5918 T>C and *APOA1* rs1799837 C>T polymorphisms in Turkish Cypriot population which will also offer valuable insights to understand the susceptibility of the Turkish Cypriot population to diseases such as cardiovascular conditions, dyslipidemia and hypercholesterolemia.

So far, several variants of the *ITGB3* gene have been identified.[6] In the current study, the allele and genotype frequencies of the *ITGB3* rs5918 T>C polymorphism were determined in a group of patients with CAD and control group. Minor Allele Frequency (MAF) was higher (MAF: 0.24 C) when compared with European and global MAF (EUR MAF: 0.13 C; global MAF: 0.09) (Ensembl Genome Browser (http://www.ensembl.org). Earlier studies including Egyptian population pinpointed that the *ITGB3* rs5918 T>C variant has a strong association with the etiology of CAD.[2] In contrast, it has been indicated that the carriage of the *ITGB3* rs5918 T>C polymorphism is not a major risk factor for the development of myocardial infarction in Iranian patients with premature CAD.[20] Furthermore, it has been found that there is a strong association between the *ITGB3* rs5918 T>C with triglycerides in non-Hispanic blacks who are one of the major ethnic groups in the US population.[3]

In another study, the researchers investigated the association between the PlA2 (C) allele and acute coronary syndrome (ACS) in a case control study of 71 Caucasians patients with a diagnosis of MI or unstable angina. It has been documented that the PlA2 (C) allele was overexpressed in patients with CAD compared to 68 healthy controls (39.4% versus 19.10%; $p = 0.01$, respectively).[21] Considerably, in our study, the frequency of the C allele was more frequent in CAD group compared to the control group ($p = 0.001$) and a significant association has been observed between *ITGB3* rs5918 CC genotype and serum total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) ($p = 0.0006$, $p = 0.016$, respectively).

More importantly, as it is known *ITGB3* is a membrane receptor for fibrinogen and von-Willebrand factor which has a critical role in platelet aggregation.[22] Although newer antiplatelet drugs were developed, acetylsalicylic acid is still one of the most commonly used antiplatelet agent all around the world to prevent thrombotic events in patients with cardiovascular diseases.[4] However, many patients have had adverse situations in spite of acetylsalicylic acid intake which is also known as "aspirin resistance" (AR), the AR term indicates that a mechanistic reason limits acetylsalicylic acid's efficiency.[23]

There is limited evidence for the biological reasons that explain the anti-platelet effect of acetylsalicylic acid in patients, the mechanisms involved in AR are likely to be multifactorial.[24] For instance, diabetes mellitus, hyperlipidemia, severe unstable angina, heart failure, and obesity are some of the risk factors associated with increased lipid peroxidation and overproduction of isoprostanes which may lead to the development of AR.[24] Additionally, by understanding the role of genetic variation or polymorphisms in drug response can be useful to discover if an individual will develop an altered clinical effect.[25]

Undas et al.[26] suggested that individuals homozygous for the *ITGB3* rs5918 CC genotype have a higher risk of developing myocardial infarction (MI) and aspirin resistance. Therefore, testing for genetic polymorphisms before prescribing drug therapy could be a valuable strategy to identify additional risk factors. Screening patients with cardiovascular disease for antiplatelet polymorphisms may help optimize treatment options and improve outcomes.[21]

Similarly, the allele and genotype frequencies of the *APOA1* rs1799837 C>T polymorphism were analyzed in a cohort of patients with coronary artery disease (CAD) and a control group. Although *APOA1* polymorphisms have been widely studied in various diseases, their as-

sociation with cardiovascular diseases remains controversial. Liao et al.[27] reported that individuals carrying the *APOA1*-75 T allele had a lower risk of developing CAD, as this variation was significantly associated with increased serum HDL-C levels in a Chinese Han population (p <0.001). In contrast, Wang et al. (2017) found no significant association between the *APOA1* rs1799837 C>T polymorphism and HDL-C levels in a study involving interactions between *APOA1* single nucleotide polymorphisms (SNPs) and obesity subtypes in the Chinese population.

Moreover, Villard et al.[9] explored the impact of genetic variants involved in the biogenesis, maturation, and intravascular remodeling of high-density lipoprotein (HDL) particles on plasma efflux capacity. Their study also found no significant association between the *APOA1* rs1799837 C>T variant and plasma HDL-C levels. In line with these findings, our current study did not observe a significant association between the *APOA1* rs1799837 C>T polymorphism and serum lipid concentrations.

Limitations

This study has several limitations. Firstly, it is volunteer--based, and the sample size is relatively small. Secondly, CAD is a multifactorial disease involving various genetic and environmental influences, which makes identifying significant associations between candidate genes and disease risk more challenging. Thirdly, considering the unique and underexplored genetic profile of the Turkish Cypriot population, these polymorphisms might exhibit different effects on plasma lipid levels compared to other populations. Nonetheless, despite the small sample size, our study adds important preliminary data to the literature. For instance, the *ITGB3* gene rs5918 C allele could serve as a useful screening marker for Turkish Cypriots during routine medical check-ups, enabling personalized lifestyle modifications based on genetic susceptibility.

Furthermore, the absence of comprehensive polymorphic data for many genes in the Turkish Cypriot population underscores the need for additional studies. Future research should focus on larger cohorts and incorporate more detailed biochemical and genetic analyses to strengthen the findings and explore additional candidate gene associations.

Conclusion

Overall, our study highlights the potential role of the *ITGB3* rs5918 T>C and *APOA1* rs1799837 C>T polymorphisms in determining serum lipid concentrations. Notably, individuals with the *ITGB3* rs5918 CC genotype exhibited higher total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) levels. These findings suggest that the *ITGB3* rs5918 T>C variant may contribute to an increased susceptibility to CAD, providing insights for further investigation in diverse genetic populations.

Conflict of interest

The authors declare no conflict of interest.

Funding

None.

References

1. Shabana NA, Ashiq S, Ijaz A, et al. Genetic risk score (GRS) constructed from and ALDH2 genes is associated with the risk of coronary artery disease in Pakistani subjects. Lipids Health Dis 2018;17:224.
2. Fawzy MS, Toraih EA, Aly NM, Fakhr-Eldeen A, Badran DI, Hussein MH. Atherosclerotic and thrombotic genetic and environmental determinants in Egyptian coronary artery disease patients : a pilot study. BMC Cardiovasc Disord. 2017 Jan 13;17(1):26.
3. Chang MH, Yesupriya A, Ned RM, Mueller PW, Dowling NF. Genetic variants associated with fasting blood lipids in the U.S. population: Third National Health and Nutrition Examination Survey. BMC Med Genet. 2010 Apr 20;11:62.
4. Rai H, Sinha N, Finn J, Agrawal S, Mastana S. Association of serum lipids and coronary artery disease with polymorphisms in the apolipoprotein AI-CIII-AIV gene cluster. Cogent Med. 2016 Dec 31;3(1):1266789.
5. Komsa-Penkova R, Golemanov G, Tsankov B, Ivanov P, Beshev L, Tonchev P. Rs5918ITGB3 Polymorphism, Smoking, and BMI as Risk Factors for Early Onset and Recurrence of DVT in Young Women. Clin Appl Thromb Hemost. 2017 Sep;23(6):585-595.
6. Khatami M, Heidari MM, Soheilyfar S. Common rs5918 (PlA1/A2) polymorphism in the ITGB3 gene and risk of coronary artery disease. Arch Med Sci Atheroscler Dis. 2016 Apr 27;1(1):e9-e15.
7. Bridge KI, Philippou H, Ariëns RAS. Clot properties and cardiovascular disease. Thromb Haemost. 2014 June;112(11):901–908.
8. Wang F, Ji Y, Chen X, Song Y, Huang S, Zhou C, et al. ABCA1 variants rs2230806 (R219K), rs4149313 (M8831I), and rs9282541 (R230C) are associated with susceptibility to coronary heart disease. J Clin Lab Anal. 2019 Jul;33(6):e22896.
9. Villard EF, El Khoury P, Frisdal E, Bruckert E, Clement K, Bonnefont-Rousselot D, et al. Translational Science Genetic Determination of Plasma Cholesterol Efflux Capacity Is Gender-Specific and Independent of HDL-Cholesterol Levels. Arterioscler Thromb Vasc Biol. 2013 Apr;33(4):822-8.
10. Fahrioğlu U, Ergören MÇ. The Association Between APOA5 Gene Polymorphisms and Plasma Lipids in the Turkish Cypriot Population: A Possible Biomarker for Preventing Cardiovascular Diseases. Biochem Genet. 2018 Jun;56(3):176-187.
11. Ergoren MC, Turkgenc B, Teralı K, Rodoplu O, Verstraeten A, Van Laer L, et al. Identification and characterization of a novel FBN1 gene variant in an extended family with variable clinical phenotype of Marfan syndrome. Connect Tissue Res. 2019 Mar;60(2):146-154.
12. Temel SM, Ergören MC. The association between the chromosome 9p21 CDKN2B-AS1 gene variants and the lipid metabolism: A pre-diagnostic biomarker for coronary artery disease. Anatol J Cardiol. 2019 Jan; 21(1): 31–38. Published online 2018 Dec 7.
13. Temel SG, Ergoren MC, Yilmaz I, Oral HB. The use of ACE INDEL polymorphism as a biomarker of coronary artery disease (CAD) in humans with Mediterranean-style diet. Int J Biol Macromol. 2019 Feb 15;123:576-580.
14. Conkbayir C, Fahrioglu Yamaci R, Gencer P, Barin B, Yucel G, Yildiz CE, et al. Impact of genetic defects on coronary atherosclerosis among Turkish Cypriots. Heart Surg Forum. 2017 Oct 30;20(5):E223-E229.
15. Martínez-Quintana E, Chirino R, Nieto-Lago V, Pérez-Jiménez P, López-Ríos L, Rodríguez-González F. Prognostic value of ACE I/D, AT1R A1166C, PAI-I 4G/5G and GPIIIa a1/a2 polymorphisms in myocardial infarction. Cardiol J. 2014;21(3):229-37.
16. Yin RX, Li YY, Lai CQ. Apolipoprotein A1/C3/A5 haplotypes and serum lipid levels. Lipids Health Dis. 2011 Aug 19;10:140.
17. Khera AV, Kathiresan S. Genetics of coronary artery disease: discovery, biology and clinical translation. Nat Rev Genet. 2017 Jun;18(6):331-344.

18. Önalan MA, Bahşeliyev Ş, Beyaz MO, Öztaş DM, Önal Y, Uğurlucan M, Tireli E. Karotis endarterektomi operasyonu geçiren hastalarda alt ekstremite periferik arter hastalığı sıklığının belirlenmesi. İst Tıp Fak Derg 83 (1), 40-41 .
19. Tada H, Nohara A, Kawashiri M. Serum triglycerides and atherosclerotic cardiovascular disease: Insights from clinical and genetic studies. Nutrients. 2018 Nov; 10(11): 1789. Published online 2018 Nov 17.
20. Sheikhvatan M, Boroumand MA, Behmanesh M, Ziaee S, Cheraghee S. Integrin Beta-3 Gene Polymorphism and Risk for Myocardial Infarction in Premature Coronary Disease. Iran J Biotechnol. 2019 Apr; 17(2): e1921. Published online 2019 Apr 20.
21. Gandhi PJ, Cambria-Kiely JA. Aspirin resistance and genetic polymorphisms. J Thromb Thrombolys. 2002 Sep; 14(1):51–58.
22. Verdoia M, Cassetti E, Schaffer A, Barbieri L, Giovine GD, Nardin M, et al. Relationship between glycoprotein IIIa platelet receptor gene polymorphism and coronary artery disease. Angiology. 2015 Jan;66(1):79-85.
23. Kenneth A. Schwartz. Aspirin Resistance: A Clinical Review Focused on the Most Common Cause, Noncompliance. Neurohospitalist 2011;1:94–103.
24. Chadha DS, Sumana B, Karthikeyan G, Jayaprasad V, Arun SS. Prevalence of aspirin resistance in Asian-Indian patients with stable coronary artery disease. Catheter Cardiovasc Interv 2016;88:E126–E131.
25. Knowles JW, Wang H, Itakura H, et al. Association of polymorphisms in platelet and hemostasis system genes with acute myocardial infarction. Am Heart J 2007;154:1052–1058.
26. Undas A, Brummel K, Musial J, et al. Pl(A2) polymorphism of beta(3) integrins is associated with enhanced thrombin generation and impaired antithrombotic action of aspirin at the site of microvascular injury. Circulation 20017;104:2666–2672.
27. Liao B, Cheng K, Dong S, et al. Effect of apolipoprotein A1 genetic polymorphisms on lipid profiles and the risk of coronary artery disease. Diagn Pathol. 2015;16:102.

Původní sdělení | Original research article

Efficacy of Left Atrial Radiofrequency Surgical Ablation in Patients with Atrial Fibrillation and Concomitant Cardiac Surgical Pathology

Olha Shepetko-Dombrovska[a], Serhii Varbanets[a], Pavlo Shepetko-Dombrovskyi[a], Ivanna Zubovych[b], Nadiya Rudenko[c]

[a] *Department of Adult Cardiac Surgery, Clinic for Adults, Scientific-Practical Medical Center for Pediatric Cardiology and Cardiac Surgery, Kyiv, Ukraine*
[b] *Department of Cardiometabolic Diseases, Clinic for Adults, Scientific-Practical Medical Center for Pediatric Cardiology and Cardiac Surgery, Kyiv, Ukraine*
[c] *Department of Children's Cardiology and Cardiac Surgery, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine*

ARTICLE INFO

Article history:
Submitted: 29. 11. 2024
Revised: 6. 1. 2025
Accepted: 14. 1. 2025
Available online: 17. 6. 2025

Klíčová slova:
Hybridní techniky
Kardiovaskulární choroby
Operace Cox-Maze IV
Srdeční arytmie
Torakoskopický přístup

SOUHRN

Cíl: Cílem studie bylo zjistit proveditelnost chirurgické ablace levé síně u pacientů s fibrilací síní a souběžnými kardiovaskulárními onemocněními.
Soubor a metodika: Experiment byl proveden ve Vědecko-praktickém lékařském centru dětské kardiologie a kardiochirurgie, Klinika pro dospělé (Kyjev, Ukrajina, 2024). Studie se zúčastnilo celkem 69 pacientů, kteří podstoupili chirurgickou léčbu fibrilace síní a souběžných kardiovaskulárních onemocnění.
Výsledky: Bylo zjištěno, že po provedení chirurgické ablace levé síně zaměřené na ložisko fibrilace síní byl sinusový uzel hlavním rytmogenerátorem u 45 pacientů (65 % z celkového počtu). U 18 pacientů (26 %) přetrvávaly poruchy rytmu ve formě fibrilace síní, 4 pacienti (6 %) měli síňový flutter a u 2 pacientů (3 %) byl diagnostikován flutter levé síně. Mezi účastníky studie mělo téměř 61 % (42 pacientů) dlouhotrvající formu fibrilace síní a průměrnou velikost levé síně 5,2 ± 0,6 cm, což významně zhoršovalo výsledky chirurgické léčby. Účinnost radiofrekvenční ablace byla nižší u pacientů s tradičními prediktory neúspěchu, konkrétně u pacientů starších 70 let, s velikostí levé síně 5 cm nebo více, s fibrilací síní trvající déle než pět let a u pacientů s perzistující a dlouhotrvající fibrilací síní.
Závěr: Studie dospěla k závěru, že samotná radiofrekvenční ablace levé síně byla podmíněně úspěšná u pacientů s kratší dobou trvání fibrilace síní a menší velikostí levé síně.

ABSTRACT

Aim: The aim of the study was to determine the feasibility of left atrial surgical ablation in patients with atrial fibrillation and concomitant cardiovascular diseases.
Methods: The experiment was conducted at the Scientific and Practical Medical Centre of Paediatric Cardiology and Cardiac Surgery, Adult Clinic (Kyiv, Ukraine, 2024). A total of 69 patients who underwent surgical treatment for atrial fibrillation and concomitant cardiovascular disease took part in the study.
Results: It was found that after the procedure of left atrial surgical ablation of the atrial fibrillation focus, the sinus node was the rhythm driver in 45 patients (65% of all). In 18 patients (26%), rhythm disturbances remained in the form of atrial fibrillation, 4 patients (6%) had atrial flutter, and 2 patients (3%) had left atrial flutter. Among the study participants, almost 61% (42 patients) had a long-standing form of atrial fibrillation and an average left atrial size of 5.2 ± 0.6 cm, which significantly worsened the results of surgical treatment. The efficacy of radiofrequency ablation was lower in patients with traditional predictors of failure, namely, patients over 70 years of age, left atrial size of 5 cm or more, atrial fibrillation duration of more than 5 years, and persistent and long-standing atrial fibrillation.
Conclusions: The study concluded that radiofrequency ablation of the left atrium alone was conditionally successful in patients with shorter duration of atrial fibrillation and smaller left atrial size.

Keywords:
Cardiac arrhythmias
Cardiovascular diseases
Thoracoscopic access
Hybrid techniques
Cox-Maze IV surgery

Address: Olha Shepetko-Dombrovska, MD, Department of Adult Cardiac Surgery, Clinic for Adults, Scientific-Practical Medical Center for Pediatric Cardiology and Cardiac Surgery 04050, 24 Yuriy Illienko Str., Kyiv, Ukraine, e-mail: shepetk.olha@gmail.com
DOI: 10.33678/cor.2025.007

Please cite this article as: Shepetko-Dombrovska O, Varbanets S, Shepetko-Dombrovskyi P, et al. Efficacy of Left Atrial Radiofrequency Surgical Ablation in Patients with Atrial Fibrillation and Concomitant Cardiac Surgical Pathology. Cor Vasa 2025;67:367–375.

Introduction

Atrial fibrillation (AF) is a common cardiac rhythm disorder diagnosed in 33.5 million people worldwide.[1] In the population of European countries, this pathology occurs with a frequency of 3% starting from the age of 20. It affects mainly Caucasian men.[2] In Asians, the prevalence of AF is less than 1%. At the same time, Sagris et al.[1] note that in 10 years, the prevalence of atrial fibrillation among European residents will double. Aldaas et al.[2] and Al-Ezzi et al.[3] found that the risk factors for AF are hypertension, obesity, coronary heart disease, and smoking. Predictors of the progression of persistent atrial fibrillation in patients awaiting ablation are: hypertension, advanced age, and ischaemic attacks. This cardiac rhythm disorder can be a complication of any pathology of the valvular heart apparatus. For example, AF is most commonly diagnosed in patients with mitral valve damage due to rheumatic diseases. In people with mild to moderate aortic stenosis, the prevalence of AF is 10%, and in severe stenosis – 33.7%. In isolated mitral insufficiency, AF is detected in 15% of cases; in isolated mitral stenosis – in 29% of cases; in a combination of stenosis and regurgitation – in 52%. The incidence of atrial fibrillation is 65–75% in the case of a combination of mitral and tricuspid valve pathology.[2]

Ren et al.[4] and Volgman et al.[5] note that patients with AF have a fourfold higher risk of stroke and heart attack. AF also increases the risk of cognitive impairment and anxiety. Scientists Ferro et al.,[6] Cheng et al.,[7] and Skybchyk et al.[8] note that AF mainly affects people aged 70–80 years, with a frequency of 10–20%. From 2010 to 2020, many studies were conducted to investigate the features of atrial fibrillation and the effects of ablation in AF in the elderly. At the same time, more attention should be paid to strategies for developing effective treatments and prevention of AF in younger people. Leszto et al.[9] studied the relationship between the type of diet and the effectiveness of prevention and treatment of atrial fibrillation; the possibilities of non-drug treatment of cardiac pathology were assessed.

Since 2000, catheter-based and surgical ablation for AF has transitioned from primarily diagnostic measures to well-established therapeutic interventions for managing heart disease. Surgical ablation techniques have diversified, encompassing standard, minimally invasive, and hybrid approaches. Among these, radiofrequency ablation has demonstrated considerable success, particularly in enhancing patients' quality of life and postoperative survival.[10,11] Transcatheter radiofrequency ablation has proven effective in reducing recurrence rates, especially in symptomatic AF. However, selecting the optimal therapeutic approach remains a significant challenge, as the severity and progression of AF are closely influenced by various comorbidities. For instance, Peigh et al.[12] note that permanent AF is associated with a significantly higher risk of thromboembolism and mortality compared to paroxysmal AF. Additionally, paroxysmal AF has been linked to a higher prevalence of depressive disorders, further emphasizing the complex interplay between AF types and patient well-being.[4]

However, the exact mechanism of psychological disorders in cardiac pathology is still under investigation. Thus, there are currently many controversial issues when choosing the optimal type of surgery, access, indications, and contraindications for atrial fibrillation. The aim of the present study was to evaluate the effectiveness of left atrial surgical ablation of atrial fibrillation in patients with concomitant cardiac surgery pathology. The following objectives were set: determining the prevalence of atrial fibrillation, its types and mechanisms of development; analysing the risk factors for AF and ways to prevent this pathology; studying the types of possible surgical interventions for AF; investigating the predictors of surgical ablation failure in AF.

Materials and methods

The present open-label retrospective study was conducted in 2024 at the Scientific and Practical Medical Centre for Paediatric Cardiology and Cardiac Surgery, Clinic for Adults, Ministry of Health of Ukraine, Kyiv. The trial involved 69 patients who underwent surgical treatment for atrial fibrillation and related pathology. **Table 1** shows the main clinical and morphological characteristics of the patients who participated in the study. Thirty-seven patients were male and 32 were female, which made up 54% and 46%, respectively. The average age of the study group was 63 years. Among the parameters of transthoracic echocardiography, the mean ejection fraction and left atrial dimensions were evaluated. The diameter of the left atrium (2D-guided linear LA measurement) was determined by cardiac ultrasound. Taking into account the patients' symptoms and objective examination data, patients with heart failure were classified according to *the New York Heart Association* (NYHA) scale. Thirty-four (49%) patients had severe symptoms of heart failure, so they were classified as NYHA class III.

The analysis was conducted using SPSS version 27.0 (IBM Corp., Armonk, NY, USA), ensuring accurate statistical computations and enhancing the reproducibility of the study. Continuous variables, such as left atrial diameter and ejection fraction, were analysed using Student's t-test, while categorical variables, including NYHA class and severe heart failure symptoms, were analysed using chi-square tests. Logistic regression was employed to assess associations between clinical variables (e.g., left atrial size, NYHA class) and treatment outcomes, accounting for confounders. Transthoracic echocardiography was performed using a GE Vivid E95 system with a 4Vc-D

Table 1 – Patient characteristics

Indicator		Data
Age, years		63 ± 9
Gender	women (%)	37 (53%)
	men (%)	32 (47%)
Dimensions of the left atrium, mm		52 ± 6
Ejection fraction, %		51 ± 8.4%
Cross-clamp time, min		138 ± 43 min
HF according to NYHA III		34 (49%)

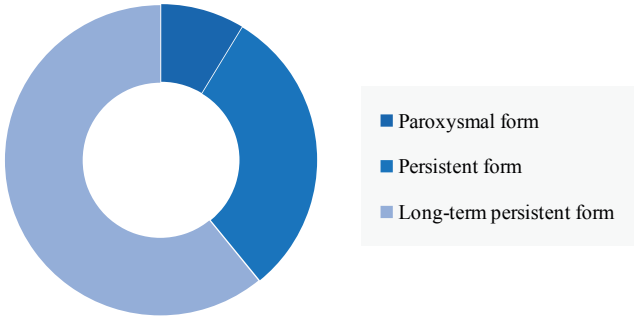


Fig. 1 – Percentage of patients according to the form of atrial fibrillation.

transducer, measuring left atrial diameter (via 2D-guided linear LA measurement) and ejection fraction. Heart failure symptoms were classified using the NYHA functional scale based on clinical evaluation. Outcomes included sinus rhythm restoration, NYHA class improvement, and recurrence rates of atrial fibrillation or flutter. These were assessed during follow-up visits at 1-, 3-, and 6-months post-surgery, ensuring a comprehensive evaluation of treatment effectiveness.

Figure 1 shows the breakdown of patients by arrhythmia type before the surgical ablation procedure. Among all patients, 6 had paroxysmal atrial fibrillation, 21 had persistent atrial fibrillation, and 42 had long-standing atrial fibrillation.

The inclusion criteria for the study required patients to have a confirmed diagnosis of atrial fibrillation (paroxysmal, persistent, or long-standing), be classified as NYHA functional class I–III (mild to moderate symptoms of heart failure without severe limitations on physical activity), demonstrate clear consciousness as assessed using the Glasgow Coma Scale with a minimum score of 15 (indicating full alertness and orientation), and provide voluntary informed consent to participate. Exclusion criteria encompassed the presence of decompensated neurological or cognitive disorders, defined as conditions causing significant functional impairment such as advanced dementia or uncontrolled epilepsy. Psychiatric illnesses diagnosed by a specialist, uncontrolled pathological conditions such as severe infections or metabolic disorders, NYHA class IV heart failure, or stage 3 heart failure (indicating severe functional limitation and end-stage disease) also led to exclusion from the study.

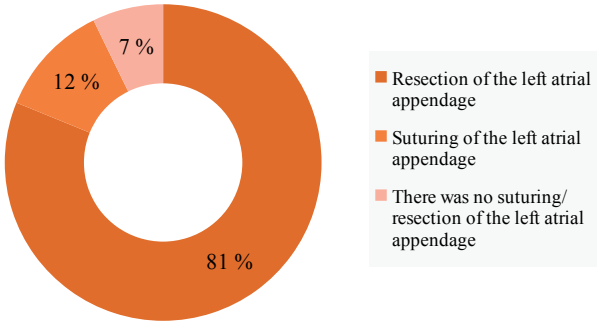


Fig. 2 – Percentage of left atrial annulus interventions.

Table 2 – Surgeries in conjunction with which left atrial surgical ablation of atrial fibrillation was performed

Operations	No. of procedures	Percentage, %
Mitral valve procedure (± tricuspid procedure)	34	49.3
CABG + mitral valve procedure (± tricuspide procedure)	16	23.3
Aortic valve procedure and mitral valve procedure (± tricuspid procedure)	12	17.4
CABG	1	1.4
CHD (cor triatriatum)	1	1.4
Aortic valve procedure (± tricuspid procedure)	3	4.3
ASD repair (± tricuspid procedure)	2	2.9
Total	69	100

All patients underwent left atrial radiofrequency surgical ablation of atrial fibrillation and concomitant operations, depending on the type of concomitant pathology, under general anaesthesia and with a cardiopulmonary bypass. The average time of surgery was 4.5 hours. **Table 2** shows the distribution of patients into groups according to the type of surgical treatment.

In the course of surgical interventions, the left atrial appendage was resected or sutured (**Fig. 2**).

Prior to the study, all patients signed a voluntary informed consent to surgery and the processing of their personal data for participation in the study.

In order to study the risk factors for AF, its prevalence, mechanisms of development and treatment methods, a search for relevant information in PubMed and Google Scholar databases published in 2018-2024 was conducted. A combined set of keywords was used: "atrial fibrillation", "surgical ablation", "radiofrequency ablation", "left atrial ablation". The received publications were carefully studied and selected by title, abstract, relevance of the topic and appropriate level of evidence for case studies. The present study includes papers that fully met the selected criteria. In total, 30 papers are cited in the presented research.

Results

Results of the surgical intervention

All patients underwent left atrial radiofrequency surgical ablation of atrial fibrillation, surgical treatment of coronary heart disease, and valve pathology. The choice of surgical intervention depended on the presence of concomitant pathologies, complications, and the age of the patients. The study revealed that after the left atrial radiofrequency surgical ablation of atrial fibrillation, 45 patients (65% of all patients) had a sinus node as the rhythm driver (**Fig. 3**). Rhythm disturbance in the form of atrial fibrillation remained in 18 patients, atrial flutter was observed in 4 patients, and left atrial flutter was observed in 2 patients.

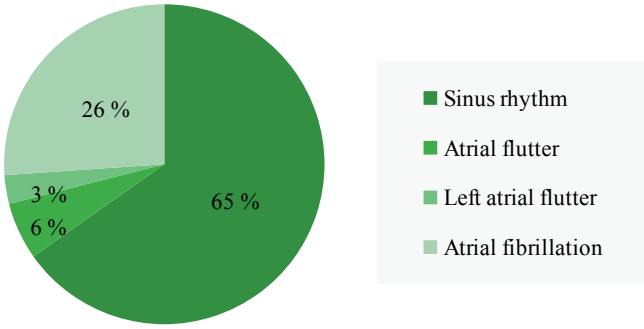


Fig. 3 – Percentage distribution of left atrial surgical ablation results.

After analysing the data obtained, it was concluded that radiofrequency ablation of the left atrium alone was conditionally successful, primarily in patients with shorter AF duration and smaller left atrial size. At the same time, the effectiveness of radiofrequency ablation was lower in patients with traditional predictors of failure, namely, age 75 years or older, left atrial size of 5 cm or more, atrial fibrillation duration of more than 5 years, and non-paroxysmal AF. Among the study participants, almost 61% (42 patients) had long-standing atrial fibrillation and a mean left atrial size of 5.2 ± 0.6 cm, which significantly worsened the results of surgical treatment. Therefore, for patients with traditional predictors of surgical ablation failure, it is necessary to implement the classical Cox-Maze IV procedure and cryoablation as an independent technique.

Atrial fibrillation: aetiology, mechanism of development, and classification

Atrial fibrillation is a supraventricular tachyarrhythmia based on discoordinated electrical activation of the atria and impaired contractile function of the heart. On an electrocardiogram, this pathology is manifested by irregular RR intervals, the absence of clear repeated P waves and irregular atrial activation. The main risk factors (RF) that cannot be influenced include: old age, male gender, and Caucasian race. At the same time there are many more factors that depend on the individual: physical activity level, weight control, diabetes mellitus, high blood pressure.

Age is a major risk factor for AF.[13] This is because people over 65–70 years of age have chronic subclinical inflammation, increased reactive oxygen species concentration, endothelial dysfunction, increased collagen breakdown, and vascular ageing at all levels. A quarter of AF cases is associated with high blood pressure. This is due to the fact that chronically high blood pressure causes the left atrium (LA) and left ventricle (LV) to be restructured, and contributes to profibrotic changes in the heart. The risk of developing AF among people with obstructive sleep apnoea increases fourfold.[14] This is due to the repeated cessation of ventilation caused by the collapse of the upper airway, which leads to hypoxia, increased intrathoracic pressure, hyperactivity of the autonomic nervous system of the heart, systemic inflammation, and oxidative stress.

Atrial stretch caused by fluctuations in negative chest pressure during apnoea, which contributes to further chronic structural remodelling, as well as acute dysregulation of calcium handling and electrical function. Type 2 diabetes mellitus is associated with a one-and-a-half-fold increase in the risk of AF. In this disease, oxidative stress and inflammation are the main factors of mitochondrial dysfunction and DNA damage, which creates the basis for the formation of AF. Obesity causes electroanatomical remodelling, increases neurohormonal activation, which modulates LA enlargement, and electrical instability; in obesity, the thickness of epicardial fat increases, which worsens atrial electrophysiology. A number of comorbidities also increase the risk of AF. For example, in patients with HF, the development of AF is 4–6 times higher; albuminuria, mild renal impairment, and reduced renal function are associated with a higher incidence of AF (with an GFR <30 ml/min/1,73 m^2, the risk was 60% higher).

One of the main mechanisms of AF development is fibrosis, due to its ability to electrically and structurally remodel heart muscle tissue.[15] Fibrosis is divided into: reparative fibrosis (replacement of necrotic cells) and interstitial fibrosis (excessive deposition of pathological proteins without the need to replace damaged cells). These changes are based on the excessive accumulation of extracellular matrix proteins in the interstitium of the inner layer of the heart due to a significant proliferation of fibroblasts in response to pathology. Under normal conditions, fibroblasts are responsible for maintaining the normal structure of the heart.[16] With the development of the fibrosis process, fibroblasts turn into myofibroblasts, which contribute to a decrease in myocardial conduction and arrhythmogenic effect.[2] This is due to the fact that an increase in the number of myofibroblasts disrupts the continuity of myocardial bundles and makes it impossible to form gap junctions between cardiomyocytes. Consequently, conduction abnormalities and the formation of unidirectional conduction blocks occur.

The inflammatory process is also a link in the pathogenesis of AF. C-reactive protein levels are associated with recurrence after cardioversion, while the restoration of sinus rhythm contributed to a decrease in this marker. During inflammation, angiotensin II promotes the formation of proinflammatory cytokines and causes cardiac tissue remodelling through the activation of MAPK mediators AngII/AT1R and the subsequent expression of profibrotic TGFβ1, which promotes fibroblast differentiation. The effect of angiotensin II is associated with impaired calcium handling and subsequent electrical remodelling of the atria.[17,18]

Atrial fibrillation is classified into:

1. Paroxysmal form (episodes stop within a week as a result of treatment or on their own, with attacks recurring with an uncertain frequency).
2. Persistent form (in the presence of continuous episodes lasting more than a week that do not stop).
3. Long-term persistent form (continuous episodes lasting more than a year).
4. Permanent form (continuous episodes, with no attempts to restore or maintain normal sinus rhythm).

5. Non-valvular form (symptoms occur in the absence of rheumatic heart disease or an artificial heart valve).[18,19]

Non-invasive diagnostic methods for predicting af recurrence after surgical ablation

Echocardiography is a non-invasive, painless, fast, and affordable examination method. This method allows determining the diameter and volume of the LA, left atrial appendage, and LA ejection fraction, which correlate with the risk of AF recurrence. Epicardial adipose tissue performs endocrine and inflammatory functions; increased thickness of this tissue, measured by ultrasound, is associated with recurrent AF. Speckle tracking echocardiography is a new effective noninvasive echocardiographic technique that allows detecting LA stretch during the filling and contraction phases and, on this basis, predicts the risk of recurrent AF. Lower peak values of LA longitudinal strain measured by this technique were independent predictors of AF recurrence after radiofrequency ablation.

Cardiac CT is a non-invasive method for assessing the anatomy of the left atrium and an accurate tool for diagnosing left atrial appendage. A contrast defect of the left atrial appendage detected on preoperative CT images was a predictor of AF recurrence. This is because contrast defects are caused by a decrease in function. In addition, the volume of atrial septal fat, pericardial fat volume, and pericoronary adipose tissue weakening detected during CT diagnostics are directly related to an increased risk of AF recurrence. Magnetic resonance imaging (MRI) determines the volume of the left and right atria, biventricular volume, LA sphericity, dilation index, LA ejection fraction, intraatrial dyssynchrony during sinus rhythm, total relative length of the ablation line, fibrosis, which is used to determine the risk of AF recurrence. LA fibrosis determined on MRI images using gadolinium contrast material shows promising efficacy in predicting the risk of recurrence after ablation in patients with.[20]

Surgical treatment of atrial fibrillation

Catheter ablation is the first line of treatment for paroxysmal atrial fibrillation. This method is more effective than antiarrhythmic drugs in terms of efficacy and improved survival in patients with AF and HF. The ablation catheter leads to the establishment of sinus rhythm in patients. However, most patients require several ablation procedures to restore a stable sinus rhythm.[12,17] New endocardial catheters provide favourable results in persistent AF. In 54.8% of patients with a mean duration of persistent AF of 7 months, atrial arrhythmias were absent 12 months after cryoballoon ablation.[19]

There are different ablation techniques: bi-atrial ablation, Cox IV method, left atrial ablation, and pulmonary vein isolation. These techniques are relatively minimally invasive, reduce the time of surgery, and reduce the risks of early mortality and complications. The rate of early recurrence after radiofrequency ablation is 20-40%. This is due to early inflammation, incomplete scar formation, and reconnection of the pulmonary vein. Compared to radiofrequency ablation, the cryoballoon technique is more effective. Very late recurrences, which occur a year or more after the operation, are described in 9% of patients. They are diagnosed with elevated blood pressure and low-density lipids. Factors that contribute to recurrence are overweight, metabolic syndrome, and a large amount of pericardial fat. Obstructive sleep apnoea is an accurate predictor of AF recurrence, as it promotes atrial remodelling in patients.[17]

Not all patients with AF need coronary artery bypass grafting or valve surgery or replacement.[21] In such cases, autonomous Cox's labyrinth operations are performed through sternotomy or right thoracotomy. Surgical ablation is performed without stopping the heart, so no atriotomy or endocardial incision is required. The effectiveness of epicardial surgical video thoracoscopic ablation is higher than endocardial catheter ablation. Cox IV labyrinth surgery demonstrates better results in persistent and long-term persistent AF. In its original form, this technique was based on cutting and stitching using numerous incisions and stitching to create a labyrinth of transmural conduction blocks. However, such surgical intervention was not effective enough and as a result of many years of modifications, the Cox-Maze IV technique was developed. It is based on only one incision in the left atrium and two incisions in the right atrium. The hybrid epicardial and endocardial ablation technique was developed to create a minimally invasive method of surgery without cardiac arrest, while combining the advantages of existing surgical and electrophysiological approaches.

There are two approaches to hybrid ablation, which differ in terms of pericardial access and epicardial ablation technique. The first method of hybrid ablation provides access to the posterior part of the left atrium thoracoscopically, and the second – endoscopically. Thoracoscopic ablation of atrial fibrillation in combination with hybrid AF ablation is an effective treatment for patients with symptomatic, drug-resistant paroxysmal or persistent AF. When using the standard hybrid ablation technique, the gentlest bilateral thoracoscopic ablation of the epicardium is performed with transvenous endocardial electrophysiological testing and correction of incomplete epicardial lesions. This treatment significantly reduces the risk of AF recurrence (in paroxysmal AF, the recurrence rate is 20%, and in persistent AF, 21% within 3 years). The main complications in the early postoperative period encompass: perioperative major complications included: bleeding, with the need for repeated surgery, cardiac tamponade, myocardial infarction, and pneumothorax.[18,22,23] Hybrid convergent surgery is performed under endoscopic visualization followed by catheter ablation. This technique is the least invasive hybrid surgery for AF.

Prevention of atrial fibrillation and cardiovascular diseases

Regular physical activity reduces the risk of AF by 2 mechanisms: directly by reducing the likelihood of AF, and indirectly by controlling body weight and blood pressure. 500 MET-min/week (metabolic equivalent of a minute's work per week) of regular exercise is recommended. Patients with already diagnosed AF are also recommended to exercise. It reduces the risk of ischaemic and haemorrhagic strokes and diseases of the white matter of the brain. Moderate-intensity exercise has been shown to

reduce symptoms and improve the functional capacity of the cardiovascular and respiratory systems.[23–26]

The choice of diet has a significant impact on the health of the cardiovascular system. A properly selected dietary pattern normalizes body weight, blood pressure and cholesterol levels. The anti-inflammatory properties of food can reduce chronic inflammation, reducing the risk of AF. For example, such components of the Mediterranean diet as lean fish and olive oil reduce oxidative stress, which is the primary and secondary prevention of AF. A plant-based diet has an anti-inflammatory effect, and its high fibre content improves the functioning of the gastrointestinal and cardiovascular systems.[27] Regular consumption of nuts reduces the level of low-density lipoprotein by 10–12%. Antioxidants and polyphenols contained in fruits and vegetables enhance the growth of *Bacteroides*, reducing inflammation and oxidative stress.[28] Cruciferous vegetables (e.g., cabbage and broccoli) promote the conversion of trimethylamine to trimethylamine-N-oxide, which reduces ventricular remodelling, improves hemodynamic parameters, and reduces the risk of atrial fibrillation.[29–31]

Patients with heart disease should avoid ultra-processed foods, as they increase inflammation and dyslipidaemia. Caffeine and methylxanthine contained in coffee and tea have a neurohormonal effect and affect the sympathetic nervous system. Caffeine causes a decrease in atrial muscle contractility and a decrease in the activity of the sinoatrial node. Alcohol exposure causes oxidative stress, release of fatty acids into the blood plasma, and reduction of atrial action potential, which leads to the development of AF. Chronic alcohol intake causes electrical disturbances, increased sympathetic tone, decreased sodium channel expression, and the development of hypertension and cardiomyopathy. At the same time, a small amount of alcohol <15 g/day for women and <30 g/day for men has a protective effect against coronary diseases. Resveratrol contained in red wine has antioxidant properties. It is necessary to exclude tobacco smoking. Daily poisoning with nicotine from cigarettes causes a violation of ionic conduction in atrial myocytes. This slows down ventricular repolarization and prolongs the refractory period by blocking the flow of K ions. Smoking increases fibrosis in the heart tissue, increases blood pressure and heart rate, increases the systemic release of catecholamines and promotes coronary vasospasm, which leads to myocardial ischaemia.[32,33] Thus, for the normal functioning of the cardiovascular system, it is important to avoid ultra-processed foods, giving preference to fresh vegetables and fruits, regularly devote time to physical activity and monitor blood pressure.

Discussion

As a result of the study, 34 patients, which is almost half of all patients, underwent mitral valve surgery with/without tricuspid valve surgery, and 16 patients (23.3%) underwent mitral valve surgery with/without tricuspid valve surgery with coronary artery bypass grafting. Aortic valve surgery in combination with mitral valve surgery with/without tricuspid valve surgery was performed in 12 patients (17.4%). Aortic valve surgery with/without tricuspid valve surgery was performed in 3 patients (4.3%). Atrial septal defect repair with/without tricuspid valve surgery was performed in 2 patients (4.3%). One surgery was performed due to congenital heart disease and one isolated coronary artery bypass grafting. The most favourable treatment results were found in patients with shorter AF duration and smaller left atrial size.

The study by Malagoli et al.[34] also indicated that structural remodelling of the left atrium and an increase in its volume positively correlated with the onset of AF and was one of the predictors of AF recurrence after pulmonary vein isolation. Zolotarova et al.[35] found that the duration of the QT interval before radiofrequency ablation and its prolongation after surgery were independent predictors of atrial fibrillation recurrence; the diameter of the left atrium before ablation was a highly sensitive predictor in patients with chronic heart failure with preserved LV ejection fraction. Patients with normal LA size but a reduced left atrial ejection fraction have more frequent recurrence after ablation.[36] Cardiac endothelin-1 concentration correlates with increased left atrial size, promoting myocyte hypertrophy and myocardial interstitial fibrosis. Atrial fibrosis causes a slowing of conduction and changes in dynamic repolarization. Khan et al.[37] found that the decrease in LA volume due to ablation was associated with the formation of a postoperative scar directly on the atrium. This was described in all patients, regardless of the existing heart rhythm. Taking into account the left ventricular diastolic function, it is possible to predict the recurrence of AF after ablation. This is because LA function is directly related to normal left ventricular filling. At the same time, the assessment of LA function by visualization of its deformities is more sensitive than the measurement of conventional LV filling parameters to determine the presence of LV diastolic dysfunction.

Scientists Tian et al.[38] noted that the volume of the LA annulus is an important predictor of atrial fibrillation recurrence after radiofrequency ablation. Patients who had an LA annulus volume of more than 25 ml were diagnosed with recurrent AF. The LA annulus is involved in the regulation of heart rate and fluid balance through its expandable reservoir function and the ability to secrete atrial natriuretic peptides and sensitive stretch receptors. The volume of the left atrial annulus is a reliable parameter for determining the function and structure of the left atrium in the early stages of AF.[39] In this study, during surgical interventions, 81% of patients underwent resection of the left atrial appendage, and 12% underwent ligation.

According to the results of the study, it is recommended to implement the classic Cox-Maze IV procedure for patients with traditional predictors of surgical ablation failure. Khiabani et al.[40] noted that this surgical intervention is highly effective in restoring sinus rhythm, and reduces surgical morbidity and mortality. The technique is equally successful in patients undergoing ablation for AF alone, AF in combination with concomitant cardiac surgery, including coronary artery bypass grafting, mitral valve, aortic valve, and septal myectomy procedures. Cox-Maze IV demonstrates approximately the same outcomes for patients with both paroxysmal and non-paroxysmal

(persistent and long-standing) forms of AF. MacGregor et al.[41] also described the predictors of the first recurrence of AF after Cox-Maze IV surgery: older age, peripheral vascular disease, non-paroxysmal AF, enlarged left atrium, and absence of sinus rhythm at the time of discharge from the hospital increased the risk of the first recurrence within 10 years of follow-up. At the same time, the researchers determined that obesity did not adversely affect the short-term and long-term results of Cox-Maze IV, meaning that increased BMI is not a predictor of AF recurrence in this case.

The present study identified risk factors for AF, including overweight, hypertension, and smoking, while also highlighting the significant impact of psychological conditions. Ren et al.[4] noted that anxiety, depression, and mental disorders increase the risk of AF by more than five times. Patients with a history of AF spanning 5–2 years were found to have higher levels of depression, with the prevalence of depression in AF patients ranging from 40% to 43%. Additionally, Ren et al. observed that an increased left atrial diameter is associated with a higher likelihood of recurrent AF one year after radiofrequency ablation, emphasizing the multifactorial nature of AF progression and recurrence. Patients with persistent AF had more severe manifestations of depression compared to patients with paroxysmal AF. Older patients with AF are more likely to suffer from depression and anxiety. This is partly explained by physical disorders, unhealthy lifestyle, and cognitive impairment. Women have higher rates of depressive disorders and sleep disturbances than men, regardless of the type of AF.[42] The greater susceptibility of women to mental disorders can be explained by sex differences, genetic factors, differences in daily life or health behaviour. At the same time, 50–70% of patients with chronic illnesses have undiagnosed depression (due to a frequent lack of awareness of symptoms, unclear clinical picture, and unwillingness to admit the problem). Also, high levels of depression were observed in patients who were not sufficiently informed about their health status and in those who had poor relationships with medical staff.

Patients with AF who receive accurate and detailed information about their condition often report fewer symptoms, improved disease management, and reduced emotional stress. This highlights the importance of patient education as a component of comprehensive AF care. Anxiety and depressive disorders play a significant role in the progression and recurrence of AF by activating the renin-angiotensin-aldosterone system, which leads to fibrosis, delayed atrial conduction, increased atrial pressure, and electrophysiological remodelling. These effects are further compounded by chronic depressive states, which elevate inflammatory cytokines, reactive oxygen species, and catecholamines, contributing to nervous system dysfunction and creating conditions favourable for AF recurrence. Research has shown that the presence of even mild depressive symptoms significantly increases the likelihood of AF recurrence following surgical or medical interventions. This association underscores the need for healthcare providers to recognize and address mental health as a critical factor in AF management. Routine screening for anxiety and depression should be integrated into standard care protocols, particularly for patients undergoing surgical treatment or those with advanced forms of AF.

Incorporating psychological support measures, such as stress management programs, counselling, or appropriate pharmacological interventions, could enhance treatment outcomes and improve patients' overall quality of life. This multidisciplinary approach aligns with current evidence, suggesting that addressing mental health factors not only reduces recurrence rates but also contributes to better long-term management of AF. Expanding clinical guidelines to include mental health support for AF patients, especially those with comorbid cardiac conditions, could lead to more effective and patient-centred care. Such efforts are essential to improving outcomes and reducing the burden of AF on both patients and healthcare systems.

Limitations

The limitations of this experiment were a small sample of study participants, a single-centre study, and the lack of randomization. Therefore, it is necessary to conduct further large-scale randomized clinical trials to determine the most effective methods of surgical treatment of atrial fibrillation, taking into account predictors of failure.

Conclusions

It was found that after the procedure of left atrial radiofrequency surgical ablation of atrial fibrillation, the sinus node served as the rhythm driver in 45 patients (65% of all). In 18 patients (26%), rhythm disturbances in the form of atrial fibrillation persisted, while 4 patients (6%) had atrial flutter, and 2 patients (3%) had left atrial flutter. Notably, 61% (42 patients) had a long-term persistent form of atrial fibrillation and an average left atrial size of 5.2 ± 0.6 cm, which significantly affected the outcomes of surgical treatment. The efficacy of radiofrequency ablation was lower in patients with traditional predictors of failure, such as being over 70 years of age, left atrial size of 5 cm or more, atrial fibrillation duration of more than 5 years, and persistent or long-standing AF. These findings emphasize the need for alternative approaches in patients with these predictors of failure. For such cases, the implementation of the classic Cox-Maze IV procedure or cryoablation as an independent technique is recommended to improve treatment success. Beyond surgical interventions, preventive measures play a crucial role in managing atrial fibrillation and reducing its recurrence. Adopting a healthy lifestyle that includes daily physical activity of moderate intensity, a balanced diet rich in fresh vegetables and fruits, lean meat and fish, along with controlling alcohol consumption, blood pressure, and body weight, and avoiding smoking, can significantly contribute to the prevention and better management of AF. By integrating these preventive strategies with tailored surgical approaches for high-risk patients, clinical outcomes can be optimized, providing a more comprehensive and patient-centred management of atrial fibrillation.

Conflict of interest
The authors declare none.

Funding
No funding was obtained for this study.

Ethical statement and consent to participate
All procedures performed in the study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. Prior to the study, all patients signed a voluntary informed consent for participation in the study.

Consent for publication
All patients signed a voluntary informed consent to the processing of their personal data for the study.

Author contributions statement
O.Sh-D.: Conceptualization, Methodology, Supervision, Writing – Original Draft; S.V.: Conceptualization, Data Curation, Investigation, Writing – Review & Editing; P.Sh.-D.: Methodology, Formal Analysis, Writing – Original Draft; I.Z.: Investigation, Visualization, Resources, Writing – Review & Editing. N.R.: Formal Analysis, Project Administration, Validation, Writing – Review & Editing.

References

1. Sagris M, Vardas EP, Theofilis P, et al. Atrial fibrillation: Pathogenesis, predisposing factors, and genetics. Int J Mol Sci 2022;23:6.
2. Aldaas OM, Malladi CL, Hsu JC. Catheter ablation of atrial fibrillation in patients with heart failure. Am J Cardiol 2019;123:187–195.
3. Al-Ezzi SMS, Bista I, Al-Ezzi MM, et al. Updates in the management of atrial fibrillation: Emerging therapies and treatment. Dis Mon 2024;70:101633.
4. Ren L, Li W, Su X, et al. Follow-up study of depressive state on patients with atrial fibrillation 1 year after radio-frequency ablation. Front Psychiatr 2022;13:1046924.
5. Volgman AS, Nair G, Lyubarova R, et al. Management of atrial fibrillation in patients 75 years and older: JACC state-of-the-art review. J Am Coll Cardiol 2022;79:166–179.
6. Ferro EG, Reynolds MR, Xu J, et al. Outcomes of atrial fibrillation ablation among older adults in the United States: A nationwide study. JACC Clin Electrophysiol 2024;10:1341–1350.
7. Cheng EP, Liu CF, Yeo I, et al. Risk of mortality following catheter ablation of atrial fibrillation. J Am Coll Cardiol 2019;74:2254–2264.
8. Skybchyk YV, Mikhaliev K□, Zharinov OJ. Association of left atrial spontaneous echo contrast with clinical and hemodynamic characteristics of patients with long-term episodes of persistent atrial fibrillation. Med News 2022;75:2652–2657.
9. Leszto K, Frąk W, Kurciński S, et al. Associations of dietary and lifestyle components with atrial fibrillation. Nutrients 2024;16:456.
10. Joglar JA, Chung MK, Armbruster AL, et al. ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: A report of the American college of cardiology/American heart association joint committee on clinical practice guidelines. Circ 2024;149: e1–e156.
11. Bisleri G, Pandey AK, Verma S, et al. Combined minimally invasive surgical and percutaneous catheter ablation of atrial fibrillation. J Am Coll Cardiol 2023;81: 606–619.
12. Peigh G, Zhou J, Rosemas SC, et al. Association of atrial fibrillation burden and mortality among patients with cardiac implantable electronic devices. Circ 2024;150:350–361.
13. Ravshanov AX, Suhail M, Komilova N, et al. Medical geographical zoning in part of Uzbekistan – A regional synthesis. Reg Sci Pol Pract 2024;16:100142.
14. Sokól-Szawlowska M. Paternal perinatal depression: cases. Psych Pol 2020;54:1123–1135.
15. Tomasz O, Waldemar K, Kajetan Ł, et al. Robotics in Neurosurgery – Past, Presence and Future. Adv Intell Syst Comp 2021;1362:1–8.
16. Serkova VK, Pavlov SV, Romanava VA, et al. Medical expert system for assessment of coronary heart disease destabilization based on the analysis of the level of soluble vascular adhesion molecules. Proc SPIE Int Soc Optic Eng 2017;10445:104453O.
17. Hanafy DA, Erdianto WP, Husen TF, et al. Three ablation techniques for atrial fibrillation during concomitant cardiac surgery: A systematic review and network meta-analysis. J Clin Med 2023;12:5716.
18. van der Heijden CAJ, Weberndörfer V, Luermans JGLM, et al. Hybrid ablation of atrial fibrillation: A unilateral left-sided thoracoscopic approach. J Card Surg 2022;37:4630–4638.
19. Kaba RA, Ahmed O, Behr E, Momin A. A chronicle of hybrid atrial fibrillation ablation therapy: From Cox Maze to convergent. Arrhythm Electrophysiol Rev 2022;11:e12.
20. Jing M, Li D, Xi H, et al. Value of imaging in the non-invasive prediction of recurrence after catheter ablation in patients with atrial fibrillation: An up-to-date review. Rev Cardiovasc Med 2023;24:241.
21. Rudyk DV, Tutchenko MI, Chub SL, et al. Portal hypertension and emergency care. Wiad Lek Wars Pol 2024;77:1485–1489.
22. Koutsaki S, Koutelekos I, Gerogianni G, et al. Atrial fibrillation in hypertension: Patients' characteristics. Mater Sociomed 2018;30:4–9.
23. Lapa ME, Swabe GM, Magnani JW. Association of depression and adherence to oral anticoagulation in patients with atrial fibrillation. J Am Heart Assoc 2023;12:e031281.
24. Zhang S, Zhang N, Liu L, et al. Global epidemiology of mental disorder in atrial fibrillation between 1998-2021: A systematic review and meta-analysis. World J Psychiatr 2024;14:179–193.
25. Le Grande MR, Salvacion M, Shwaita L, et al. Does coping style mediate the relationship between knowledge and psychosocial outcomes in women with atrial fibrillation? Front Psychiatr 2024;15:1328111.
26. Holmes DN, Piccini JP, Allen LA, et al. Defining clinically important difference in the atrial fibrillation effect on quality-of-life score: Results from the outcomes registry for better informed treatment of atrial fibrillation. Circ Cardiovasc Qual Outcomes 2019;12:e005358.
27. Chen YP, Li D, Xu YQ, et al. 5-Azacytidine accelerates mandarin fruit post-ripening and enhances lignin-based pathogen defense through remarkable gene expression activation. Food Chem 2024a;458:140261.
28. Chen YP, Xu YQ, Han XY, et al. Azacytidine shows potential in controlling the chilling injury of banana peel during cold storage. Food Cont 2024b;159:110283.
29. Vos LM, Vos R, Nieuwkerk PT, et al. Quality of life improvement from thoracoscopic atrial fibrillation ablation in women versus men: A prospective cohort study. Interdiscip Cardiovasc Thorac Surg 2024;39:ivae132.
30. Gupta D, Vijgen J, De Potter T, et al. Quality of life and healthcare utilisation improvements after atrial fibrillation ablation. Heart 2021;107:1296–1302.
31. Terricabras M, Mantovan R, Jiang C-Y, et al. Association between quality of life and procedural outcome after catheter ablation for atrial fibrillation: A secondary analysis of a randomized clinical trial. JAMA Netw Open 2020;3:e2025473.
32. Keum H, Cevik E, Kim J, et al. Tissue ablation: Applications and perspectives. Adv Mater 2024;36:e2310856.
33. Boersma L, Andrade JG, Betts T, et al. Progress in atrial fibrillation ablation during 25 years of Europace journal. EP Europace 2023;25:euad244.

34. Malagoli A, Rossi L, Bursi F, et al. Left atrial function predicts cardiovascular events in patients with chronic heart failure with reduced ejection fraction. J Am Soc Echocardiogr 2019;32:248–256.
35. Zolotarova TV, Brynza MS, Volkov DY, et al. Predictors of atrial fibrillation recurrence after radiofrequency ablation in patients with chronic heart failure. Med News 2021;74:1850–1855.
36. Oliinyk Y, Maltsev D, Shydlovska O, et al. Integrated Approach to Diagnosis and Treatment in Clinical Medicine: Search for Optimal Solutions. J Pion Med Sci 2024;13:12–21.
37. Khan HR, Yakupoglu HY, Kralj-Hans I, et al. Left atrial function predicts atrial arrhythmia recurrence following ablation of long-standing persistent atrial fibrillation. Circ Cardiovasc Imaging 2023;16:e015352.
38. Tian X, Zhang X-J, Yuan Y-F, et al. Morphological and functional parameters of left atrial appendage play a greater role in atrial fibrillation relapse after radiofrequency ablation. Sci Rep 2020;10:8072.
39. Smiyan OI, Loboda AM, Manko YA, et al. Dynamics of content of some minerals in teenagers with cardiovascular system pathology against the background of chronic tonsillitis. Wiad Lek Wars Pol 2018;71:861–864.
40. Khiabani AJ, MacGregor RM, Bakir NH, et al. The long-term outcomes and durability of the Cox-Maze IV procedure for atrial fibrillation. J Thorac Cardiovasc Surg 2022;163:629.e7–641.e7.
41. MacGregor RM, Khiabani AJ, Bakir NH, et al. Impact of obesity on atrial fibrillation recurrence following stand-alone Cox Maze IV procedure. Innov Technol Tech Cardiothorac Vasc Surg 2021;16:434–440.
42. Efremov A. Psychosomatics: Communication of the Central Nervous System through Connection to Tissues, Organs, and Cells. Clin Psychopharm Neurosci 2024;22:565–577.

Původní sdělení | Original research article

The Effect of Cigarette Exposure on Intima-Media Thickness (IMT) and VCAM-1 Expression in the Aorta of Mus musculus Mice

Meity Ardiana[a], Andrianto[a], Hanestya Oky Hermawan[a], Primasitha Maharany Harsoyo[a], Bagas Setiawan Ihsan Zaini[b], Akbar Reza Muhammad[b]

[a] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Academic Hospital, Surabaya, Indonesia*
[b] *Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia*

ARTICLE INFO

Article history:
Submitted: 26. 12. 2024
Accepted: 21. 1. 2025
Available online: 12. 6. 2025

Klíčová slova:
Ateroskleróza
Kouření cigaret
Tkáň aorty
Tloušťka intimy-medie
VCAM-1

SOUHRN

Kontext: Kouření je nadále jednou z hlavních příčin endotelové dysfunkce, která spouští proces rozvoje aterosklerózy a přispívá k rozvoji řady kardiovaskulárních onemocnění. Jedním ukazatelem endotelové dysfunkce je zvýšení hodnot vaskulární buněčné adhezní molekuly (vascular cell adhesion molecule-1, VCAM-1), molekuly podporující shlukování monocytů a urychlující rozvoj aterosklerózy. Běžným ukazatelem poškození endotelu je i ztluštění vrstvy intimy-medie (intima-media thickness, IMT), jež lze často pozorovat u kuřáků. Cílem této studie bylo zkoumat vliv kouření cigaret na hodnoty VCAM-1 a IMT.
Metody: Byla provedena experimentální studie s kontrolní skupinou hodnocenou až na konci studie. Dvanáct myší domácích (*Mus musculus*) bylo náhodně rozděleno do čtyř skupin: skupiny K (-), kontrolní (nevystavena tabákovému kouři); skupiny P1, s denní expozicí kouři po dobu 14 dní; skupiny P2, vystavené kouři denně po dobu 21 dní, a skupiny P3 s expozicí kouři po dobu 28 dní. Po 28 dnech expozice byly vzorky aorty všech skupin analyzovány z hlediska exprese VCAM-1 a hodnoty IMT.
Výsledky: Expozice tabákovému kouři zvětšuje IMT aorty. Měření IMT prokázalo statisticky významné rozdíly mezi „třítýdenní", „dvoutýdenní" skupinou a kontrolní skupinou ($p < 0,05$). Marker endotelové dysfunkce VCAM-1 ve vzorcích aorty nicméně statisticky významné změny nevykazoval ($p > 0,05$).
Závěr: Po třítýdenní expozici cigaretovému kouři se sice statisticky významně zvýšila hodnota IMT, délka expozice však nebyla dostatečně dlouhá na to, aby došlo ke statisticky významnému zvýšení hodnot VCAM-1 v tkáni myší aorty.

Keywords:
Aortic tissue
Atherosclerosis
Cigarette smoking
Intima media thickness
VCAM-1

ABSTRACT

Background: Smoking remains one of the leading causes of endothelial dysfunction, which triggers the atherosclerotic process and contributes to various cardiovascular diseases. One marker of endothelial dysfunction is an increase in VCAM-1, a molecule that promotes monocyte aggregation and accelerates the development of atherosclerosis. Thickening of the intima-media layer (IMT) is also a common indicator of endothelial damage, frequently observed in smokers. The aim of this study is to investigate the effect of cigarette smoking on vascular cell adhesion molecule-1 (VCAM-1) levels and intima-media thickness (IMT).
Methods: An experimental study with a post-test only controlled group design was conducted. Twelve mice (*Mus musculus*) were randomly subdivided into four groups: Group K (-), the control group (not exposed to tobacco smoke); Group P1, exposed to smoke daily for 14 days; Group P2, exposed to smoke daily for 21 days; and Group P3, exposed to smoke daily for 28 days. After the 28-day exposure period, samples from all groups were analyzed for VCAM-1 expression and aortic intima-media thickness (IMT).
Results: The tobacco smoke exposure leads to an increase in aortic intima-media thickness (IMT). The IMT measurements showed a significant difference between the 3-week group compared to the 2-week group and the baseline ($p < 0.05$). However, the endothelial dysfunction marker, VCAM-1, did not show a significant change in the aortic samples ($p > 0.05$).
Conclusion: The IMT measurement increased significantly after 3 weeks of cigarette smoke exposure, but the exposure duration was not sufficient to significantly elevate VCAM-1 levels in the aortic tissue of the mice.

Address: Andrianto, MD. Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Airlangga Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, e-mail: andrianto@fk.unair.ac.id
DOI: 10.33678/cor.2025.015

Please cite this article as: Ardiana M, Andrianto, Hermawan HO, et al. The Effect of Cigarette Exposure on Intima-Media Thickness (IMT) and VCAM-1 Expression in the Aorta of Mus musculus Mice. Cor Vasa 2025;67:376–380.

Introduction

Smoking is recognised as a major cause of cardiovascular disease (CVD), accounting for one in every four CVD-related deaths worldwide.[1,2] Smoking is the most significant modifiable risk factor, proven to greatly contribute to premature death, both related and unrelated to CVD.[3] Smoking just 1–4 cigarettes per day has also been shown to increase the risk of death from ischemic heart disease by 2.74 times compared to never having smoked.[4] A recent meta-analysis revealed that smoking increases the risk of atrial fibrillation and coronary artery disease by 1.23 (95% CI 1.10–1.36) and 1.33 (95% CI 1.27–1.40), respectively.[5]

From a pathogenic perspective, cardiovascular diseases (CVDs) are recognised as some of the most complex human conditions, arising from the interplay between genetics, environment, and lifestyle.[6] Smoking is one of the most significant modifiable risk factors, and among lifestyle risks, it remains the most complex and least understood due to the 9,000 different chemicals in cigarettes (ranging in size from atoms to particulate matter), which contribute to the development of complex CVDs that are difficult to fully comprehend.[7]

One of the well-known harmful substances that contribute to atherosclerosis is nicotine. Nicotine is absorbed in the alveoli of the lungs and rapidly enters the bloodstream, reaching the brain within just 10–12 seconds. This triggers the release of dopamine, which is the primary reason for nicotine addiction, encouraging continued smoking.[8]

A critical review of the current scientific literature leads to the hypothesis that nicotine mediates the effects of cigarette smoke on the cardiovascular system by enhancing MAPK signalling, inflammation, and oxidative stress via NADPH oxidase 1 (Nox1), which induces vascular smooth muscle cell (VSMC) ageing.[9] In fact, atherosclerosis is driven by two key pathological mechanisms: inflammation and cell death.[10]

Previous studies on mice exposed to cigarette smoke have shown that nicotine exposure leads to atherosclerotic lesions, especially in those on a high-fat diet (HFD).[11] The combination of platelet aggregation, lipid profile modification, endothelial dysfunction, direct actions on cellular elements involved in plaque formation, and vascular smooth muscle cell (VSMC) proliferation accelerates atherosclerosis progression due to nicotine exposure.[8]

Several biomarkers have been investigated in recent years to evaluate their association with various cardiovascular diseases, as they may assist in achieving an optimal diagnosis or predicting prognosis. One important biomarker of endothelial dysfunction caused by smoking is Vascular Cell Adherens Molecule-1 (VCAM-1). VCAM-1 is a key pro-inflammatory and pro-atherogenic protein, serving as a critical indicator of endothelial dysfunction and atherosclerosis. Among other cell adhesion molecules, VCAM-1 plays a crucial role in neointima proliferation following arterial damage induced by nicotine, a major focus of research into atherosclerotic cardiovascular diseases. In the nicotine-induced arterial injury model, VCAM-1 expression is notably elevated, contributing to the proliferation and migration of neointimal smooth muscle cells.[12]

VCAM-1 is also known to have increased expression in various cardiovascular conditions, including hypertension, atherosclerosis, ischemic disease, stroke, heart failure, and atrial fibrillation. Recent studies suggest that VCAM-1 could be a potential biomarker for atrial fibrillation, post-operative atrial fibrillation, and cardiovascular mortality in patients with coronary artery disease undergoing coronary artery bypass surgery.

In this study, the researchers aim to examine whether there is a change in aortic IMT size and an increase in VCAM-1 expression in *Mus musculus* subjects exposed to cigarette smoke.

Material and method

Ethics approval

This study adhered to the ARRIVE guidelines for animal experimentation protocols. The animal experiments were conducted under the approval of the Institutional Animal Care and Use Committee of Universitas Airlangga (UNAIR), Surabaya, Indonesia (Animal Approval No: 270/EC/KEPK/FKUA/2023), with Meity Ardiana as the principal investigator. The study was carefully conducted to prevent harm or discomfort to the experimental animals. At the conclusion of the study, anesthesia was administered to minimize pain during euthanasia.

Animals

This study used 12 male Balb/c mice (Mus musculus), aged eight weeks and weighing between 30 and 50 grams. Before the experiment commenced, the mice were acclimatised to their new environment for seven days. The animals were housed in the pharmacology animal laboratory at the Faculty of Medicine, Universitas Airlangga, in individual polycarbonate cages measuring 480 mm × 265 mm × 210 mm.

Each cage contained three or four mice, with wood shavings covering the cage floor. The animals were kept in microisolator cages under controlled room temperatures ranging between 22 °C and 25 °C, with a 12-hour light/dark cycle. Humidity was maintained at a constant level of 50% to 60%. The mice were fed a standard diet and had access to water ad libitum. Group assignment was carried out using simple random sampling.

At the end of the study, the mice were administered isoflurane and either to minimise the impact on nitric oxide levels. Subsequently, the mice were euthanised by cardiac puncture, performed only after confirming deep anaesthesia, as evidenced by the absence of a pain response. Our method was approved by the Animal Ethics Committee, in accordance with the IACUC policy on laboratory animal use. The study was conducted following international standards as outlined in the National Institute of Health's Guide for the Care and Use of Laboratory Animals and adhered to the ARRIVE guidelines for reporting in vivo experiments.

After euthanasia, the aortic tissues were collected to isolate the intima-media, involving the removal of surrounding adipose tissue, longitudinal cutting along the edges, and peeling off of the adventitia.

Table 1 – Immunoreactivity Scoring System for IHC[13]		
Percentage of positive cells	**X intensity of staining**	**= IRS (0–12)**
0 = no positive cells	0 = no colour reaction	0–1 = negative
1 = < 10% of positive cells	1 = mild reaction	2–3 = mild
2 = 10–50% positive cells	2 = moderate reaction	4–8 = moderate
3 = 51–80% positive cells	3 = intense reaction	9–12 = strongly positive
4 = > 80% positive cells		

Table 2 – IRS points and classification[13]	
IRS points	**IRS classification**
0–1	0 = negative
2–3	1 = positive, weak expression
4–8	2 = positive, mild expression
9–12	3 = positive, strong expression

VCAM-1 immunohistochemistry

The VCAM-1 reagent for immunohistochemistry (IHC) was purchased from Santa Cruz Biotechnology (VCAM-1 Antibody [E-10], sc-13160; Dallas, TX, USA). The analysis was performed using the streptavidin-biotin method, with a biotin-conjugated secondary antibody used to link the primary antibody to the streptavidin-peroxidase complex. The labeled streptavidin-biotin (LSAB) method was employed to assess VCAM-1 expression in mouse aortic tissue.

The procedure began with deparaffinisation and fixation of the aortic tissue, followed by rehydration using xylene and various concentrations of ethanol. After rehydration, the tissue was washed with Phosphate Buffer Solution and immersed in 3% H_2O_2 solution for 20 minutes. We then added 1% Bovine Serum Albumin and incubated the samples for 30 minutes.

The primary anti-VCAM-1 antibody was applied, incubated, and washed, followed by the addition of the secondary antibody and further incubation. The SA-HRP complex was then added and incubated for 10 minutes. DAB chromogen was applied and incubated, followed by another wash.

Finally, counterstaining with Haematoxylin-Eosin was carried out, and VCAM-1 expression was measured and analysed using a biological microscope at 400× magnification. Semiquantitative analysis was performed using an immunoreactivity scoring system (**Tables 1, 2**).[13]

IMT measurement and histology

The thoracic aorta was prepared by cutting the distal arch from the left ventricle of each mouse. Post-mortem samples of the descending thoracic aorta, obtained through dissection, were then fixed using 10% formaldehyde to preserve tissue integrity. Following fixation, the samples were embedded in paraffin and sectioned into 6 µm slices for histological analysis.

After sectioning, the tissue slices were stained with haematoxylin and eosin to enhance contrast and facilitate the observation of cellular morphology. The intima-media thickness of the aorta was measured using a Leica DMD 108 (Leica Microsystems GmbH, Wetzlar, Germany), which enables precise and consistent measurements.

Each sample was measured in micrometres (µm) at six different locations along the vessel wall, providing a comprehensive view of tissue thickness. The arithmetic mean of these six measurements was calculated and presented in the results section to offer detailed data on the morphological characteristics of the aorta.

Results

Smoking causes increased aortic intima-media thickness due to the progression of atherosclerosis

This study evaluated the thickness of the aortic intima-media layer, measured using the MIT scale. The statistical analysis employed was a one-way ANOVA test, conducted after confirming the normality and homogeneity of the data. The results showed a significant difference between the treatment groups (**Fig. 1**).

Based on the results of the post hoc LSD test, the study demonstrated a significant difference between the control group and the group exposed to cigarette smoke for 3 weeks, as well as between the 2-week and 3-week exposure groups. These findings confirm that cigarette smoke exposure at certain doses and durations can lead to endothelial dysfunction and thickening of the aortic intima-media layer, which is clinically significant in the development of atherosclerosis.

Lack of significant increase in VCAM-1 expression in mice exposed to cigarette smoke for 1 month

This study examined VCAM-1 expression using IHC staining, evaluated by an anatomical pathology expert according to the Immunoreactivity Scoring System (IRS) (Kaemmerer, 2012). Initial assessment results indicated that the data were not normally distributed or homogeneous. The statistical analysis employed was the Kruskal-Wallis test, with the results presented in **Figure 2**.

Based on the Kruskal-Wallis statistical analysis, no significant differences were found between the groups. This suggests that the level of cigarette smoke exposure may have been insufficient to cause an increase in the exposure groups. The brown colour observed on the elastic fibers and blood cells was identified as a false positive and was not included in the analysis. Adjustments were made before evaluation to avoid false positives in the samples. Not all samples could be observed across 10 fields of view due to the small or overlapping aortas; however, a re-

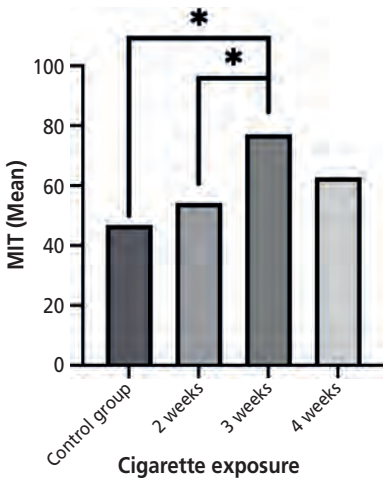


Fig. 1 – Measurement of aortic IMT in mice exposed to cigarette smoke (Sig <0.05).

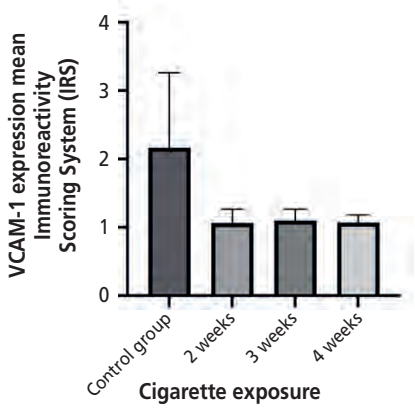


Fig. 2 – Assessment of VCAM-1 expression in the aorta of mice exposed to cigarette smoke.

duced number of fields still adequately represented the entire aortic wall.

Discussion

The effect of smoking on the IMT aortic

The thickening of carotid intima-media (IMT) is recognised as a proxy indicator of early-stage atherosclerosis and serves as a predictor of cardiovascular disease (CVD) development, independent of conventional CVD risk factors.[14] Prior studies have highlighted the significant role of inflammation in the initial thickening of IMT resulting from exposure to cigarette smoke. Smoking's impact on IMT is partially mediated by leukocytes, high-sensitivity C-reactive protein, and fibrinogen, all of which are early biomarkers of atherosclerosis.[15]

Based on the results of the study above, it shows that there is a significant difference between giving smoked cigarettes to mice on increasing aortic IMT with a *p*-value <0.05, especially between the control group and the group exposed to cigarette smoke for 3 weeks. This finding is consistent with another research,[16] that there is a significant relationship to the aortic IMT exposed to cigarette smoke in experimental animals. Another research[17] also showed that there was an increase in the average carotid artery IMT in smokers than in non-smokers.

One of the most harmful components of cigarettes known to cause various cardiovascular diseases is nicotine. Nicotine is recognised for causing systemic hemodynamic disturbances, reducing coronary blood flow, and inducing myocardial tissue remodelling. It is also known as a pro-atherogenic agent with several effects, such as: 1. triggering endothelial dysfunction, 2. increasing inflammatory response, 3. modifying lipid profile, 4. inducing catecholamines, which are responsible for raising blood pressure and heart rate, 5. enhancing platelet aggregability, 6. triggering smooth muscle cell proliferation and migration into the intima, and 7. promoting vascular smooth muscle cell (VSMC) proliferation and migration to the lesion cap.[8] These pathogenic mechanisms contribute to permanent vascular damage and the progression of atherosclerosis.

Based on the number of cigarettes smoked per day,[18] showed that the lowest average IMT value was in the study population, who consumed 1–5 cigarettes per day, and the highest average IMT value was in the study population, who consumed 11–15 cigarettes per day. This shows that IMT increases with the number of cigarettes smoked per day, especially in chronic smokers. He showed significant changes in the structure and function of the carotid artery IMT in respondents who had smoked for 5–10 years.[18]

However, another research[19] obtained different results where there were no changes in the tunica intima observed from the mouse experiment. Another experimental study[20] found that exposure to cigarette smoke for eight weeks only resulted in disorganization of vascular smooth muscle cells in the tunica media. Vacuolization is one of the complications of the cytotoxic process in cells and an early marker of preclinical atherosclerosis. Vacuolization is a sign of oxidative stress in blood vessels due to exposure to cigarette smoke. Vacuolization makes vascular smooth muscle cells have different shapes and sizes, resulting in cells becoming irregular and causing atherosclerosis.[21]

VCAM-1 expression in mice exposed to cigarette smoke

Based on the results of the study above, it showed that there was no significant difference in VCAM-1 expression between control and treatment. This result is appropriate with the study of Ardiana et al. (2023)[16] that there is no significant difference in VCAM-1 expression between the group exposed to cigarette smoke and the control group. VCAM-1 is expressed in vascular endothelial cells, and VCAM-1 expression can increase leukocyte adhesion to endothelial cells. VCAM-1 accelerates the migration of adherent leukocytes along the endothelial surface, and promotes the proliferation of vascular smooth muscle cells. So, VCAM-1 may play an important role as a pro-atherogenic molecule.[22]

It is believed that smoking can cause increased oxidative stress due to direct damage by reactive oxygen species (ROS) and inflammatory responses. The production of oxidative stress and ROS due to cigarette smoke is

expected to increase VCAM-1 expression and decrease e-NOS levels.[23] According to previous studies,[24,25] there was an increase in oxidative stress, ROS, and VCAM-1 expression in endothelial cell cultures after exposure to cigarette smoke.

However, increased VCAM-1 expression is a multifactorial process, smoking cannot increase VCAM-1 independently without other risk factors such as dyslipidemia.[26] have proven this hypothesis by examining VCAM-1 expression in aortic tissue of dyslipidemia patients. The results showed that VCAM-1 expression was positively correlated with triglycerides, total cholesterol, and LDL levels while VCAM-1 and HDL had a negative correlation.[26] VCAM-1 expression in endothelial cells requires a trigger which is high lipid levels, especially LDL. Increased oxidized LDL in the endothelium will be phagocytized by macrophages which require the role of VCAM-1.[27] In our study, other factors contributing to the development of atherosclerosis such as dyslipidemia were not included. Our study did not use experimental animals with high-fat diets and serial lipid profile measurements. Therefore, our results showed that there was no significant difference of VCAM-1 expression between the group exposed to cigarette smoke and the control group.

Conclusion

IMT increased significantly after 3 weeks of cigarette smoke exposure, but the exposure duration was not sufficient to significantly elevate VCAM-1 levels in the aortic tissue of the mice.

Conflict of intereset

The authors declare no conflict of interest.

Acknowledgment

The authors would like to express their sincere gratitude to the advisors for the valuable guidance and support throughout this research journey.

References

1. WHO. Global Health Risks. Published online 2009. Available from: http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf [cited 2025-06-12].
2. Centers for Disease Control and Prevention (US), U.S. Department of Health and Human Services. The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General. Publications and Reports of the Surgeon General. Published online 2006. Available from: https://www.ncbi.nlm.nih.gov/books/NBK44324/. [cited 2025-06-12].
3. Zhu J, Nelson K, Toth J, Muscat JE. Nicotine dependence as an independent risk factor for atherosclerosis in the National Lung Screening Trial. BMC Public Health. 2019;19(1). doi: 10.1186/s12889-019-6419-8
4. Bjartveit K, Tverdal A. Health consequences of smoking 1-4 cigarettes per day. Tob Control 2005;14:315–320.
5. Larsson SC, Burgess S. Appraising the causal role of smoking in multiple diseases: A systematic review and meta-analysis of Mendelian randomization studies. EBioMedicine 2022;82. doi:10.1016/j.ebiom.2022.104154
6. Messner B, Bernhard D. Smoking and cardiovascular disease: Mechanisms of endothelial dysfunction and early atherogenesis. Arterioscler Thromb Vasc Biol 2014;34:509–515.
7. Münzel T, Hahad O, Kuntic M, et al. Effects of tobacco cigarettes, e-cigarettes, and waterpipe smoking on endothelial function and clinical outcomes. Eur Heart J 2020;41:4057–4070.
8. Centner AM, Bhide PG, Salazar G. Nicotine in Senescence and Atherosclerosis. Cells 2020;9(4). doi:10.3390/cells9041035
9. Chang KH, Park JM, Lee CH, et al. NADPH oxidase (NOX) 1 mediates cigarette smoke-induced superoxide generation in rat vascular smooth muscle cells. Toxicology in Vitro 2017;38:49–58.
10. Welsh P, Grassia G, Botha S, et al. Targeting inflammation to reduce cardiovascular disease risk: a realistic clinical prospect? Br J Pharmacol 2017;174:3898–3913.
11. Wu X, Zhang H, Qi W, et al. Nicotine promotes atherosclerosis via ROS-NLRP3-mediated endothelial cell pyroptosis. Cell Death Dis 2018;9(2). doi:10.1038/s41419-017-0257-3
12. Dos Santos JC, Cruz MS, Bortolin RH, De Oliveira KM, et al. Relationship between circulating VCAM-1, ICAM-1, E-selectin and MMP9 and the extent of coronary lesions. Clinics 2018;73. doi:10.6061/clinics/2018/e203
13. Kaemmerer D, Peter L, Lupp A, et al. Comparing of IRS and Her2 as immunohistochemical scoring schemes in gastroenteropancreatic neuroendocrine tumors. Int J Clin Exp Pathol 2012;5:187–194.
14. Libby P, Ridker PM, Hansson GK. Progress and challenges in translating the biology of atherosclerosis. Nature 2011;472:317–325.
15. Benowitz NL, Burbank AD. Cardiovascular toxicity of nicotine: Implications for electronic cigarette use. Trends Cardiovasc Med 2016;26:515–523.
16. Ardiana M, Santoso A, Hermawan HO, et al. Acute effects of cigarette smoke on Endothelial Nitric Oxide synthase, vascular cell adhesion molecule 1 and aortic intima media thickness. F1000Res 2023;10:1–20.
17. Alsiddig AM, Ali IA. Effects of Smoking on Intima-Media Thickness of the Common Carotid Artery Using Ultrasonography. Artery Res 2024;30. doi:10.1007/s44200-024-00044-w.
18. Mahmoud M. Effect of cigarettes smoking on common carotid arteries intima-media thickness in current smokers. Ozean J Appl Sci 2012;5:259–269.
19. Ali SS, Ayuob NN, Al Ansary AK, Soluman ER. Antioxidants protect against increased risk of atherosclerosis induced by exposure to cigarette smoke: Histological and biochemical study. Saudi J Biol Sci 2012;19:291–301.
20. Jaldin R, Castardelli É, Perobelli J, et al. Morphologic and biomechanical changes of thoracic and abdominal aorta in a rat model of cigarette smoke exposure. Ann Vasc Surg 2013;27:791–800.
21. Harrington J, Peña AS, Gent R, et al. Aortic intima media thickness is an early marker of atherosclerosis in children with type 1 diabetes mellitus. J Pediatr 2010;156:237–241.
22. Lembas A, Zawartko K, Sapuła M, et al. VCAM-1 as a Biomarker of Endothelial Function among HIV-Infected Patients Receiving and Not Receiving Antiretroviral Therapy. Viruses 2022;14:578.
23. Yang G, Li Y, Wang Z, et al. Protective effect of melatonin on cigarette smoke-induced restenosis in rat carotid arteries after balloon injury. J Pineal Res. 2014;57(4):451-458.
24. Teasdale JE, Hazell G, Newby AC, White SJ. Paradoxical effects of cigarette smoke extract and high laminar flow on tumour necrosis factor-alpha induced VCAM-1 up-regulation – Implications for endothelial dysfunction. Atherosclerosis 2014;237:e13–e14.
25. Kamceva G, Arsova-Sarafinovska Z, Ruskovska T, et al. Cigarette smoking and oxidative stress in patients with coronary artery disease. Open Access Maced J Med Sci 2016;4:636–640.
26. Mu W, Chen M, Gong Z, et al. Expression of vascular cell adhesion molecule-1 in the aortic tissues of atherosclerotic patients and the associated clinical implications. Exp Ther Med 2015;10:423–428.
27. Toma L, Sanda GM, Deleanu M, et al. Glycated LDL increase VCAM-1 expression and secretion in endothelial cells and promote monocyte adhesion through mechanisms involving endoplasmic reticulum stress. Mol Cell Biochem 2016;417:169–179.

Přehledový článek | Review article

Konstriktívna perikarditída po očkovaní proti SARS-CoV-2 – kazuistika a prehľad literatúry

(Constrictive pericarditis after SARS-CoV-2 vaccination: a case report and literature review)

Veronika Šimovičová[a], Marcela Danková[a], Erika Drangová[b], Michal Hulman[c], Eva Gonçalvesová[a]

[a] *Kardiologická klinika, Lekárska fakulta Univerzita Komenského v Bratislave a Národný ústav srdcových a cievnych chorôb a.s., Bratislava, Slovenská republika*
[b] *Oddelenie diagnostickej a intervenčnej rádiológie, Národný ústav srdcových a cievnych chorôb a.s., Bratislava, Slovenská republika*
[c] *Klinika kardiochirurgie, Lekárska fakulta Univerzita Komenského v Bratislave a Národný ústav srdcových a cievnych chorôb a.s., Bratislava, Slovenská republika*

INFORMACE O ČLÁNKU

Historie článku:
Vložen do systému: 3. 12. 2024
Přijat: 23. 12. 2024
Dostupný online: 4. 6. 2025

Kľúčové slová:
Konstritívna perikarditída
Očkovanie proti covidu-19
Perikardiektómia

SÚHRN

Konstriktívna perikarditída po očkovaní proti SARS-CoV-2 je pravdepodobne veľmi zriedkavá a vyznačuje sa pomerne závažnou klinickou manifestáciou. Opisujeme prípad 42-ročného pacienta, bez závažného predchorobia, ktorý prekonal perimyokarditídu po druhom očkovaní proti covidu-19. Tá bola liečená nesteroidnými antiflogistikami. Po polroku od epizódy perimyokarditídy sa u pacienta manifestovali znaky a príznaky srdcového zlyhávania. Bolo vyslovené podozrenie na konstriktívnu perikarditídu. Diagnózu sme potvrdili echokardiograficky, kde boli typické prejavy konstrikcie a CT srdca s nálezom zhrubnutého perikardu s kalcifikátmi. U pacienta bola indikovaná perikardiektómia s parciálnou resekciou perikardu pre lokálne výrazné zrasty perikardu a epikardu, ktoré bránili totálnej perikardiektómii. Výkon mal dobrý hemodynamický aj klinický výsledok.

Keywords:
Constrictive pericarditis
COVID-19 vaccination
Pericardiectomy

ABSTRACT

Constrictive pericarditis following SARS-CoV-2 vaccination is likely to be very rare and is characterized by a relatively severe clinical manifestation. We describe the case of a 42-year-old patient, without significant comorbidities, who developed perimyocarditis after the second dose of the COVID-19 vaccine. It was treated with nonsteroidal anti-inflammatory drugs. Six months after the perimyocarditis episode, the patient presented signs and symptoms of heart failure. A suspicion of constrictive pericarditis was raised. The diagnosis was confirmed by echocardiography, which showed typical signs of constriction, and cardiac CT, revealing a thickened pericardium with calcifications. Pericardiectomy with partial resection of the pericardium was indicated due to local significant adhesions between the pericardium and epicardium, which prevented total pericardiectomy. The procedure resulted in good hemodynamic and clinical outcomes.

Adresa pro korespondenci: MUDr. Marcela Danková, PhD., Kardiologická klinika, Lekárska fakulta Univerzita Komenského v Bratislave a Národný ústav srdcových a cievnych chorôb a.s., Pod Krásnou hôrkou 1, 833 48 Bratislava, Slovenská republika, e-mail: marcela.dankova@nusch.sk
DOI: 10.33678/cor.2024.107

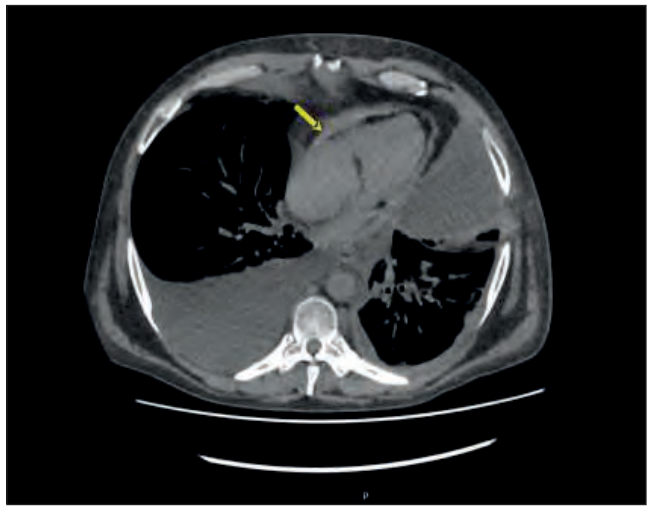
Tento článek prosím citujte takto: Šimovičová V, Danková M, Drangová E, et al. Konstriktívna perikarditída po očkovaní proti SARS-CoV-2 – kazuistika a prehľad literatúry. Cor Vasa 2025;67:381–385.

Úvod

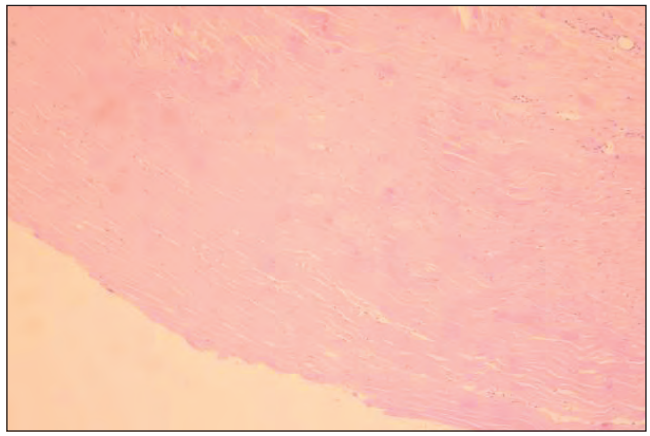
Konstriktívna perikarditída po očkovaní proti SARS-CoV-2 je pravdepodobne veľmi zriedkavá. Nie je jasný jej reálny výskyt. V literatúre je opísaných niekoľko prípadov. Aj keď jej výskyt nie je častý, klinická manifestácia je závažná. Manifestuje sa rozvojom syndrómu srdcového zlyhávania s nízkym minútovým objemom. Dôležitá je včasná diagnostika a terapia. V niektorých prípadoch je potrebná chirurgická perikardiektómia.

Popis prípadu

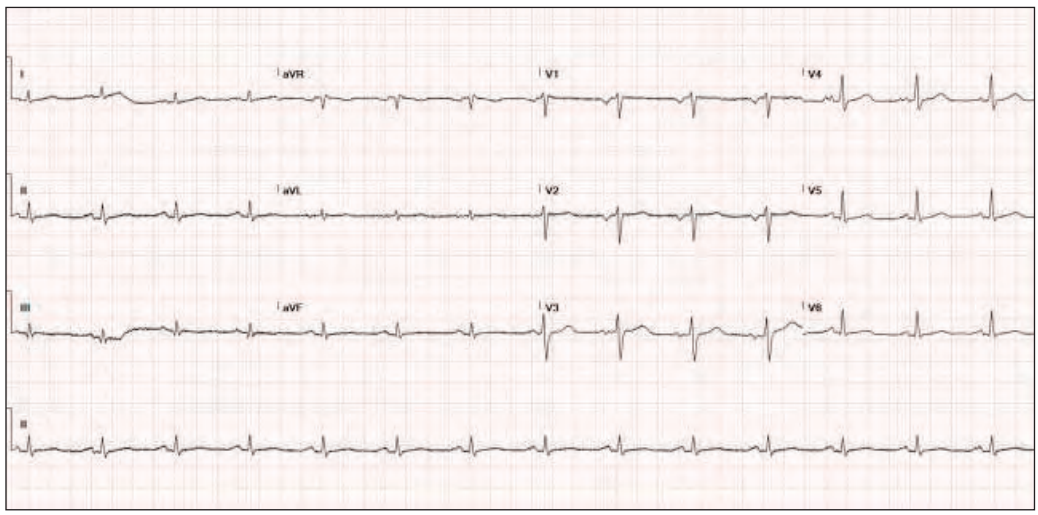
42-ročný pacient bez závažnejšieho predchorobia prekonal lete v lete 2021 perimyokarditídu, ktorá bola diagnostikovaná týždeň po druhej dávke mRNA vakcíny proti covidu-19. Odporučená bola terapia nesteroidnými antiflogistikami. Dodatočne udával, že rovnaké ťažkosti – bolesti na hrudníku, palpitácie – mal aj po prvej dávke vakcíny. Pre krátke trvanie a spontánny ústup ťažkostí tomu nevenoval pozornosť. Koncom roka 2021 sa začal zadýchavať pri námahe, postupne netoleroval horizontálnu polohu, pozoroval rýchly nárast veľkosti brucha. Bol hospitalizovaný. Po rozsiahlej diferenciálnej diagnostike, kedy boli vylúčené infekčná, hepatologická, onkologická, endokrinologická príčina, bol stav hodnotený ako polyserozitída. V kontexte prekonanej perimyokarditídy sa vyslovilo podozrenie na konstriktívnu perikarditídu. Pacient bol následne hospitalizovaný. Pri vstupnom vyšetrení bol pacient funkčne na úrovni triedy NYHA IV, mal zvýšenú náplň pulzujúcich jugulárnych vén s Kussmaulovým príznakom a výrazné kongestívne prejavy dominantne vo veľkom obehu (ascites, obojstranný fluidothorax, opuchy nôh). Na EKG (**obr. 1**) bol prítomný sínusový rytmus, horizontálne depresie ST vo V_3–V_6 a nízka voltáž. V laboratórnom náleze ľahko zvýšený C-reaktivný protein (CRP), mierna leukocytóza, elevácia N-terminálneho faktora natriuretického propetidu typu B (NT-proBNP), hepatálnych enzýmov a nízka saturácia O_2 vo venóznej krvi. Echokardiografickým vyšetrením sme zobrazili zhrubnutý perikard s perikardiálnym výpotkom, „septal bounce“, znaky konstrikcie, ľahkú dysfunkciu PK, dilatované predsiene a dilatovanú dolnú dutú žilu (VCI) bez respiračne podmienenej variability. Výpočtová tomografia (CT) srdca (**obr. 2**) potvrdila zhrubnutý denzný perikard s niekoľkými kalcifikátmi do 6 mm. Na základe výsledkov vyšetrení



Obr. 2 – CT – punktiformné kalcifikáty perikardu (šípka).



Obr. 3 – Histologický obraz perikardu, zväčšenie 100×.



Obr. 1 – EKG pri prijatí.

Tabuľka 1 – Prehľad doteraz publikovaných kazuistík postvakcinačnej konstriktívnej perimyokarditídy

Autor	Pohlavie/ Vek	Vakcína a dávka	Dg. peri(myo)-karditídy do 1 mesiaca od vakcinácie	Doba od vakcinácie po dg. konstrikcie	Prejavy SZ, NYHA	Relevantné komorbidity	Dg. metódy	Perikardiektómia	Histologický nález
Diana D.[17]	M/75	Moderna, 2d.	N	1m	VOK	AHT, CHOCHP	ECHO, MR	n.a.	n.a.
Diana D.[17]	M/68	Moderna, 2d.	N	2m	VOK	KCH, AHT, DLP, CKD	ECHO, CT	n.a.	n.a.
Bain E.[18]	M/19	Pfizer, 2d.	N	2t	VOK, dýchavica	n.a.	CT, katetrizácia, MR	A	Fibróza
Hajsadeghi S.[19]	M/72	Inaktiv. vírus, vakcína, 3d.	N	1m	VOK, dýchavica, NYHA IV	KCH, CMP, DM, AHT	ECHO, CT, MR, katetrizácia	A	Kalcifikovaný perikard
Viani GM.[20]	M/59	Pfizer, 2d.	A, 5D	5D	VOK	DM	ECHO, MR	N	n.a.
Federico C.[21]	M/32	Moderna, 2d.	A, 2D	2D	dýchavica	n.a.	ECHO, MR	N	n.a.
Nakanishi Y.[22]	F/70	mRNA, 2d.	N	1m	VOK, dýchavica	DM, AHT, DLP, fibróza pľúc	ECHO, CT, katetrizácia, MR	N	n.a.
Misumi I.[23]	M/59	Pfizer, 1d.	A, 5D	3m	Dýchavica	Syst. skleróza	ECHO	N	n.a.
Demirtas H.[24]	M/28	Pfizer, 2d.	N	4m	VOK	n.a.	ECHO, CT, katetrizácia	A	n.a.
Sharma S.[25]	M/59	Moderna, 2d.		2t	VOK, NYHA III	AHT, DM	ECHO, MR, katetrizácia	A	fibróza
Hysi I.[26]	M/63	Pfizer, 1d.	A, 3D	3m	VOK, NYHA III	PAO, EAP	ECHO, MR, katetrizácia	A	Nešpecifická zápalová infiltrácia
Penmetsa M.[27]	M/42	Pfizer, 2d.	N	3t	dýchavica	n.a.	ECHO, MR	N	n.a.
Náš pacient	M/42	Moderna, 2d.	A, 2T	12m	VOK, NYHA IV	n.a.	ECHO, CT	A	Fibróza

A – áno; AHT – artériová hypertenzia; CKD – chronická obličková choroba; CMP – cievna mozgová príhoda; CT – výpočetná tomografia; d – dávka; D – deň; DLP – dyslipidémia; DM – diabetes mellitus; EAP – embolizácia do arteria pulmonalis; ECHO – echokardiografia; F – žena; CHOCHP – chronická obštrukčná choroba pľúc; KCH – koronárna choroba; m – mesiac; M – muž; MR – magnetická rezonancia; N – nie; n.a. – neuvedené; NYHA – New York Heart Association; t – týždeň; PAO – periférne artériové ochorenie; VOK – veľkoobehová kongescia.

sme stav hodnotili ako konstriktívnu perikarditídu, u pacienta bola indikovaná perikardiektómia. Vzhľadom na to, že perikard bol intímne zrastený s epikardom, sa podarila len parciálna resekcia perikardu. Histologicky bol perikard výrazne väzivovo zhrubnutý, s proliferáciou hypocelulárneho denzného hyalizovaného kolagénového spojiva, boli zavzaté dilatované kapiláry. Zápalový infiltrát nebol signifikantne zmnožený (**obr. 3**). Pri kontrolnom ambulantnom vyšetrení 3 mesiace po operácii bol pacient funkčne na úrovni NYHA II, nemal prítomné klinické známky retencie tekutín, v 6-minútovom teste chôdzou prešiel 440 m, Borg 2. Echokardiograficky pretrvávala dilatácia oboch predsiení, PK s redukovanou funkciou a vysoké plniace tlaky oboch komôr.

Prehľad doteraz publikovaných prípadov

Doteraz bolo v literatúre opísaných 12 prípadov konstriktívnej perikarditídy asociovanej s očkovaním proti covidu-19, pacient z nášho prípadu je trinásty. V opísaných prípadoch sme hodnotili vek, pohlavie, typ a dávku vakcíny, po ktorej boli zaznamenané ťažkosti, dobu od vakcinácie po diagnózu peri(myo)karditídy, dobu od vakcinácie po diagnózu konstriktívnej perikarditídy, prítomnosť kongestívnych prejavov a funkčnú triedu NYHA, prítomnosť relevantných komorbidít, diagnostické modality, ktorými sa diagnóza konstriktívnej perikarditídy potvrdila, či pacient absolvoval perikardiektómiu a aký bol histologický nález perikardu (**tabuľka 1**). Nebolo možné zistiť uvedené informácie u všetkých opísaných pacientov. Z opísaných prípadov bolo 12 mužov a 1 žena. Jednalo sa skôr o starších pacientov, priemerný vek bol 52,9 rokov, len 5 pacienti boli mladší ako 50 rokov. Títo 5 pacienti nemali v osobnej anamnéze žiadnu relevantnú komorbiditu. U pacientov starších ako 50 rokov (8 pacientov) bola najčastejšia komorbidita artériová hypertenzia (u 5 pacientov), 4 mali diabetes mellitus, 3 pacienti mali ochorenie pľúc. Až na jedného pacienta, ktorý bol očkovaný inaktivovanou vírusovou vakcínou, boli všetci očkovaní mRNA vakcínou. Len u 5 pacientov došlo v krátkom časovom období po podaní vakcíny k rozvoju ťažkostí a diagnostike peri(myo)karditídy. Diagnóza konstriktívnej perikarditídy bola stanovená maximálne do 12 mesiacov od očkovania. Všetci pacienti mali v čase príjmu na hospitalizáciu rozvinutý syndróm srdcového zlyhávania dominantne s prejavmi veľkoo-

behovej kongescie, tiež boli funkčne významne limitovaní. Z diagnostických vyšetrovacích metód každý pacient absolvoval echokardiografické vyšetrenie, magnetická rezonancia bola realizovaná 9 pacientom, u 6 pacientov aj CT srdca a obojstranná katetrizácia. U 6 pacientov bola potrebná perikardiektómia. Histologický nález z perikardu bol nešpecifický, s nálezom fibrózneho tkaniva, kalcifikátov alebo zápalovej infiltrácie.

Diskusia

Je známe, že myoperikarditída môže byť jednou zo zriedkavých komplikácií očkovania. Avšak po začatí očkovania mRNA vakcínou proti covidu-19 začali pribúdať hlásenia o myoperikarditíde, hlavne u adolescentov a mladých dospelých.[1]

Mechanizmus vzniku perikarditídy či myokarditídy po očkovaní vakcínou mRNA proti covidu-19 nie je jednoznačne stanovený. Existujú viaceré hypotézy.[2,3] Rozdiel medzi pohlaviami možno vysvetliť prozápalovým účinkom testosterónu u mužov, na rozdiel od protizápalového účinku estrogénu u žien.[4]

Celkový výskyt myoperikarditídy v bežnej populácii po podaní vakcín proti covidu-19 sa udáva 18,2 prípadov na milión dávok vakcíny, pričom súhrnný výskyt myoperikarditídy pre vakcíny proti covidu-19 a iné ako covid-19 je približne rovnaký. Pri vakcínach proti covidu-19 bol vyšší výskyt myoperikarditídy u tých, ktorí dostali vakcínu mRNA (22,6 prípadov na milión dávok) v porovnaní s tými, ktorí dostali vakcínu bez mRNA (7,9 prípadov na milión dávok).[1] Náchylnejší na vznik myoperikarditídy po očkovaní proti covidu-19 sú muži a mladšie vekové skupiny.[5] Najvyšší výskyt myokarditídy bol zaznamenán po druhom očkovaní (83 zo 117 pacientov bolo vo veku ≤ 30 rokov a len 15 zo 117 pacientov boli ženy).[6]

Ako myoperikarditída sa označuje perikarditída so známym alebo klinicky suspektným sprievodným postihnutím myokardu. Myokardiálne postihnutie sa zvyčajne potvrdí magnetickou rezonanciou. Klinicky sa manifestuje bolesťou na hrudníku, ktorú môžu sprevádzať príznaky ako perikardiálny trecí šelest, elevácia segmentu ST na EKG a perikardiálny výpotok. Zároveň je prítomná elevácia markerov myokardiálneho poškodenia – troponínov.[7]

Perikarditída súvisiaca s očkovaním proti covidu-19 sa typicky prejavuje miernymi klinickými príznakmi u mladých jedincov mužského pohlavia niekoľko dní po druhej alebo tretej dávke vakcíny a väčšinou sa vyznačuje rýchlym úplným zotavením.[8] Zdá sa, že u niektorých pacientov nedochádza ku kompletnému vyhojeniu, ale stav progreduje a rozvíja sa konstriktívna perikarditída.

Podobne je to aj pri myokarditíde po očkovaní proti covidu-19. Symptómy sa väčšinou prejavia v priebehu prvých dní po podaní druhej vakcíny.[9] Klinický obraz a závažnosť myokarditídy je rôzna. Najčastejšie symptómy, ktorými sa manifestuje myokarditída, sú bolesť na hrudníku, dýchavica, palpitácie alebo synkopa.[10] Niektorí pacienti môžu mať aj asymptomatický priebeh.[11] V súčasnosti nie sú dostupné údaje, či a u koľkých pacientov s prekonanou myokarditídou po vakcinácii dôjde k vývoju do chronického kardiálneho postihnutia. V krátkodobom sledovaní sa preukázalo zlepšenie alebo normalizácia ejekčnej frakcie ľavej komory u takmer všetkých pacientov po myokarditíde.[12] Údaje zo strednodobého (5 – 6 mesiacov) sledovania malého počtu pacientov preukázali normalizáciu koncentrácií troponínu, žiadne reziduálne srdcové symptómy alebo funkčné poškodenie a žiadne srdcové príhody.[13,14] Na to, aby sa zistilo pretrvávanie poškodenia myokardu, eventuálne vývoj srdcového zlyhávania či akútnych kardiovaskulárnych príhod, je potrebné dlhodobé sledovanie tejto skupiny pacientov.

Výskyt konstriktívnej perikarditídy je relatívne zriedkavý.[15] V literatúre sa uvádza rozvoj chronickej konstriktívnej perikarditídy po epizóde akútnej perikarditídy u 1,8 % pacientov. Nižší výskyt bol u pacientov s idiopatickou/vírusovou perikarditídou ako u pacientov s neidiopatickou/nevírusovou.[16] Reálny výskyt konstriktívnej perikarditídy po akútnej perikarditíde asociovanej s očkovaním proti covidu-19 nie je známy. Rovnako tak aj výskyt konstriktívnej perikarditídy pri alebo po prekonaní ochorenia covidu-19 nie je známy. V oboch prípadoch je opísaných niekoľko raritných prípadov.

Záver

Konstriktívna perikarditída asociovaná s očkovaním proti covidu-19 sa vyskytuje zriedkavo. U väčšiny opísaných prípadov konstriktívnej perikarditídy po očkovaní proti covidu-19 dôjde ku vzniku konstrikcie v relatívne krátkom čase, bez ohľadu na to, či bola predtým potvrdená diagnóza peri(myo)karditídy vo včasnom postvakcinačnom období. Je veľmi dôležité myslieť na túto diagnózu hlavne u tých pacientov, ktorí po očkovaní perimyokarditídu prekonali a v neskoršom období dôjde u nich k rozvoju syndrómu srdcového zlyhávania. Nie je vylúčené, že čím neskôr sa diagnóza konstriktívnej perikarditídy stanoví od začiatku manifestácie vo forme veľkoobehovej kongescie, tým je väčšia pravdepodobnosť vzniku spojenia perikardu s epikardom, prípadne vrastanie kalcifikátov do myokardu, čo môže znemožniť totálnu perikardiektómiu. V prípade parciálnej perikardiektómie, ako u nášho pacienta, môže zostať určitý stupeň konstrikcie, v dôsledku ktorej pretrváva mierny stupeň klinických ťažkostí.

Prehlásenie autorov o možnom konflikte záujmov
Autori nemajú konflikt záujmov.

Financovanie
Žiadne.

Prehlásenie autorov o etických aspektoch publikácie
Spracovanie kazuistiky bolo realizované v súlade s etickými štandardmi. Schvaľovanie etickou komisiou nie je potrebné.

Informovaný súhlas
Požiadavky týkajúce sa informovaného súhlasu sa nevzťahujú na tento článok.

Literatúra

1. Ling RR, Ramanathan K, Tan FL, et al. Myopericarditis following COVID-19 vaccination and non-COVID-19

vaccination: a systematic review and meta-analysis. Lancet Respir Med 2022;10:679–688.
2. Heymans S, Cooper LT. Myocarditis after COVID-19 mRNA vaccination: clinical observations and potential mechanisms. Nat Rev Cardiol 2022;19:75–77.
3. Kadkhoda K. Post RNA-based COVID vaccines myocarditis: Proposed mechanisms. Vaccine 2022;40:406–407.
4. Girón-González JA, Moral FJ, Elvira J, et al. Consistent production of a higher TH1:TH2 cytokine ratio by stimulated T cells in men compared with women. Eur J Endocrinol 2000;143:31–36.
5. Dagan N, Barda N, Balicer RD. Adverse Effects after BNT162b2 Vaccine and SARS-CoV-2 Infection, According to Age and Sex. N Engl J Med 2021;385:2299.
6. Mevorach D, Anis E, Cedar N et al. Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel. N Engl J Med 2021;385:2140–2149.
7. Adler Y, Charron P, Imazio M, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC). Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2015;36:2921–2964.
8. Collini V, Imazio M, De Biasio M, et al. Coronavirus disease 2019 vaccination-related pericarditis: a single tertiary-center experience. J Cardiovasc Med 2022;23:779–783.
9. Woo W, Kim AY, Yon DK, et al. Clinical characteristics and prognostic factors of myocarditis associated with the mRNA COVID-19 vaccine. J Med Virol 2022;94:1566–1580.
10. Gargano JW, Wallace M, Hadler SC, et al. Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices – United States, June 2021. MMWR Morb Mortal Wkly Rep 2021;70:977–982.
11. Verma AK, Lavine KJ, Lin CY. Myocarditis after Covid-19 mRNA Vaccination. N Engl J Med 2021;385:1332–1334.
12. Simone A, Herald J, Chen A, et al. Acute Myocarditis Following COVID-19 mRNA Vaccination in Adults Aged 18 Years or Older. JAMA Intern Med 2021;181:1668–1670.
13. Fronza M, Thavendiranathan P, Karur GR, et al. Cardiac MRI and Clinical Follow-up in COVID-19 Vaccine-associated Myocarditis. Radiology 2022;304:E48–E49.
14. Rosner CM, Atkins M, Saeed IM, et al. Patients With Myocarditis Associated With COVID-19 Vaccination. J Am Coll Cardiol 2022;79:1317–1319.
15. Welch TD. Constrictive pericarditis: diagnosis, management and clinical outcomes. Heart 2018;104:725–731.
16. Imazio M, Brucato A, Maestroni S, et al. Risk of constrictive pericarditis after acute pericarditis. Circulation 2011;124:1270–1275.
17. Diana D, Cardillo I, Polizzi V, et al. Two cases of constrictive pericarditis temporally associated with mRNA-1273 COVID-19 vaccination. Eur Heart J Suppl 2021;8:23(Suppl G).
18. Bain E, Guglin M. A case report of constrictive pericarditis following COVID-19 vaccination. Eur Heart J Case Rep 2023;7:ytad540.
19. Hajsadeghi S, Gholizadeh Mesgarha M, Saberi Shahrbabaki E, et al. Constrictive pericarditis following inactivated virus COVID-19 vaccine: a case report with review of the literature. Radiol Case Rep 2022;17:3774–3778.
20. Viani GM, Pedrotti P, Seregni R, et al. Effusive-constrictive pericarditis after the second dose of BNT162b2 vaccine (Comirnaty): a case report. Eur Heart J Case Rep 2022;6:ytac012.
21. Federico C, Paolo T, Carlo L, et al. A case of constrictive pericarditis after COVID-19 vaccine. J Clin Images Med Case Rep 2022;3:1827.
22. Nakanishi Y, Honda S, Yamano M, et al. Constrictive pericarditis after SARS-CoV-2 vaccination: A case report. Int J Infect Dis 2022;116:238–240.
23. Misumi I, Ogata A, Fukuda K, et al. Constrictive pericarditis following mRNA COVID-19 vaccination in a patient with systemic sclerosis. J Cardiol Cases 2022;26:97–100.
24. Demirtas H, Ozer A, Burak Gulcan M, et al. Pericardiectomy after constrictive pericarditis associated with second dose of BNT162b2 vaccine: A case report. Turk Gogus Kalp Damar Cerrahisi Derg 2024;32:97–100.
25. Sharma S, Pham S, Martin A, et al. Effusive constrictive pericarditis in the era of COVID-19. AIM Clinical Cases 2024;3:e231360.
26. Hysi I, Rebet O, Vaquette B, et al. Subacute constrictive pericarditis after mRNA COVID-19 vaccination. Arch Clin Med Case Rep 2022;6:189–192.
27. Penmetsa M, Shaik A, Nadig V. Effusive constrictive pericarditis after COVID-19 Vaccination. Circulation 2022;146(Suppl 1):A15745.

Přehledový článek | Review article

Využití magnetické rezonance srdce ve stratifikaci nemocných s dilatační kardiomyopatií

(The use of cardiac magnetic resonance in the stratification of patients with dilated cardiomyopathy)

Tatiana Štípalová[a], Roman Panovský[a], Mary Mojica-Pisciotti[b], Jan Krejčí[a]

[a] *I. interní kardioangiologická klinika, Lékařská fakulta Masarykovy univerzity a Fakultní nemocnice u sv. Anny v Brně a Mezinárodní centrum klinického výzkumu Fakultní nemocnice u sv. Anny v Brně, Brno, Česká republika*
[b] *Klinika zobrazovacích metod, Fakultní nemocnice u sv. Anny v Brně a Mezinárodní centrum klinického výzkumu Fakultní nemocnice u sv. Anny v Brně, Brno, Česká republika*

INFORMACE O ČLÁNKU

Historie článku:
Vložen do systému: 7. 12. 2024
Přijat: 9. 2. 2025
Dostupný online: 10. 6. 2025

Klíčová slova:
Dilatační kardiomyopatie
Magnetická rezonance srdce
Parametrické mapování

SOUHRN

Dilatační kardiomyopatie (DKMP) patří mezi nejčastější kardiomyopatie, její etiologie je multifaktoriální a manifestuje se především srdečním selháním se zvýšeným rizikem komorových arytmií a/nebo náhlé srdeční smrti.[1] V době manifestace a stanovení diagnózy DKMP je často přítomna těžká kontraktilní dysfunkce s remodelací obou komor, které nezřídka předchází dlouhé období asymptomatické tiché progrese onemocnění s rozvojem myokardiální fibrózy.[2] Detailní zhodnocení tohoto procesu hraje klíčovou roli v prognostické stratifikaci pacientů s DKMP a také může přispívat k optimalizaci léčby. Magnetická rezonance srdce (CMR) se stala jedním ze základních nástrojů pro hodnocení pacientů postižených nebo ohrožených rozvojem kardiomyopatií.[2] Poskytuje nejen přesné údaje o srdečních objemech, tloušťce stěny, hmotnosti a systolické funkci, ale umožňuje také neinvazivní tkáňovou charakteristiku myokardu, čímž napomáhá nejen včasné diagnostice a přesné fenotypizaci různých kardiomyopatií, ale také etiologické diferenciální diagnostice, což je nezbytné pro včasnou a individualizovanou léčbu pacientů.[2]
Účelem tohoto článku je zdůraznit užitečnost CMR v diagnostice DKMP a poskytnout přehled klinické použitelnosti standardních a novějších kontrastních technik CMR.

Keywords:
Cardiac magnetic resonance
Dilated cardiomyopathy
Parametric mapping

ABSTRACT

Dilated cardiomyopathy (DCM) is one of the most common multifactorial cardiomyopathies that manifests mostly as heart failure with an increased risk of ventricular arrhythmias and/or sudden cardiac death.[1] At the time of manifestation and establishing the diagnosis of DCM, there is often severe contractile dysfunction with remodeling of both ventricles, which is preceded by a long period of asymptomatic silent disease progression with the development of myocardial fibrosis.[2] Detailed characterization of this process plays a key role in the prognostic stratification of DCM patients and in improving clinical therapy. Cardiac magnetic resonance (CMR) has become essential for evaluating patients affected or at risk of developing cardiomyopathies.[2] CMR not only provides precise data on cardiac volumes, wall thickness, mass, and systolic function, but it also provides a non-invasive characterization of myocardial tissue, thus helping the early diagnosis and the precise phenotyping of the different cardiomyopathies, which is essential for early and individualized treatment of patients.[2] The purpose of this article is to highlight the utility of CMR in the management of idiopathic DCM and provide an overview of the clinical applicability of standard and emerging CMR techniques.

Adresa pro korespondenci: MUDr. Tatiana Štípalová, I. interní kardioangiologická klinika, Lékařská fakulta Masarykovy univerzity a Fakultní nemocnice u sv. Anny v Brně a Mezinárodní centrum klinického výzkumu Fakultní nemocnice u sv. Anny v Brně, Pekařská 664/53, 602 00 Brno, Česká republika,
e-mail: tatiana.stipalova@gmail.com
DOI: 10.33678/cor.2025.038

Tento článek prosím citujte takto: Štípalová T, Panovský R, Mojica-Pisciotti M, Krejčí J. Využití magnetické rezonance srdce v stratifikaci nemocných s dilatační kardiomyopatií. Cor Vasa 2025;67:386–392.

Úvod

Dilatační kardiomyopatie (DKMP) je charakterizována dilatací a systolickou dysfunkcí levé komory (LK), kterou nelze vysvětlit abnormálním zatížením levé komory způsobeným arteriální hypertenzí, chlopenní vadou ani ischemickou chorobou srdeční. Magnetická rezonance srdce je podle nových doporučení Evropské kardiologické společnosti (ESC) pro kardiomyopatie vydaných v roce 2023 indikována u všech nemocných s DKMP v rámci počátečního zhodnocení.[3] Magnetická rezonance srdce (CMR) pomáhá zlepšit stratifikaci rizika díky charakteristice tkání myokardu využitím techniky pozdního sycení (late gadolinium enhancement, LGE) a parametrickým mapováním. Stratifikace rizika u pacientů s DKMP definuje pravděpodobnost komorových arytmií a náhlé srdeční smrti.[3] CMR je vysoce efektivní při odhalování příčin dysfunkce LK u nově diagnostikovaných pacientů se srdečním selháním s nejasnou etiologií.[4] Dále může být cenným nástrojem také při analýze pravé komory, často špatně vizualizované echokardiografií, která se také ukázala jako důležitý nástroj ve stratifikaci rizika pacientů s DKMP.[5]

V následujících odstavcích budou představeny různé techniky CMR používané k hodnocení DKMP.

CINE sekvence

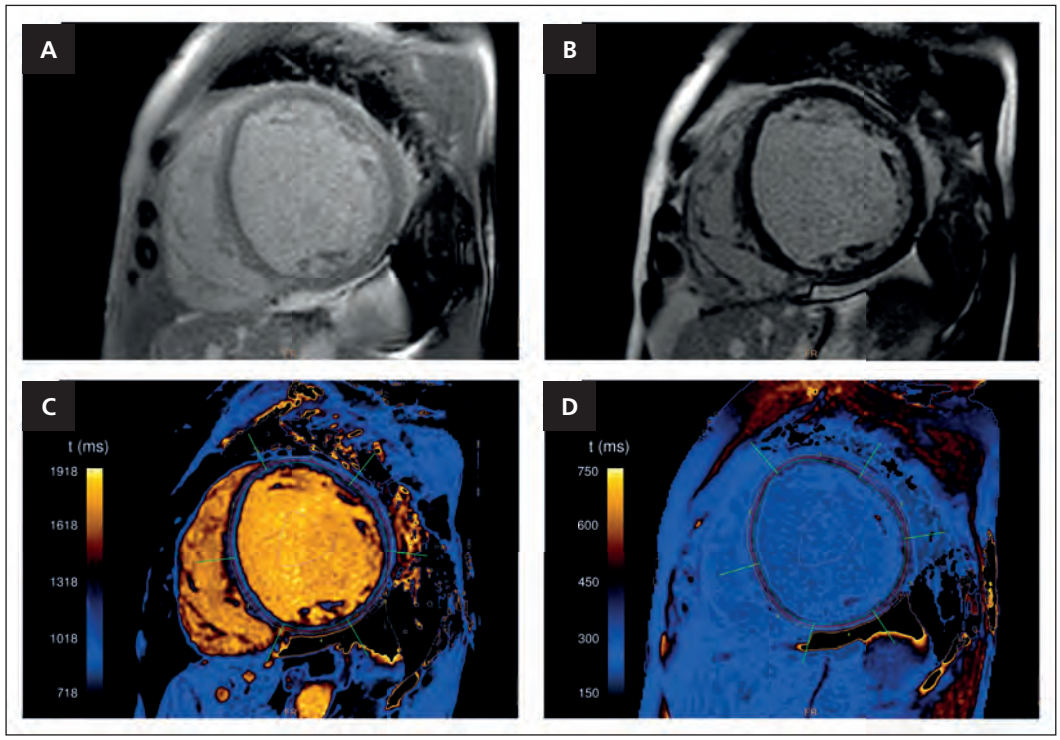
CMR je považována za zlatý standard v měření objemů srdečních dutin a stanovení funkce levé komory srdeční.[6] K zobrazení pohybu struktur srdce se v současnosti nejčastěji používá kinematická (CINE) sekvence SSFP (steady-state free precession), obvyklá frekvence je 25–30 obrazů na srdeční stah, avšak je možné získat i vyšší časové rozlišení.[7] Z obrazů pokrývajících celé komory v krátké ose se vypočítají objemy a ejekční frakce komor.[7]

LGE

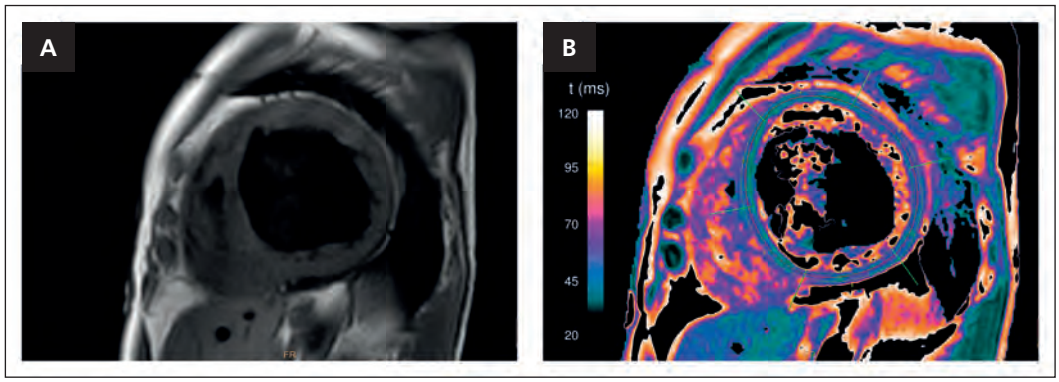
Technika pozdního sycení kontrastní látkou na bázi gadolinia je používána za účelem charakterizace tkáně myokardu a zejména k identifikaci lokalizované fibrózy nebo jizvy pomocí použití gadolinia, paramagnetické kontrastní látky.[4] Gadolinium se podává intravenózně a šíří se mimo intravaskulární prostor. Přibližně 10–15 minut po podání gadoliniové kontrastní látky jsou naskenovány T1 vážené obrazy. Zatímco ve zdravém myokardu dojde k vyplavení většiny kontrastní látky do oběhu, myokard fibroticky či jinak změněný naopak kontrastní látku retinuje.[7]

Histologické studie poukázaly na to, že u DKMP se fibróza může vyskytovat ve dvou formách.[8] Jednou z nich je ireverzibilní substituční fibróza odpovídající přítomnosti LGE, která zobrazuje oblasti myokardiálního zjizvení vzniklého v důsledku buněčné smrti myocytů.

LGE poskytuje klíčové informace s ohledem na etiologii kardiomyopatií. U DKMP je prevalence LGE až v 45 % případů a tato ložiska se vyskytují typicky midmyokardiálně (v septu či volných stěnách LK), možná je i lokalizace subepikardiální. Naopak pacienti s ischemickou etiologií vykazují subendokardiální/transmurální LGE v povodí jedné nebo více koronárních tepen.[4]



Obr. 1 – Ukázka měření nativního (A) a postkontrastního (B) T1 relaxačního času myokardu a odpovídající nativní (C) a postkontrastní (D) T1 mapy ve středním segmentu levé komory v krátké ose u pacienta s těžkou dilatací obou komor a difuzní hypokinezí. Hodnoty globálního nativního T1 času, postkontrastního T1 času a extracelulárního objemu (ECV) byly 1 098 (90) ms, 369 (32) ms a 30,4 %, v tomto pořadí.



Obr. 2 – Ukázka měření T2 relaxačního času myokardu (A) a T2 mapy (B) ve středním segmentu levé komory v krátké ose u pacienta s výraznou dilatací obou komor a difuzní hypokinezí. Bez detekce edému nebo prodloužených hodnot T2 relaxačního času. Globální T2 čas byl 53,9 (6,8) ms.

Druhá forma fibrózy je intersticiální a je způsobena akumulací kolagenu i bez buněčné smrti.[9] Tato forma fibrózy může být detekována a kvantifikována nativními relaxačními časy myokardu T1 a extracelulárním objemem myokardu (ECV).[2]

Parametrické mapování

Parametrické mapování jsou sekvence umožňující kvantifikaci relaxačních časů a prostorovou vizualizaci kvantitativních změn v myokardu.[4] K dispozici je využití T1 váženého mapování a T2 váženého mapování. Ve srovnání s konvenčním zobrazováním umožňují mapovací sekvence absolutní kvantifikaci T1 a T2 relaxačních časů (ms) pro každou tkáň, což vytváří pixelové kvantitativní mapy myokardu,[10,11] které odrážejí změny způsobené několika onemocněními myokardu (**obr. 1, obr. 2**).[12] Na rozdíl od T1 a T2 vážených snímků umožňuje mapování jak vizualizaci, tak kvantifikaci procesu onemocnění, nezávisle na tom, zda je onemocnění myokardu fokální nebo difuzní.[13]

T1 mapování

T1 mapování je technika, která měří longitudinální relaxační čas (T1) tkáně.[14] Je to doba, za kterou se tkáň vrátí do stavu magnetické rovnováhy poté, co byla narušena radiofrekvenčním impulsem.[14] Různé typy tkání mají různé hodnoty T1, což umožňuje rozlišovat a charakterizovat tkáně podle jejich magnetických vlastností.[14] T1 mapování se provádí nativně i postkontrastně, získáme díky němu informaci o nativním T1 relaxačním času myokardu, postkontrastním T1 relaxačním času myokardu a extracelulárním objemu myokardu.[6] T1 mapování dokáže identifikovat a kvantifikovat různé stavy, jako je fibróza myokardu, zánět, edém a hromadění tuku v myokardu.[14]

Extracelulární objem myokardu

ECV je měřítkem objemového podílu extracelulárního prostoru ve vztahu k celkovému objemu tkáně.[4] Vypočítá se z pre- a postkontrastního T1 mapování a hematokritu a koreluje s rozsahem intersticiálního prostoru (kde se hromadí kontrastní látka na bázi gadolinia). Nejčastějšími příčinami zvýšeného ECV jsou nekróza myokardu, intersticiální edém, fibróza a amyloidóza.[15,16] Na rozdíl od LGE, mapování ECV nevyžaduje přítomnost lokálních rozdílů v myokardu, a umožňuje tak detekci difuzních změn myokardu (tj. difuzní intersticiální fibrózy). T1 mapování a ECV umožňují kvantifikaci difuzní fibrózy a poskytují komplementární informaci k LGE. Nehomogenita tkáně způsobená difuzní fibrózou je potenciálním substrátem pro vznik život ohrožujících komorových arytmií.[4] Změny hodnot T1 se mohou objevit v raných stadiích DKMP, kdy je systolická funkce levé komory (ejekční frakce levé komory [EF LK]) jen mírně snížena.[4] T1 mapování a ECV tak mohou zlepšit stratifikaci rizika u pacientů s DKMP, zejména u těch s negativním LGE.[3]

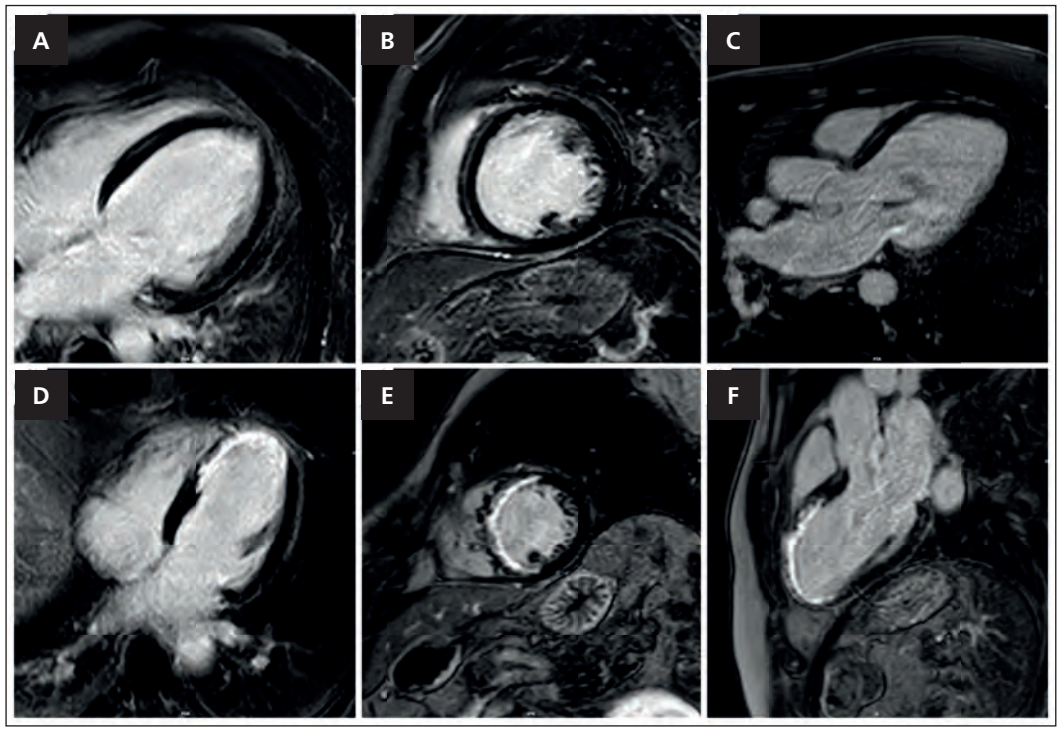
Cadour a spol.[17] provedli prospektivní longitudinální multicentrickou studii s dvouletým sledováním 225 pacientů s diagnózou DKMP. Zdokumentovali, že mapování T1 bylo nezávislým prediktorem příhod souvisejících s arytmiemi v této populaci. Rovněž bylo zjištěno, že prognostická role mapování T1 byla významně spojena se srdeční smrtí a transplantací srdce u pacientů s pozitivním i negativním LGE.[18] Puntmann a spol.[19] sledovali 637 pacientů s DKMP v prospektivní longitudinální, observační, multicentrické studii po dobu 22 měsíců. Dokumentovali, že výsledek mapování T1 je nezávislým prediktorem mortality ze všech příčin u DKMP. Nedávná metaanalýza[20] ukázala významnou prognostickou hodnotu T1 mapování v populaci 1 242 pacientů s DKMP.

T2 mapování

T2 mapování je technika, která měří transverzální relaxační čas (T2) tkáně. T2 mapování dokáže detekovat edém myokardu a následně aktivní zánět, protože relaxace T2 je přímo úměrná obsahu vody v tkáni. T2 mapování je vysoce účinné při identifikaci časného stadia DKMP, zejména pokud je morfologie myokardu obtížně odlišitelná od atletické adaptace myokardu.[21]

T2 mapování*

Kromě klasických metod mapování je k dispozici i T2* relaxační mapování, které je metodou volby pro hodnocení depozit železa v myokardu, např. u hemochromatózy. Ukládání železa v myokardu může být způsobeno i řadou



Obr. 3 – Postkontrastní snímky pozdního sycení gadoliniem (LGE). (A–C) Pacient s dilatační kardiomyopatií, vykazující významnou dilataci levé komory (LK) a difuzní hypokinezi, zejména interventrikulárního septa (IVS). Je přítomen intramurální LGE v bazální a střední části IVS, který odpovídá neischemické pozánětlivé fibróze. (D–F) Pacient po infarktu myokardu (IM) se subendokardiálním LGE apikální poloviny IVS a hrotu LK. Snímky odpovídají čtyřdutinovým projekcím (A, D), projekcím na krátkou osu (SAX) (B, E) a třídutinovým projekcím (C, F).

hematologických onemocnění (jako je talasemie, hemolytická anémie a sideroblastická anémie) nebo jinými stavy. Přetížení železem narušuje systolickou funkci levé komory, což může vést k fenotypu podobnému DKMP. Hodnota T2* rovná nebo nižší než 10 ms je spojena se závažným přetížením železem a u 98 % pacientů s talasemií s hodnotami T2* v tomto rozmezí se po jednom roce sledování rozvinulo manifestní srdeční selhání.[22]

Deformace myokardu

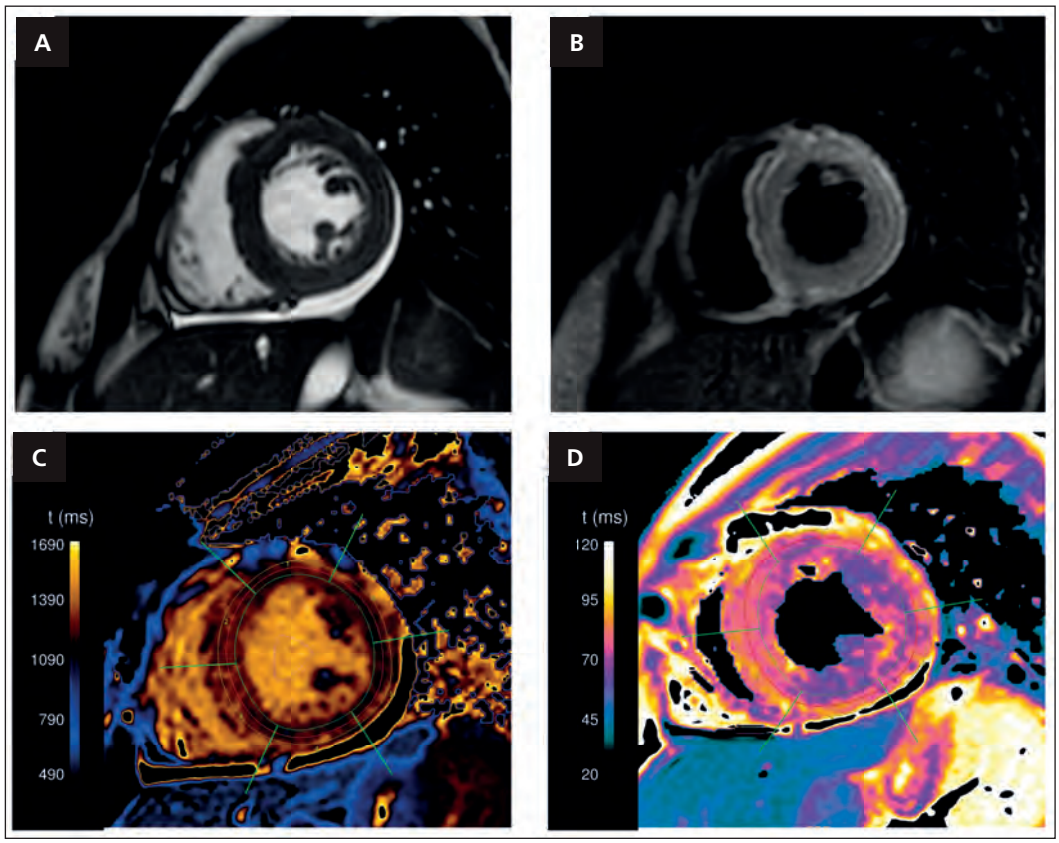
Dalším funkčním parametrem, který lze z CMR získat, je strain, který podobně jako při hodnocení pomocí echokardiografie stanovuje deformaci myokardu a je parametrem jeho funkce.[23] Rozlišujeme longitudinální, cirkumferenciální a radiální strain a dále torzi.[23] Longitudinální strain je kontrakce podél podélné osy srdce v důsledku zkrácení myokardu od baze k apexu. Cirkumferenciální strain je kontrakce po obvodu v krátké ose v důsledku koncentrického intramurálního zkrácení myokardu podél zakřivené linie rovnoběžné s povrchem epikardu.[23] Radiální strain zahrnuje zesílení myokardu v radiálním směru směrem ke středu komorové dutiny. Torze je rotační pohyb způsobený rotací bazálních segmentů ve směru hodinových ručiček a rotací apikálních segmentů proti směru hodinových ručiček.[23]

Stanovení globálního longitudinálního strainu (GLS) je nejpřesnější a nejužitečnější a zahrnuje řadu různých technik. Historicky nejstarší je metoda taggingu, která má nevýhodu v nutnosti skenování sekvence navíc. Častěji jsou využívány novější metody, tzv. tissue tracking nebo feature tracking (FT).[6] U těchto přístupů odpadá nezbytnost skenování sekvence navíc, lze k nim využít rutinně snímané CINE sekvence. Limitací je potřeba speciálního softwaru k realizaci analýzy.[6] GLS koreluje lépe s rizikem srdeční smrti, transplantace srdce a adekvátního výboje z implantabilního kardioverteru-defibrilátoru (ICD) v důsledku komorové tachykardie nebo fibrilace komor než EF LK a hodnota natriuretických peptidů (N-terminální fragment natriuretického propeptidu typu B [NT-pro BNP]) u pacientů s DKMP.[2] Je tedy považován za silný nezávislý prediktor mortality.

Přínos CMR v diferenciální diagnostice

Magnetická rezonance srdce má zásadní význam pro rozlišení ischemické a neischemické etiologie DKMP. Jak již bylo zmíněno, subendokardiální distribuce LGE odpovídající oblasti koronární tepny identifikuje ischemické poškození na rozdíl od fibrózy s midmyokardiální nebo subepikardiální distribucí, typickou pro neischemické postižení (**obr. 3**).[24]

U pacientů s akutním infarktem myokardu bez obstrukce koronárních tepen (myocardial infarction with non-obstructive coronary arteries, MINOCA) se doporučuje provedení CMR po invazivní angiografii, pokud není konečná diagnóza jasná.[25] Přínos CMR zde spočívá zejména v hodnocení tkáňové charakteristiky myokar-



Obr. 4 – CMR snímky a parametrické mapování u pacienta s perimyokarditidou a perikardiálním výpotkem. (A) Cine SAX řez na úrovni střední části LK, s normální systolickou funkcí levé a pravé komory a mírnou hypokinezí bazálních a středních segmentů přední a laterální stěny levé komory. (B) Snímek T2 STIR, ukazující edém přední a laterální stěny levé komory. (C) Nativní mapování T1 s difuzně prodlouženými relaxačními časy T1 (globální T1: 1 290 [60] ms, segmentální T1: s1: 1 293 [56] ms, s2: 1 316 [34] ms, s3: 1 316 [54] ms, s24: 67 [62] ms, s6: 1 274 [61] ms) v myokardu levé komory. (D) Mapování T2 s difuzně zvýšenými hodnotami T2 (globální T2: 79,7 [6,8] ms) a heterogenními hodnotami T2 ve stěně pravé komory a perikardu (segmentální T2: s1: 78,8 [6,7] ms, s2: 80,8 [4,8] ms) (2,8 ms, 2,3 ms). s4: 79,3 (8,1) ms, s5: 76,9 (6,6) ms, s6: 79,0 (7,3) ms. CMR – magnetická rezonance srdce.

du. Nepřítomnost typického LGE obrazu ischemického postižení má velmi vysokou negativní prediktivní hodnotu (94 %) z hlediska vyloučení ischemické etiologie.[25] Je nutno zdůraznit, že negativní nález při koronarografickém vyšetření nemusí vylučovat ischemickou etiologii kardiálního postižení. Kombinace normálního koronarografického nálezu s výsledkem CMR neprokazujícím ischemický typ LGE s velmi vysokou pravděpodobností odliší ischemickou a neischemickou etiologii kardiálního postižení.[26]

Publikované práce udávají, že až polovina případů dilatační kardiomyopatie se rozvíjí v důsledku prodělané myokarditidy. Pokud je zánět myokardu spojen s jeho dysfunkcí, označuje se jako zánětlivá kardiomyopatie (inflammatory cardiomyopathy, ICM).[11] Přechod akutního zánětu do subakutního až chronického stadia spojeného s remodelací myokardu, rozvojem fibrózy a ztrátou kontraktilní funkce myokardu vede k rozvoji dilatační kardiomyopatie.[27] CMR má zásadní význam v diagnostice myokarditidy. Původní kritéria CMR pro diagnostiku myokarditidy z roku 2009, známá jako Lake Louis Criteria, byla v roce 2018 akutalizována a doplněna především o využití T1 a T2 mapování a ECV, které umožňují detekci zejména difuzních fibrotických změn.[7] Pro potvrzení myokarditidy je potřeba splnit: T2-vážené kritérium (obraz edému na T2-vážených snímcích nebo zvýšené hodnoty T2 mappingu) a zároveň T1-vážené kritérium (pozitivní LGE, zvýšený signál T1 mappingu nebo zvýšené ECV). Pozitivita obou kritérií současně svědčí pro diagnózu myokarditidy, nicméně i splnění pouze jednoho z kritérií může svědčit pro přítomnost myokarditidy s nižší specifitou, pokud tomu odpovídá klinický obraz pacienta (**obr. 4**). [28]

Regionální a globální T2 časy jsou významně zvýšené u pacientů s myokarditidou. T2 mapování spolehlivě rozlišuje mezi biopsií prokázanou myokarditidou a zdravým myokardem u pacientů s nově vzniklým srdečním selháním.[29] T2 mapování je užitečné nejen pro stanovení diagnózy, ale také pro stratifikaci rizika.[30] Stupeň prodloužení relaxační doby T2 je spolehlivým prediktorem závažných nežádoucích srdečních příhod (MACE) a hospitalizací pro srdeční selhání.[30] T2 relaxační čas má tendenci se zkracovat po odeznění zánětu, zatímco LGE může přetrvávat.[30] Přetrvávající prodloužení T2 času po akutní fázi koreluje s výskytem MACE, hospitalizací pro srdeční selhání a s dysfunkcí LK.[30]

Prognostická stratifikace

Mezi hlavní komplikace u pacientů s neischemickou DKMP patří srdeční selhání a výskyt arytmií. Tradičně se doporučuje implantace ICD v primární prevenci náhlé srdeční smrti (SCD) na základě třídy New York Heart Association (NYHA) a EF LK. Jsou to však právě pacienti nesplňující tato kritéria, kteří by pravděpodobně měli prospěch z implantace ICD, a toto bylo reflektováno v nejnovějších doporučených postupech ESC pro léčbu komorových arytmií a prevenci SCD vydaných v roce 2022, na základě kterých je doporučena (třída doporučení IIa) implantace ICD u pacientů s neischemickou DKMP s EF LK > 35 % (EF LK < 50 %) a dvěma nebo více rizikovými faktory.[31] Mezi tyto rizikové faktory patří synkopa, přítomnost LGE, setrvalá monomorfní komorová tachykardie vyvolaná při programované elektrické stimulaci a vysoce rizikové genetické varianty.[31]

Jak již bylo zmíněno, Cadour a spol.[17] zkoumali v multicentrické prospektivní studii prediktivní hodnotu T1 a ECV u pacientů s DKMP a zjistili, že pacienti s neischemickou DKMP a srdečním selháním nebo arytmiemi měli vyšší nativní hodnoty T1 a ECV ve srovnání s pacienty s DKMP bez MACE. Zvýšená hodnota ECV zůstala jediným významným nezávislým prediktorem výskytu srdečního selhání a arytmií. Naproti tomu nativní T1 byl pouze nezávisle spojen s arytmickými příhodami, a proto by mohl být užitečnější pro výběr pacientů vhodných pro ICD. Výsledky týkající se ECV byly v souladu s dalšími pracemi. Dvě nedávné studie analyzovaly prognostickou hodnotu T1 a ECV při výskytu arytmií u pacientů s neichemickou DKMP.[32,33] Obě studie zjistily, že ECV je nejsilnější nezávislý prediktor arytmií.

Di Marco a spol.[33] poukázali na to, že mezní hodnota ECV ≥ 30 % navíc dokázala dále rozlišit arytmické riziko jak u pacientů s přítomností LGE, tak u pacientů s EF LK ≤ 35 %. ECV by proto mohlo pomoci určit, kteří pacienti s LGE mají nejvyšší riziko a mohou mít z implantace ICD největší prospěch a kteří naopak z takového zásahu pravděpodobně prospěch mít nebudou. ECV by také mohlo zlepšit rozpoznání pacientů s nízkým rizikem mezi pacienty s EF LK ≤ 35 %. Současně vyzdvihují vysokou negativní prediktivní hodnotu ECV < 30 % (99,8 %). Na základě těchto výsledků vypracovali model stratifikace rizik, založený na EF LK ≤ 35 %, přítomnosti/nepřítomnosti LGE a ECV ≥ 30 %, který identifikuje tři kategorie – s nízkým, středním a vysokým rizikem. Tento model měl vynikající prediktivní schopnosti a reklasifikoval riziko u 32 % pacientů ve srovnání s kritériem EF LK ≤ 35% použitým samostatně.[33] Umožnil dále identifikovat velkou skupinu pacientů (83 % z celé studované populace) s velmi nízkým arytmickým rizikem a 71 % pacientů s EF LK ≤ 35 %, kteří měli indikaci k preventivní implantaci ICD, byli reklasifikováni jako pacienti s nízkým rizikem.[34] Podle tohoto modelu je arytmické riziko v podstatě koncentrováno mezi pacienty s LGE i ECV ≥ 30 %; v takových případech je EF LK užitečná pro další zlepšení stratifikace rizika. Na podskupinu pacientů se středním rizikem by se měl zaměřit další výzkum s cílem identifikovat pacienty s vyšším rizikem, kteří mohou mít prospěch z preventivní implantace ICD.

Ačkoli prognostická hodnota GLS byla prokázána v předchozích studiích,[34–36] údaje o prognostické hodnotě různých typů strainů a zejména torze LK u pacientů s DKMP jsou vzácné. Ochs a spol.[37] hodnotili prognostický význam globálního longitudinálního, cirkumferenciálního (GCS) a radiálního strainu (GRS) a torze LK pomocí metody feature tracking (FT). U pacientů s DKMP vykazoval GLS přídatnou prognostickou hodnotu a napomáhá přesné stratifikaci rizika u pacientů s DKMP. Torze LK jako rotační parametr měla významnou prognostickou hodnotu, která byla však nižší než jiné deformační parametry jako GLS nebo GCS. GLS a GCS tak představují nejsilnější deformační prognostické parametry.[37]

Závěr

CMR s využitím široké škály technik, včetně parametrického mapování, poskytuje velmi přesné a diagnosticky cenné informace o srdeční anatomii a funkci. Jejich začlenění do běžné klinické praxe je klíčové v diagnostice, léčbě a prognostické stratifikaci DKMP a neodmyslitelně patří do diagnostického algoritmu u většiny pacientů se srdečním selháním.[24]

Prohlášení autorů o možném střetu zájmů
Žádný střet zájmů.

Financování
Tato publikace vznikla za podpory specifického výzkumu LX22NPO5104.

Prohlášení autorů o etických aspektech publikace
Zpracování článku bylo provedeno v souladu s etickými standardy. Schválení etickou komisí není nutné.

Literatura

1. Elliott P, Andersson B, Arbustini E, et al. Classification of the cardiomyopathies: a position statement from the european society of cardiology working group on myocardial and pericardial diseases. Eur Heart J 2007;29:270–276.
2. Merlo M, Gagno G, Baritussio A, et al. Clinical application of CMR in cardiomyopathies: evolving concepts and techniques: A position paper of myocardial and pericardial diseases and cardiac magnetic resonance working groups of Italian society of cardiology. Heart Fail Rev 2023;28:77–95.
3. Perone F, Dentamaro I, La Mura L, et al. Current Insights and Novel Cardiovascular Magnetic Resonance-Based Techniques in the Prognosis of Non-Ischemic Dilated Cardiomyopathy. J Clin Med 2024;13:1017.
4. Mitropoulou P, Georgiopoulos G, Figliozzi S, et al. Multi-Modality Imaging in Dilated Cardiomyopathy: With a Focus on the Role of Cardiac Magnetic Resonance. Front Cardiovasc Med 2020;7:97.
5. Gulati A, Ismail TF, Jabbour A, et al. The Prevalence and Prognostic Significance of Right Ventricular Systolic Dysfunction in Nonischemic Dilated Cardiomyopathy. Circulation 2013;128:1623–1633.
6. Panovský R. Stručný přehled možností a limitací magnetické rezonance srdce. Interv Akut Kardiol 2021;20:233–237.
7. Táborský M, Kautzner J, Linhart A, et al., eds. Kardiologie. Praha: Česká kardiologická společnost, 2021.
8. Gigli M, Merlo M, Graw SL, et al. Genetic Risk of Arrhythmic Phenotypes in Patients With Dilated Cardiomyopathy. J Am Coll Cardiol 2019;74:1480–1490.
9. Halliday BP, Gulati A, Ali A, et al. Association Between Midwall Late Gadolinium Enhancement and Sudden Cardiac Death in Patients With Dilated Cardiomyopathy and Mild and Moderate Left Ventricular Systolic Dysfunction. Circulation 2017;135:2106–2115.

10. Chow K, Flewitt JA, Green JD, et al. Saturation recovery single--shot acquisition (SASHA) for myocardial T1 mapping. Magn Reson Med 2014;71:2082–2095.
11. Higgins DM, Ridgway JP, Radjenovic A, et al. T1 measurement using a short acquisition period for quantitative cardiac applications. Med Phys 2005;32:1738–1746.
12. Weingärtner S, Akçakaya M, Basha T, et al. Combined saturation/inversion recovery sequences for improved evaluation of scar and diffuse fibrosis in patients with arrhythmia or heart rate variability. Magn Reson Med 2014;71:1024–1034.
13. Messroghli DR, Moon JC, Ferreira VM, et al. Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI). J Cardiovasc Magn Reson 2017;19:75. Erratum in: J Cardiovasc Magn Reson 2018;20:9.
14. Haaf P, Garg P, Messroghli DR, et al. Cardiac T1 Mapping and Extracellular Volume (ECV) in clinical practice: a comprehensive review. J Cardiovasc Magn Reson 2017;18:89.
15. Sado DM, Flett AS, Banypersad SM, et al. Cardiovascular magnetic resonance measurement of myocardial extracellular volume in health and disease. Heart 2012;98:1436–1441.
16. Ugander M, Oki AJ, Hsu L-Y, et al. Extracellular volume imaging by magnetic resonance imaging provides insights into overt and sub-clinical myocardial pathology. Eur Heart J 2012;33:1268–1278.
17. Cadour F, Quemeneur M, Biere L, et al. Prognostic Value of Cardiovascular Magnetic Resonance T1 Mapping and Extracellular Volume Fraction in Nonischemic Dilated Cardiomyopathy. J Cardiovasc Magn Reson 2023;25:7.
18. Li S, Zhou D, Sirajuddin A, et al. T1 Mapping and Extracellular Volume Fraction in Dilated Cardiomyopathy: A Prognosis Study. JACC Cardiovasc Imaging 2022;15:578–590.
19. Puntmann VO, Carr-White G, Jabbour A, et al. T1-Mapping and Outcome in Nonischemic Cardiomyopathy: All-Cause Mortality and Heart Failure. JACC Cardiovasc Imaging 2016;9:40–50.
20. Kiaos A, Antonakaki D, Bazmpani MA, et al. Prognostic Value of Cardiovascular Magnetic Resonance T1 Mapping Techniques in Non-Ischemic Dilated Cardiomyopathy: A Systematic Review and Meta-Analysis. Int J Cardiol 2020;312:110–116.
21. Mordi I, Carrick D, Bezerra H, Tzemos N. T1 and T2 mapping for early diagnosis of dilated non-ischaemic cardiomyopathy in middle-aged patients and differentiation from normal physiological adaptation. Eur Heart J Cardiovasc Imaging 2016;17:797–803.
22. Kirk P, Roughton M, Porter JB, et al. Cardiac T2* magnetic resonance for prediction of cardiac complications in thalassemia major. Circulation 2009;120:1961–1968.
23. Rajiah PS, Kalisz K, Broncano J, et al. Myocardial Strain Evaluation with Cardiovascular MRI: Physics, Principles, and Clinical Applications. Radiographics 2022;42:968–990.
24. Eichstaedt HW, Felix R, Danne O, et al. Imaging of Acute Myocardial Infarction by Magnetic Resonance Tomography (MRT) Using the Paramagnetic Relaxation Substance Gadolinium-DTPA. Cardiovasc Drugs Ther 1989;3:779–788.
25. Byrne RA, Rossello X, Coughlan JJ, et al. ESC Scientific Document Group, 2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the Task Force on the Management of Acute Coronary Syndromes of the European Society of Cardiology (ESC). Eur Heart J 2023;44:3720–3826.
26. Panovsky R, Borova J, Pleva M, et al. The unique value of cardiovascular magnetic resonance in patients with suspected acute coronary syndrome and culprit-free coronary angiograms. BMC Cardiovasc Disord 2017;17:170.
27. Poloczková H, Honek T, Chaloupka A, et al. News in diagnostics and treament of cardiomyopathies. Vnitr Lek 2023;69:89–104.
28. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation: Expert Recommendations. J Am Coll Cardiol 2018;72:3158–3176.
29. Bohnen S, Radunski UK, Lund GK, et al. Performance of t1 and t2 mapping cardiovascular magnetic resonance to detect active myocarditis in patients with recent-onset heart failure. Circ Cardiovasc Imaging 2015;8:e003073.
30. Spieker M, Haberkorn S, Gastl M, et al. Abnormal T2 mapping cardiovascular magnetic resonance correlates with adverse clinical outcome in patients with suspected acute myocarditis. J Cardiovasc Magn Reson 2017;19:38.
31. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J 2022;43:3997–4126.
32. Rubiś PP, Dziewięcka EM, Banyś P, al. Extracellular volume is an independent predictor of arrhythmic burden in dilated cardiomyopathy. Sci Rep 2021;11:24000.
33. Di Marco A, Brown PF, Bradley J, et al. Extracellular volume fraction improves risk-stratification for ventricular arrhythmias and sudden death in non-ischaemic cardiomyopathy. Eur Heart J Cardiovasc Imaging 2023;24:512–521.
34. Romano S, Judd RM, Kim RJ, et al. Feature-tracking global longitudinal strain predicts death in a multicenter population of patients with ischemic and nonischemic dilated cardiomyopathy incremental to ejection fraction and late gadolinium enhancement. JACC Cardiovasc Imaging 2018;11:1419–1429.
35. Buss SJ, Breuninger K, Lehrke S, et al. Assessment of myocardial deformation with cardiac magnetic resonance strain imaging improves risk stratification in patients with dilated cardiomyopathy. Eur Heart J Cardiovasc Imaging 2015;16:307–315.
36. Romano S, Mansour IN, Kansal M, et al. Left ventricular global longitudinal strain predicts heart failure readmission in acute decompensated heart failure. Cardiovasc Ultrasound 2017;15:6.
37. Ochs A, Riffel J, Ochs MM, et al. Myocardial mechanics in dilated cardiomyopathy: prognostic value of left ventricular torsion and strain. J Cardiovasc Magn Reson 2021;23:136.

Přehledový článek | Review article

Pelvic venous disease

Mária Rašiová[a], Martin Koščo[a], Marek Hudák[a], Veronika Pavlíková[a], Marta Bavoľárová[b]

[a] *Department of Angiology, East Slovak Institute of Cardiovascular Diseases, Faculty of Medicine, Šafárik University, Košice, Slovakia*
[b] *Department of Internal Medicine, Štefan Kukura Hospital, Michalovce, Slovakia*

ARTICLE INFO

Article history:
Submitted: 18. 10. 2024
Revised: 26. 3. 2025
Accepted: 28. 3. 2025
Available online: 11. 6. 2025

Kľúčové slová:
Inkompetencia
Kompresia
Obštrukcia
Panvové venózne ochorenie

Keywords:
Compression
Incompetence
Obstruction
Pelvic venous disease

SÚHRN

Panvové venózne ochorenie je po endometrióze druhou najčastejšou príčinou chronickej panvovej bolesti a predstavuje príčinu 10 – 20 % gynekologických vyšetrení. U žien je jeho hlavnou príčinou reflux a inkompetencia ľavej ovariálnej žily. U mužov sa ochorenie panvových žíl môže prejaviť ako varikokéla a často je dôsledkom venóznej obštrukcie v iliokaválnej oblasti. Tento článok poskytuje prehľad symptómov, prejavov, diagnostiky a liečby najčastejších príčin panvového venózneho ochorenia.

ABSTRACT

Pelvic venous disease is the second most common cause of chronic pelvic pain in women after endometriosis and accounts for 10–20% of gynecological consultations. Its main cause in women is reflux and incompetence of the left ovarian vein. In men, pelvic venous disease can manifest as varicocele and is often the result of venous obstruction in the iliocaval region. This article provides an overview of the symptoms, signs, diagnosis, and treatment of the most common causes of pelvic venous disease.

Introduction

Pelvic venous disease is a spectrum of symptoms and signs arising from the pelvic veins, namely, gonadal veins, internal iliac veins, and their tributaries, pelvic venous plexuses, and their drainage pathways including the left renal vein, common iliac veins, inferior vena cava, and pelvic escape points.[1–4]

The disease spectrum includes symptoms arising from reflux, most commonly from the gonadal and internal iliac veins, and compression, usually of the left renal or left common iliac vein.[4] Other causes of pelvic venous disease include inferior vena cava thrombosis/aplasia or iliac vein obstruction. The hemodynamic consequence is venous hypertension, which has various clinical manifestations, such as left flank/abdominal pain and hematuria (symptoms typical for uncollateralized left renal vein compression), chronic pelvic pain (typically associated with primary reflux/incompetence of the ovarian/internal iliac veins), venous claudication (symptoms typical for obstruction of the common iliac veins or inferior vena cava), and symptomatic vulvar, perineal and lower extremity varices in atypical or typical distribution.[4] Similar symptoms may arise from different causes (e.g., chronic pelvic pain may arise from primary reflux in the left ovarian vein, left common iliac vein compression, or left renal vein compression), and a single anatomic abnormality may lead to different symptoms (e.g., left renal vein compression may be asymptomatic, associated with left flank/abdominal pain and hematuria, or chronic pelvic pain). This can lead to diagnostic and therapeutic errors and suboptimal therapeutic outcomes.[4]

The American Vein and Lymphatic Society International Working Group on Pelvic Venous Disorders has proposed a classification of the umbrella term "pelvic venous disease".[4] This classification is based on dominant symptoms, area of varicose veins, its pathophysiology and considers the anatomical zones of the abdomen and pelvis. The anatomical zones of the abdomen and pelvis are arranged in

Address: Doc. MUDr. Mária Rašiová, PhD., Department of Angiology, East Slovak Institute of Cardiovascular Diseases, Faculty of Medicine, Šafárik University, Ondavská č.8, 04011 Košice, Slovakia, e-mail: maria.rasiova@upjs.sk
DOI: 10.33678/cor.2025.059

Please cite this article as: Rašiová M, Koščo M, Hudák M, et al. Pelvic venous disease. Cor Vasa 2025;67:393–401.

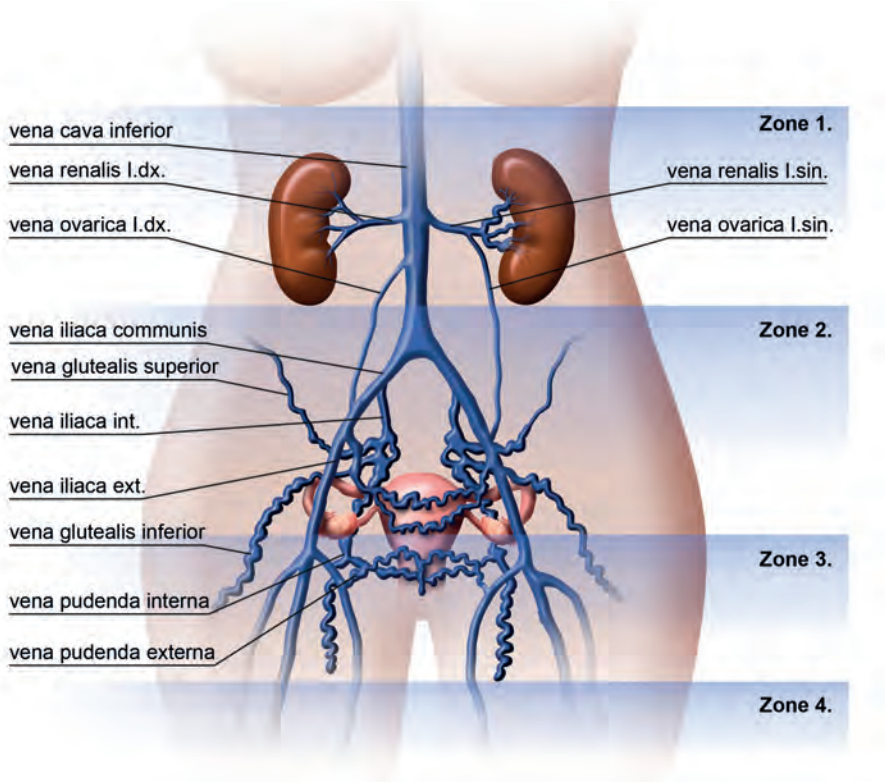


Fig. 1 – Anatomical zones of the abdomen and pelvis in relation to the symptoms–varices–pathophysiology (SVP) classification. It includes symptoms and varices associated with zones 1 (left renal vein), 2 (gonadal vein, internal iliac veins, and venous plexuses), 3 (extrapelvic veins of pelvic origin arising in the pelvis and refluxing through the pelvic escape points to the genitalia, perineum area and lower extremity veins), and 4 (superficial and deep veins of the lower limbs classified according to CEAP classification). Ext. – externa; int. – interna. Modified from 4 (an open access article published under the CC BY-NC-ND license) and drawn by Ivan Hořejší.

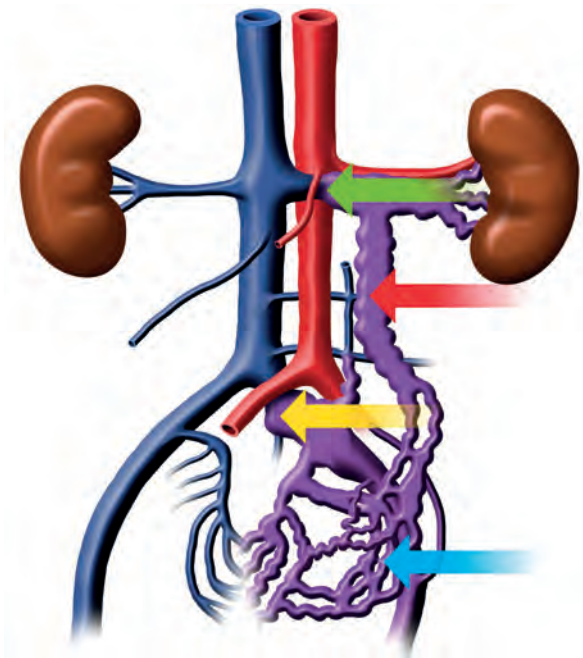


Fig. 2 – Main causes of pelvic venous disease. Purple color shows areas of venous hypertension. Green arrow: left renal vein compression between the aorta and the superior mesenteric artery; red arrow: reflux and incompetence of the left ovarian vein; yellow arrow: left common iliac vein compression by overlying right common iliac artery; blue arrow: reflux in left internal iliac vein. Modified according to 7, 9 and drawn by Ivan Hořejší.

descending order and include symptoms and varices associated with the left renal vein (zone 1); gonadal vein, internal iliac vein, and pelvic venous plexuses (zone 2) and extrapelvic veins of pelvic origin (zone 3) (**Fig. 1**). A schematic image of the causes of pelvic venous disease is shown in **Figure 2** and **Table 1** shows the anatomical zones included in the symptoms–varices–pathophysiology (SVP) classification.

Anatomy and clinical presentation of pelvic venous disease

The pelvic venous system is complex. The pelvic venous system parietal tributaries run alongside the arteries and could have various anatomical variations.[5,6] The visceral tributaries are variable and are formed by avalvular venous plexuses that drain partly into the avalvular internal iliac veins and partly into the gonadal veins.[2] The venous plexuses are interconnected, which results in a variability of symptoms. They consist of the rectal plexus (partially draining into the portal vein), the vesical plexus, the prostatic plexus in men, and the uterine and vaginal plexus in women, often collectively called the uterovaginal plexus.[7] The anatomy of the pelvic veins and ovarian veins is shown in **Figure 3**.

Most patients with pelvic venous disease are asymptomatic or have minor pelvic symptoms.[3] Asymptomatic pelvic varices have been reported in 38–47% of patients

Table 1 – Classification of pelvic venous disease according to the American Vein and Lymphatic Society International Working Group on Pelvic Venous Disorders[4]

(S) Symptoms	(V) Varices	(P) Pathophysiology
S0: no symptoms	**V0**: nonabdominal, pelvic, or extra-pelvic varices of pelvic origin	**Anatomy** Inferior vena cava (IVC) Left renal vein (LRV) Gonadal vein[1] (GV) Common iliac vein[1] (CIV) External iliac vein[1] (EIC) Internal iliac vein[1] (IIV) Pelvic escape vein[2] (PELV)
S1: renal symptoms of venous origin	**V1**: renal hilar varices	
S2: chronic pelvic pain of venous origin	**V2**: pelvic varices	
S3: extrapelvic symptoms of venous origin a. Localized symptoms associated with external genitalia veins (vulva and scrotum) b. Localized symptoms associated with pelvic origin veins of the leg c. Venous claudications	**V3**: extrapelvic varices of pelvic origin a. Genital varices (vulvar varices and varicocele) b. Varicose veins of pelvic origin extending to the thigh	**Hemodynamics:** Obstruction: thrombotic/non-thrombotic (O) Reflux: thrombotic/non-thrombotic (R) **Etiology** Thrombotic (T) Non-thrombotic: reflux, proximal obstruction, or external compression (NT) Congenital: vascular malformations (C)

[1] Further subdivision into left, right, and bilateral. [2] Includes inguinal, obturator, pudendal, and/or gluteal points.

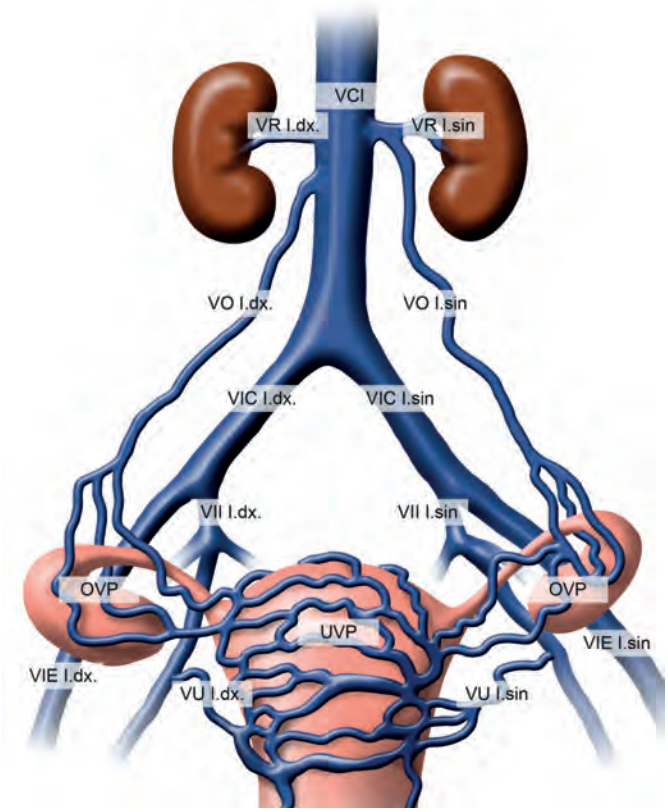


Fig. 3 – Pelvic and ovarian venous anatomy and venous plexuses. The uterine venous plexus (UVP) is drained by the right (VU l.dx.) and left uterine vein (VU l.sin.) into the internal iliac veins (VII), which have anastomoses with the external iliac veins (VIE), and the venous flow is directed to the common iliac veins (VIC). In the upper part, the UVP forms anastomoses with the ovarian venous plexus (OVP), which is drained into the ovarian veins (VO). Blood from the VO l.sin. is drained by the left renal vein (VR l.sin.), whereas blood from the right ovarian vein (VO l.dx) is drained by the inferior vena cava (VCI); however, in 10% of cases, it can drain into the right renal vein. The venous flow from the rectal, and vesicular venous plexuses is drained mainly into the VII. Modified according to 7, 9.

on computed tomography or magnetic resonance imaging.[5] Left iliac vein compression (May-Thurner syndrome) may be present in one-quarter to one-third of the population. Similarly, left renal vein (LRV) compression (nutcracker phenomenon) is common in healthy individuals.[8] Therefore, interpretation of anatomical findings is important in the context of the patient's symptoms and signs.

According to the pathophysiology and dominant clinical picture, pelvic venous disease can be divided into four main types, which can be combined with each other.

Pelvic venous disease associated with left renal vein compression

The LRV is located between the aorta and the superior mesenteric artery (SMA), and the narrow space between these structures leads to compression of the LRV (nutcracker phenomenon/syndrome). Causes of compression include a sharp angle between the SMA and the aorta, often due to loss of retroperitoneal fat during weight loss, compression due to lymphadenopathy, malignancy, pregnancy, severe lordosis, or renal ptosis. Posterior compression (posterior nutcracker phenomenon/syndrome) results from LRV compression between the aorta and the vertebral body. Patients may be asymptomatic (nutcracker phenomenon). Collateralized compression (via the perirenal collaterals, lumbar plexus, and left gonadal vein) causes hypertension in the pelvic venous plexuses. If the compression is not collateralized, symptoms are related to renal venous hypertension (micro- or macrohematuria due to rupture of peripelvic and periureteral varices and/or abdominal/left flank pain). Orthostatic proteinuria is explained by nephron damage due to venous hypertension.

Pelvic venous disease associated with reflux and incompetence of the ovarian vein

According to the American College of Gynecology and Obstetrics, chronic pelvic pain is noncyclical pain lasting at least 6 months, localized in the pelvis, anterior abdomi-

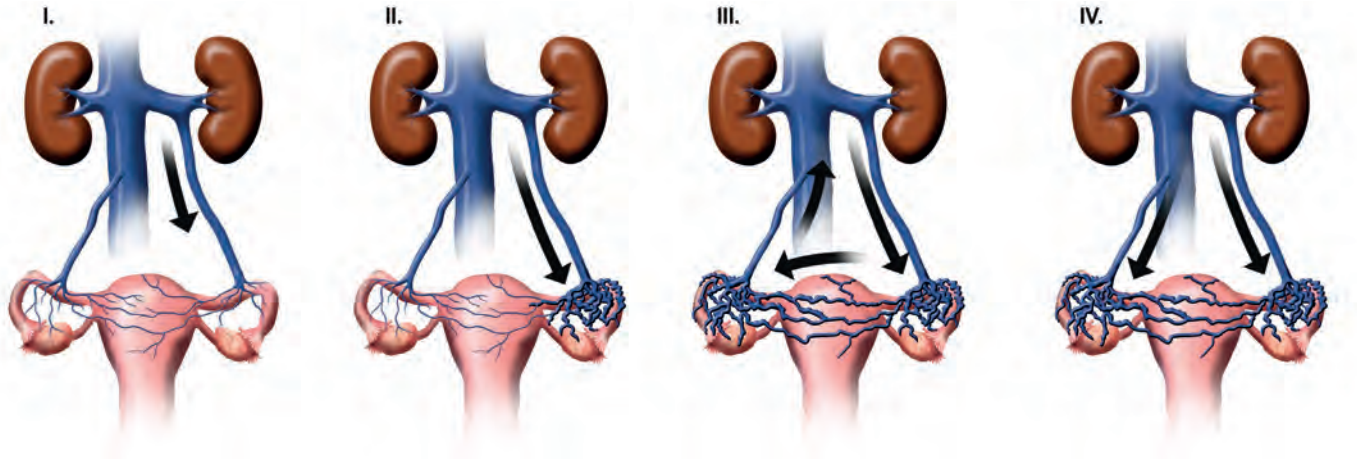


Fig. 4 – Retrograde flow in the vena ovarian vein (modified from 16).
I. Retrograde flow in the left ovarian vein does not extend into the parauterine veins.
II. Retrograde flow in the left ovarian vein with extension into the ipsilateral parauterine veins.
III. Retrograde flow in the left ovarian vein with extension into the contralateral parauterine veins.
IV. Retrograde flow in both ovarian veins.

nal wall, umbilical region, or disabling pain in the lumbosacral region requiring medical assistance.[10] Its most common vascular cause in women is reflux and incompetence of the ovarian vein spreading to the pelvic venous plexuses. Chronic pelvic pain, a sensation of dull heaviness or fullness, has variable intensity and is usually localized asymmetrically.[10] Acute severe pain may also occur.[1] Pain typically worsens during menstruation, pregnancy, with prolonged standing, and at the end of the day.[1] Postcoital pain radiates to the anus and takes several hours to resolve.[5,12] Dysmenorrhea, urological problems (dysuria, pollakisuria), rectal discomfort, and ovarian tenderness may also be present. Associated symptoms are nonspecific and include headache, back pain, bloating, nausea, and abdominal cramping.[9,11] Symptoms are often accompanied by depression and anxiety.[5] The incidence of pelvic pain increases with the number of pregnancies, and after menopause symptoms weaken or even disappear.[9]

Predisposing factors include uterine retroversion, multiple pregnancies and family history of varices. More frequent reflux in the left ovarian vein is a consequence of its greater length and perpendicular flow into the LRV, in contrast to the right ovarian vein which is shorter, and enters the inferior vena cava at an oblique angle.[1,2] Absent valves have been documented in 13–15% of women in the upper part of the left ovarian vein and in 6% of women in the upper part of the right ovarian vein.[13–15] The degrees of the retrograde blood flow extension originating from the left ovarian vein into pelvic veins are shown in **Figure 4**. Estrogens lead to the dilation of ovarian veins, and a negative effect of progesterone on venous valves has been documented. During menstruation, the ovarian veins are exposed to significantly higher estrogen concentrations compared with the estrogen concentration in the peripheral blood.[12] The increased risk of chronic pelvic pain in multiparous women may be attributed to hormonal changes during pregnancy, increased capacity, dilation, and incompetence of the pelvic veins, as well as impaired venous drainage due to uterine pressure.

Pelvic venous disease associated with proximal venous compression and obstruction

Compression of the left common iliac vein by overlying right common iliac artery against the lumbar vertebrae (May-Thurner syndrome) cause reflux and retrograde blood flow in the ipsilateral left internal iliac vein with venous drainage into the pelvic venous plexuses and contralateral iliac veins. There are also variants of compression of the right common iliac vein or compression of the inferior vena cava (in the case of a high aortic bifurcation).[1,13,17,18] In addition to chronic pelvic pain, symptoms of compression/obstruction in iliocaval region also include venous claudication, limb swelling, varicose veins, and leg ulcers.[16]

Pelvic venous disease associated with extrapelvic varices of pelvic origin

Pelvic venous hypertension may cause vulvar and perineal varices and primary or recurrent varices of the lower limbs, mainly in the gluteal and posteromedial region of the thigh (**Fig. 5**).[3] About one third of women with pelvic venous disease has vulvar varices, and up to 90% of women have leg varices in a typical or atypical location.[19] These varices are the result of pelvic venous reflux propagation through pelvic escape points. Franceschi et al. described six pelvic escape points including the perineal point: reflux through the pudendal vein; obturator point: reflux through the obturator vein; upper gluteal point: reflux through the superior gluteal vein; lower gluteal point: reflux through the lower gluteal vein; inguinal point: reflux through the veins of the round ligament of the uterus and clitoral point: reflux through the dorsal vein of the clitoris.[20] Vulvar varicosities are mostly caused by the reflux through the pudendal veins, while perineal, gluteal and posterior thigh varices are mostly caused by internal iliac vein reflux.[3] There is a strong association between hemorrhoids and internal iliac vein reflux.[3]

Table 2 – Findings supporting the left renal vein compression at the aortomesenteric angle[8,11,21,22]

Modality	Finding
Ultrasonography	Ratio between the PSV in the aortomesenteric angle and PSV in the renal hilum >4–5. (The ratio is higher in the standing position.)
CT-venography **MR-venography**	Ratio between renal vein diameter in the renal hilum and its diameter in the aortomesenteric area ≥4.9. Beak sign on axial images (sudden narrowing or interruption of the LRV in the SMA area). Left renal vein beak angle (angle of widening after narrowing at the aortomesenteric angle) >32°. Aortomesenteric angle <35°[21], <41°.[22] Dorsolateral torsion of the left kidney. Signs of pelvic congestion and dilatation of the left gonadal vein.
Catheter venography and IVUS	Renocaval gradient >3 mmHg. Renocaval gradient >1 and ≤3 mmHg with collateral veins.

IVUS – intravascular ultrasonography; LRV – left renal vein; PSV – peak systolic velocity; SMA – superior mesenteric artery.

Diagnosis of pelvic venous disease

Before diagnosing pelvic venous disease as a cause of chronic pelvic pain, all alternative pathologies should be ruled out. Differential diagnosis includes diseases of the urinary tract, digestive tract, musculoskeletal system, neurological disorders, gynecological problems, and mental health disorders. Ultrasonography (US) has limited sensitivity, lacks a method for imaging pelvic venous reflux, and cannot visualize venous valves. In addition, definitive diagnostic criteria for subtypes of pelvic venous disease are lacking, and radiological findings in symptomatic and asymptomatic patients often overlap.

Diagnosis of pelvic venous disease arising in zone 1 (renal region)

The diagnostic options are shown in **Table 2**. Patients should be adequately hydrated, as insufficient hydration may lead to overestimation of the degree of LRV compression.[6] US determines the ratio between the peak systolic velocity (PSV) in the LRV at the aortomesenteric angle and the PSV in the LRV at the renal hilum. The angle between the aorta and the SMA is determined from CT venography (CTV) and MR venography (MRV) (normal value 45–90°).[21] As the absolute diameters of the LRV vary, the ratio between the renal hilum LRV diameter and its diameter in the aortomesenteric segment is used.[1] Retrograde venography with/without intravascular ultrasonography (IVUS) provides information about the pressure gradient, collaterals veins, flow pattern and left gonadal vein. Normal pressure gradient between the LRV and inferior vena cava is <1 mmHg.[16] However, even asymptomatic patients may have renocaval pressure gradients ≥ 3 mmHg, and symptomatic patients may have a pressure gradient < 3 mmHg after collateral circulation is established. All examinations should be conducted in the left lateral position, as the supine position may lead to false-positive results. Patients examined with IVUS had a 55% significant LRV stenosis when examination was performed in the supine position compared with a 10% stenosis when examination was carried out in the left lateral position.[2] Findings supporting LRV compression are shown in **Figures 6, 7** and **8**. CTV findings of the posterior LRV vein compression between the aorta and the vertebral body shown in **Figure 9**. **Figures 10** and **11** show US findings of LRV vein

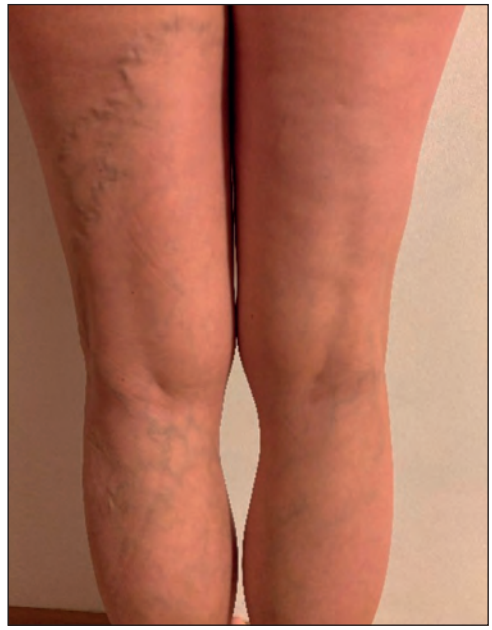


Fig. 5 – Atypical left posterior thigh varices due to pelvic reflux propagation through pelvic escape points.

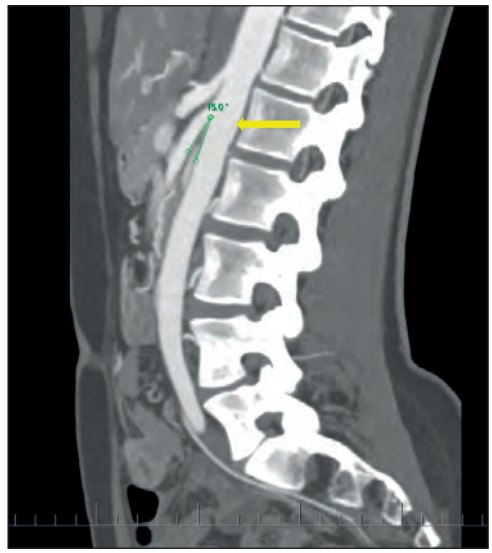


Fig. 6 – CT-venography findings of the left renal vein compression. Aortomesenteric angle = 15° (archive of the VÚSCH).

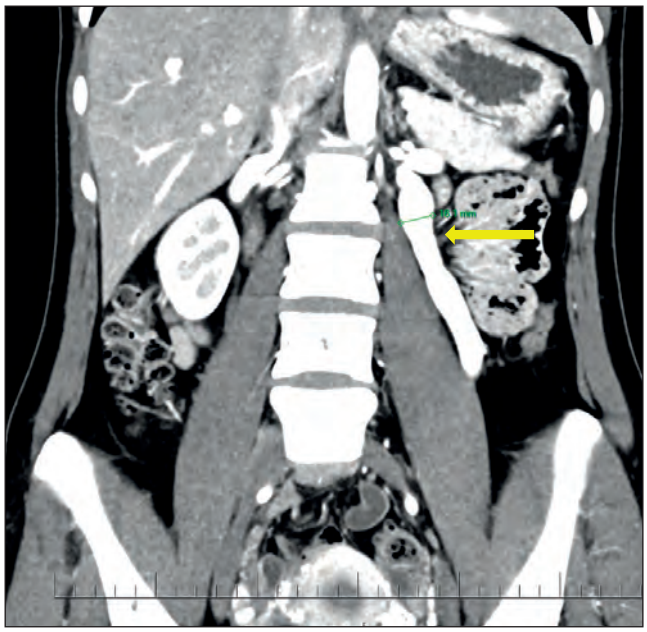


Fig. 7 – CT-venography findings of the left renal vein compression with diameter of dilated left ovarian vein = 16.1 mm (archive of the VÚSCH).

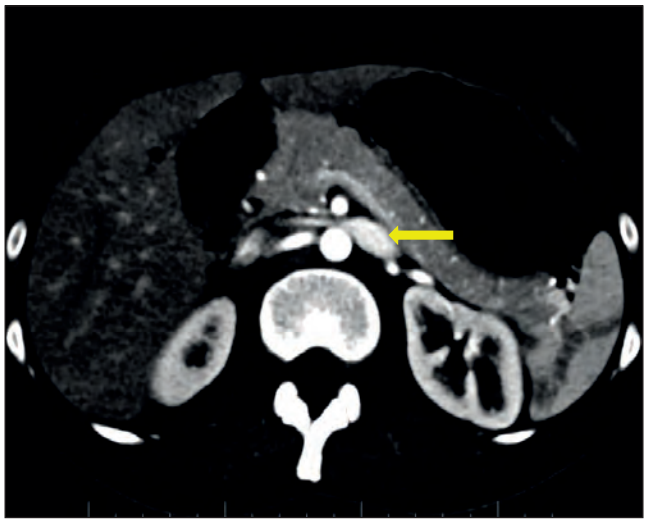
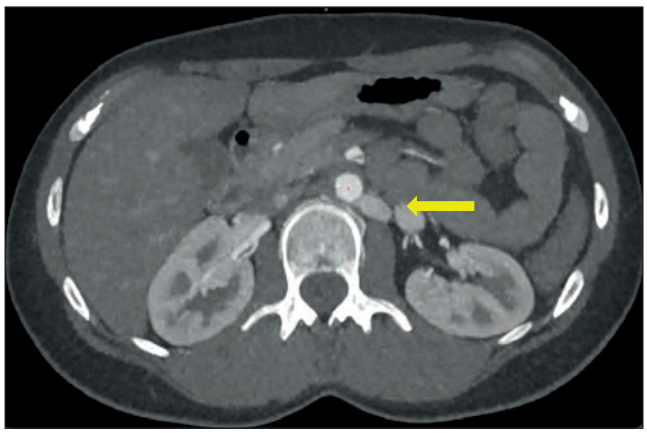


Fig. 8 – CT-venography findings of the left renal vein compression. Beak sign of the left renal vein (archive of the VÚSCH).



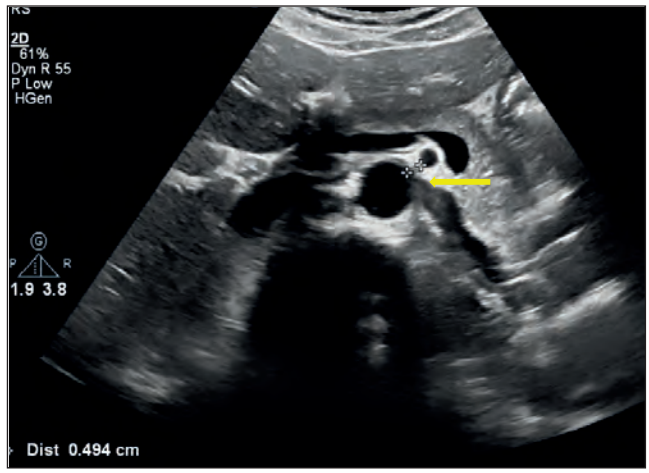


Fig. 10 – US findings of suspected left renal vein compression in supine examination (yellow arrow indicates suspected beak sign of the left renal vein). The distance between the aorta and the superior mesenteric artery is marked (archive of the VÚSCH).

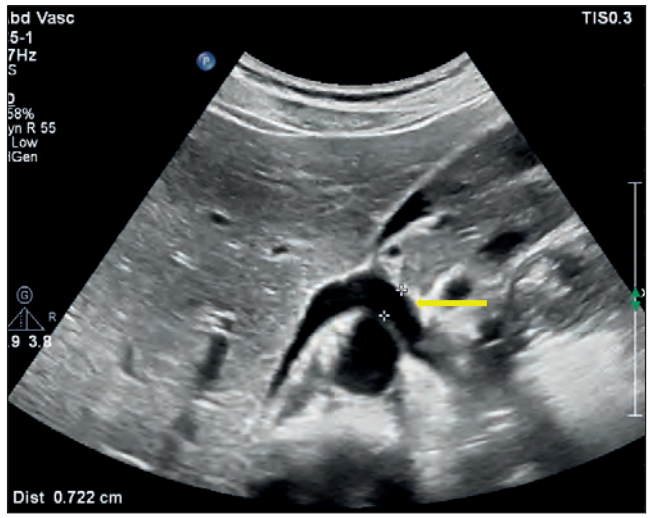


Fig. 11 – US findings of suspected left renal vein compression when the examination is performed in the left lateral position (yellow arrow indicates the absence of left renal vein compression). The diameter of the left renal vein is marked (archive of the VÚSCH).

compression when the examination is performed in the supine and in the left lateral position.

Diagnosis of pelvic venous disease arising in zone 2 (gonadal veins, internal iliac veins, and pelvic venous plexuses)

Diagnostic findings supporting pelvic venous disease arising in zone 2 are listed in **Table 3**. Transvaginal US allows better visualization of the pelvic veins and is not affected by obesity and flatulence.[3] Reflux in the pelvic and ovarian veins during the Valsalva maneuver is examined in the reverse Trendelenburg and standing position.[12] An ovarian vein diameter of 6 mm on transabdominal US is associated with a 96% positive predictive value for pelvic varices.[23,24]

Fig. 9 – CT-venography findings of the posterior left renal vein compression between the aorta and the vertebral body (posterior nutcracker phenomenon/syndrome) (archive of the VÚSCH).

Table 3 – Findings supporting the diagnosis of pelvic venous disease arising in zone 2[1,3,13,16,29,30]

Modality	Finding
Ultrasonography	Ovarian vein diameter >6 mm. Diameter of tortuous pelvic veins >5 mm. Slow pelvic vein/ovarian vein blood flow ≤3 cm/s or reversed caudal flow. Dilated arcuate veins in the myometrium communicating between the bilateral pelvic varices.
CT-venography **MR-venography**	At least four ipsilateral tortuous parauterine veins of different calibers, at least one with a diameter >4 mm or an ovarian vein diameter >8 mm.
Catheter venography	Ovarian vein diameter >6 mm with proven reflux. Contrast retention >20 s. Engorgement of the pelvic venous plexuses and/or opacification of the ipsilateral (or contralateral) internal iliac vein. Filling of vulvovaginal and femoral varices.

The sensitivity of MRV, preferred for its absence of ionizing radiation, is higher than US, but lower than catheter venography.[12] MRV and CTV should be performed in the reverse Trendelenburg position, as the results may be underestimated when examined in the supine position. CTV is not the primary imaging modality in women of reproductive potential; but it can exclude other pelvic pathologies and compressive syndromes (including LRV compression and left common iliac vein compression).[12]

Catheter venography (selective ovarian and iliac venography) during the Valsalva maneuver and in the reverse Trendelenburg position is performed in patients with a strong clinical history, inconclusive results of noninvasive investigations, and before endovascular treatment.[25] Beard's criteria include maximum ovarian vein diameter (normal < 5 mm; mildly dilated = 5–8 mm; severely dilated > 8 mm); time to resolution of contrast (0, 20, and 40 s) and degree of perfusion (normal = veins are small and straight; moderate = veins are tortuous; severe = veins are very tortuous and wide). Each criterion is scored from 1 to 3 points. A final score > 5 points determines the diagnosis of pelvic venous disease with 91% sensitivity and 89% specificity.[26]

If left common iliac vein compression by the right common iliac artery is suspected, a sufficiently hydrated patient should be examined in a semi-sitting position at 45°.[17,18] Suspicion arises when the ratio of PSV at the site of the stenosis and proximal to the compression is > 2.5 and in the absence of phasic venous flow distal to the compression.[27] Other examinations include CTV, MTV, IVUS, and catheter venography with a pressure gradient determination between the right and left common iliac veins and between inferior cava vein and left common iliac vein.[18,19,28]

Diagnosis of perineal varices and lower limb varices of pelvic origin

In the case of vulvar and perineal varices, the pelvic escape points and varices of the lower limbs should be examined by US. Further diagnostics is directed toward determining the etiology of the varices (inferior vena cava obstruction, left common iliac vein compression, LRV compression, ovarian vein incompetence, etc.).

Treatment of pelvic venous disease

Treatment of left renal vein compression and left common iliac vein compression

Treatment of LRV compression in the aortomesenteric angle depends on the patient's age, the cause of the compression, and the symptoms. Conservative treatment is recommended for patients younger than 18 years and for patients with mild and tolerable symptoms. In children, symptoms may resolve due to the increase of adipose tissue between the aorta and the SMA and also due to the collateral flow formation. Conservative treatment with an emphasis of weight gain should be the first step in treating all patients with a low body weight (body mass index <18.5 kg/m^2).[25]

In patients with severe hematuria, anemia, and intense pelvic pain (patients aged < 18 years with pain lasting > 24 months and in adults with pain lasting > 6 months), invasive treatment is considered.[14]

The first choice of surgical treatment is LRV transposition with LRV reimplantation more distally into the inferior vena cava.[14,25] Left gonadal vein transposition into the left iliac vein can be an alternative in selected patients who do not have May-Thurner syndrome.[25] In the posterior LRV compression, anterior transposition of the LRV is performed.[14]

Compared to stenting for left common iliac vein compression, the LRV stenting is controversial. It is associated with risk of stent migration (due to the short length of the vein, changes in vein diameter when changing the patient's position or during the Valsalva maneuver).[14,25] Therefore, stenting is not recommended as a primary treatment for LRV compression and open interventions are considered safer options.[25] Left ovarian vein embolization should not be done, as the left ovarian vein serves as a collateral pathway, and symptoms of renal venous hypertension may worsen following the procedure.[2,9,31]

For mild symptoms of left common iliac vein compression by the right common iliac artery, conservative treatment is recommended. For moderate and severe symptoms of compression (CEAP C4–6), angioplasty and stenting are recommended. Symptom relief after endovascular treatment was noted in 68–100% of women; however, 6–32% of women did not report significant pain improvement.[5,9,32,33]

Treatment of pelvic venous disease arising from reflux in ovarian veins, internal iliac veins, and pelvic venous plexuses

Pharmacological treatment with micronized purified flavonoid fraction (MPFF) has protective and tonic effects on the vein wall and a good clinical effect of MPFF treatment was demonstrated.[1,12,34–37] MPFF reduced the severity of pelvic symptoms, and a dose of 1,000 mg twice daily was associated with faster symptom resolution.[35]

The accepted treatment is analgesics, including short-term/intermittent treatment with nonsteroidal anti-inflammatory drugs.[12] The beneficial effects of gabapentin and amitriptyline were documented.[38] Pain relief was greater in patients who were treated with gabapentin alone or in combination with amitriptyline than in patients who received amitriptyline alone.[38] Medoxyprogesterone and the gonadotropin-releasing hormone analog goserelin may provide short-term relief of symptoms, although symptom improvement is often not permanent.[5] Furthermore, a stable effect 9 months after medoxyprogesterone treatment was achieved only in combination with psychotherapy.[39] Long-term use of hormone therapy is not recommended because of undesirable side effects (weight gain, pseudomenopausal symptoms including bone loss).[1,5,9,12,32] In case of pharmacotherapy failure in patients with chronic severe pelvic pain caused by reflux in the gonadal veins, internal iliac veins and their tributaries, endovascular treatment with transcatheter occlusion of the refluxing veins is considered.[3,33] According to the Society for Vascular Surgery and the American Venous Forum, embolization in this case is recommended with level 2B evidence.[40] However, this recommendation is based on empirical data, since the results of many published studies are limited by their heterogeneity and insufficient long-term follow-up.[9] Various agents are used in embolization, such as coils, plugs, liquid adhesives, and sclerotherapeutic agents.[3,5] Although no data support the superiority of one method over another, coils with or without liquid sclerosing agents are commonly used.[13] The entire length of the ovarian vein is embolized. The decision to perform unilateral or bilateral ovarian vein embolization remains a topic of debate.[2,41] Technical success was documented in 96–100% of patients, with complete or partial improvement of symptoms occurring in 68–100% of patients and with recurrence in 32% of patients. Small studies have reported that embolization has no impact on reproductive capacity.[9,42]

Embolization of parts of the internal iliac veins or their insufficient tributaries can be performed together with ovarian vein embolization or in a deferred treatment procedure.[1,9] Complications occur in 3.1–4.4% of patients and include coil migration (into the right ventricle and pulmonary circulation), vein perforation, local phlebitis, deep vein thrombosis, and contrast reactions.[5] Complications rise to 14.8% if self-limiting postembolization abdominal discomfort (pelvic heaviness and pain, low back pain, and fever) is considered a complication.[5] Coil migration is more common during embolization of the internal iliac veins and their tributaries; therefore, some authors prefer sclerotherapy in this area.[5] Surgical treatment, such as retroperitoneal or laparoscopic ovarian vein ligation/resection is not recommended.[2]

Treatment of perineal and lower limb varices of pelvic origin

Compression therapy using compression stockings is advised for lower limb varices of pelvic origin. Direct percutaneous sclerotherapy is used to treat atypical varices in the perineum, vulva, and posterior thigh. Coiling is not suitable in these areas, as it may cause patient discomfort.[13] For patients with lower limb varices of pelvic origin who do not exhibit symptoms of pelvic venous disease, initial treatment with a minimally invasive endovascular procedure or ligation of pelvic escape points is recommended.[3]

Conclusions

Pelvic venous disease encompasses signs and symptoms pathophysiologically caused by various diseases that result in pelvic venous hypertension. All alternative pathologies should be excluded before diagnosing pelvic venous disease as a cause of chronic pelvic pain. Determining the exact cause of pelvic venous disease and subsequent treatment is a challenge in daily practice. There is a need to establish diagnostic criteria and treatment strategies supported by prospective studies for all subunits of pelvic venous disease.

Conflict of interest
None.

Funding
This publication was supported by a grant from Scientific Grant Agency of Slovakia VEGA 1/0609/24 and by the internal scientific grant system Pavol Jozef Šafárik University vvgs-2024-3265.

Ethical statement
This review article is based on previously published literature. The authors affirm that this manuscript adheres to the ethical standards of academic publishing.

Authors' contributions
All authors contributed equally to the manuscript, read and approved the final version of the manuscript.

References

1. Knuttinen MG, Xie K, Jani A, et al. Pelvic venous insufficiency: imaging diagnosis, treatment approaches, and therapeutic issues. AJR Am J Roentgenol 2015;2004:448–458.
2. Bałabuszek K, Toborek M, Pietura R. Comprehensive overview of the venous disorder known as pelvic congestion syndrome. Ann Med 2022;54:22–36.
3. De Maeseneer MG, Kakkos SK, Aherne T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2022 Clinical Practice Guidelines on the Management of Chronic Venous Disease of the Lower Limbs. Eur J Vasc Endovasc Surg 2022;63:184–267.
4. Meissner MH, Khilnani NM, Labropoulos N, et al. The Symptoms-Varices-Pathophysiology classification of pelvic venous disorders: A report of the American Vein & Lymphatic Society International Working Group on Pelvic Venous Disorders. J Vasc Surg Venous Lymphat Disord 2021;9:568–584.

5. Meissner MH, Gibson K. Clinical outcome after treatment of pelvic congestion syndrome: sense and nonsense. Phlebology 2015;30(1 Suppl):73–80.
6. Chait J, Sen I, Kalra M. Nutcracker Syndrome: How to Diagnose It and When/How Should It Be Treated in the Pelvic Venous Disease Population. Tech Vasc Interv Radiol 2021;24:100734.
7. Jeanneret C, Beier K, von Weymarn A, Traber J. Pelvic congestion syndrome and left renal compression syndrome – clinical features and therapeutic approaches. Vasa 2016;45:275–282.
8. Ribeiro FS, Puech-Leão P, Zerati AE, et al. Prevalence of left renal vein compression (nutcracker phenomenon) signs on computed tomography angiography of healthy individuals. J Vasc Surg Venous Lymphat Disord 2020;8:1058–1065.
9. Kashef E, Evans E, Patel N, et al. Pelvic venous congestion syndrome: female venous congestive syndromes and endovascular treatment options. CVIR Endovasc 2023;6:25.
10. Chronic Pelvic Pain: ACOG Practice Bulletin, Number 218. Obstet Gynecol. 2020;135:e98–e109.
11. Bendek B, Afuape N, Banks E, Desai NA. Comprehensive review of pelvic congestion syndrome: causes, symptoms, treatment options. Curr Opin Obstet Gynecol 2020;32:237–242.
12. Antignani PL, Lazarashvili Z, Monedero JL, et al. Diagnosis and treatment of pelvic congestion syndrome: UIP consensus document. Int Angiol 2019;38:265–283.
13. Khan TA, Rudolph KP, Huber TS, Fatima J. May-Thurner syndrome presenting as pelvic congestion syndrome and vulvar varicosities in a nonpregnant adolescent. J Vasc Surg Cases Innov Tech 2019;5:252–254.
14. Gültaşli NZ, Kurt A, Ipek A, et al. The relation between pelvic varicose veins, chronic pelvic pain and lower extremity venous insufficiency in women. Diagn Interv Radiol 2006;12:34–38.
15. Phillips D, Deipolyi AR, Hesketh RL, et al. Pelvic congestion syndrome: etiology of pain, diagnosis, and clinical management. J Vasc Interv Radiol 2014;25:725–733.
16. Hiromura T, Nishioka T, Nishioka S, et al. Reflux in the left ovarian vein: analysis of MDCT findings in asymptomatic women. AJR Am J Roentgenol 2004;183:1411–1415.
17. Mangla A, Hamad H. May-Thurner Syndrome. [Updated 2024 Mar 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554377/
18. Knuttinen MG, Naidu S, Oklu R, et al. May-Thurner: diagnosis and endovascular management. Cardiovasc Diagn Ther 2017;7(Suppl 3):S159–S164.
19. Nasser F, Cavalcante RN, Affonso BB, et al. Safety, efficacy, and prognostic factors in endovascular treatment of pelvic congestion syndrome. Int J Gynaecol Obstet 2014;125:65–68.
20. Franceschi C, Bahnini A. Points de fuite pelviens viscéraux et varices des membres inférieurs. Phlébologie 2004;57:37–42.
21. Kolber MK, Cui Z, Chen CK, et al. Nutcracker syndrome: diagnosis and therapy. Cardiovasc Diagn Ther. 2021;11:1140–1149.
22. KW, Cho JY, Kim SH, et al. Diagnostic value of computed tomographic findings of nutcracker syndrome: correlation with renal venography and renocaval pressure gradients. Eur J Radiol 2011;80:648–654.
23. Basile A, Failla G, Gozzo C. Pelvic Congestion Syndrome. Semin Ultrasound CT MR 2021;42:3–12.
24. Arnoldussen CW, de Wolf MA, Wittens CH. Diagnostic imaging of pelvic congestive syndrome. Phlebology 2015;30(1 Suppl):67–72.
25. Beard RW, Highman JH, Pearce S, Reginald PW. Diagnosis of pelvic varicosities in women with chronic pelvic pain. Lancet 1984;2:946–949.
26. Labropoulos N, Borge M, Pierce K, Pappas PJ. Criteria for defining significant central vein stenosis with duplex ultrasound. J Vasc Surg 2007;46:101–107.
27. Narese D, Bracale UM, Vitale G, et al. What the young physician should know about May-Thurner syndrome. Transl Med UniSa 2016;12:19–28.
28. Park SJ, Lim JW, Ko YT, et al. Diagnosis of pelvic congestion syndrome using transabdominal and transvaginal sonography. AJR Am J Roentgenol 2004;182:683–688.
29. Ignacio EA, Dua R, Sarin S, et al. Pelvic congestion syndrome: diagnosis and treatment. Semin Intervent Radiol 2008;25:361–368.
30. Heilijgers F, Gloviczki P, O'Sullivan G, et al. Nutcracker syndrome (a Delphi consensus). J Vasc Surg Venous Lymphat Disord 2025;13:101970.
31. Wu Z, Zheng X, He Y, et al. Stent migration after endovascular stenting in patients with nutcracker syndrome. J Vasc Surg Venous Lymphat Disord 2016;4:193–199.
32. Gavrilov SG, Vasilyev AV, Krasavin GV, et al. Endovascular interventions in the treatment of pelvic congestion syndrome caused by May-Thurner syndrome. J Vasc Surg Venous Lymphat Disord 2020;8:1049–1057.
33. Lakhanpal G, Kennedy R, Lakhanpal S, et al. Pelvic venous insufficiency secondary to iliac vein stenosis and ovarian vein reflux treated with iliac vein stenting alone. J Vasc Surg Venous Lymphat Disord 2021;9:1193–1198.
34. Gora KB, Wozniak S. Evaluation of effectiveness of pharmacological treatment in pelvic congestion syndrome. Ginekol Pol 2023. doi: 10.5603/GP.a2023.0078.
35. Gavrilov SG, Karalkin AV, Moskalenko YP, Grishenkova AS. Efficacy of two micronized purified flavonoid fraction dosing regimens in the pelvic venous pain relief. Int Angiol 2021;40:180–186.
36. Tsukanov YT, Tsukanov AY, Levdanskiy EG. Secondary Varicose Small Pelvic Veins and Their Treatment with Micronized Purified Flavonoid Fraction. Int J Angiol 2016;25:121–127.
37. Gavrilov SG, Moskalenko YP, Karalkin AV. Effectiveness and safety of micronized purified flavonoid fraction for the treatment of concomitant varicose veins of the pelvis and lower extremities. Curr Med Res Opin 2019;35:1019–1026.
38. Sator-Katzenschlager SM, Scharbert G, Kress HG, et al. Chronic pelvic pain treated with gabapentin and amitriptyline: a randomized controlled pilot study. Wien Klin Wochenschr 2005;117:761–768.
39. O'Brien MT, Gillespie DL. Diagnosis and treatment of the pelvic congestion syndrome. J Vasc Surg Venous Lymphat Disord 2015;3:96–106.
40. Gloviczki P, Comerota AJ, Dalsing MC, et al. Society for Vascular Surgery; American Venous Forum. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg 2011;53(5 Suppl):2S–48S.
41. De Gregorio MA, Guirola JA, Alvarez-Arranz E, et al. Pelvic venous disorders in women due to pelvic varices: treatment by embolization: experience in 520 patients. J Vasc Interv Radiol 2020;31:1560–1569.
42. Liu J, Han L, Han X. The Effect of a Subsequent Pregnancy After Ovarian Vein Embolization in Patients with Infertility Caused by Pelvic Congestion Syndrome. Acad Radiol 2019;26:1373–1377.

Přehledový článek | Review article

Ketone Body in Heart Failure Patients with Diabetes: Pathophysiology and the Potential Therapeutic Benefit: a Literature Review

Hanestya Oky Hermawan[a], Primasitha Maharany Harsoyo[a], Faizal Ablansah Anandita[a], Aisya Ayu Shafira[b], Deasy Ardiany[c], Andrianto[a]

[a] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Airlangga University, Surabaya, Indonesia*
[b] *Faculty of Medicine, Airlangga University, Surabaya, Indonesia*
[c] *Department of Internal Medicine, Faculty of Medicine, Airlangga University, Surabaya, Indonesia*

ARTICLE INFO

Article history:
Submitted: 12. 11. 2024
Accepted: 11. 12. 2024
Available online: 18. 6. 2025

Klíčová slova:
Diabetes mellitus
Ketolátky
Ketoterapie
Srdeční selhání

SOUHRN

Kontext: Je obecně známo, že léčba srdečního selhání je založena na inhibici systému renin-angiotensin-aldosteron a snižování aktivity sympatického autonomního nervového systému. Při léčbě srdečního selhání se však zřídkakdy zvažuje možnost ovlivnění metabolismu. Je třeba poznamenat, že srdeční selhání se často vyskytuje současně s diabetem. Proto musí léčba příznivě ovlivňovat obě tato onemocnění. V průběhu patofyziologického přechodu k srdečnímu selhání může dojít k rozvoji metabolických abnormalit a jako alternativních zdrojů energie lze použít kyselinu mléčnou, ketolátky a aminokyseliny. Spojitost ketolátek s oběma onemocněními byla prokázána. Pro pacienty se srdečním selháním a diabetem by léčba s použitím ketolátek mohla být přínosná.
Cíl: Vypracovat komplexní přehled preklinických a klinických studií zkoumajících léčebné účinky ketolátek u srdečního selhání.
Metoda: Tato studie je přehledem literatury dostupné v online databázích a vyhledané pomocí klíčových slov uvedených v biomedicínském slovníku (tezauru) Medical Subject Headings (MeSH). Hledanou intervencí byla terapie ketolátkami (3-hydroxybutyrát sodný, sodium-3-OHB) nebo inhibitorem sodíko-glukózového transportéru typu 2 (SGLT2) jako aktivátorem tvorby ketolátek. Zaměřili jsme se na výsledky léčby a jakékoli zaznamenané nežádoucí účinky ketózy.
Výsledky: Bylo vybráno celkem 14 studií (šest u lidí a osm se zvířaty) zabývajících se léčebnými účinky ketolátek. Terapii ketolátkami (3-OHB sodný) nebo intervenci inhibitorem SGLT2 podstoupilo celkem 8 742 (8 zdravých jedinců) účastníků studií.
Závěr: Ketoterapie a systémová regulace ketózy se zdají být slibnými způsoby léčby díky změnám metabolismu srdcí pacientů s diabetem a srdečním selháním. Tato studie by se mohla stát literárním základem pro další výzkum s cílem určit bezpečnost a hranice účinnosti dlouhodobé léčby ketolátkami.

Keywords:
Diabetes mellitus
Heart failure
Ketone body
Ketone therapy

ABSTRACT

Background: Common knowledge of heart failure treatment target is to intervene in the renin-angiotensin-aldosterone system and the sympathetic autonomic nervous system. However, metabolic aspect in the therapy of heart failure is rarely discussed. It is worth noting that heart failure often co-exist with diabetes. Thus, there is a need for a treatment that can be beneficial for these two diseases. During the pathophysiological transition to heart failure, metabolic abnormalities may occur, and lactic acid, ketone bodies, and amino acids may be used as alternative energy sources. Ketone body has been shown to be associated with these two diseases. Treatment using ketone body may be beneficial to treat patients with heart failure and diabetes.
Objective: To provide a comprehensive review of preclinical and clinical studies on the therapeutic effects of ketone bodies for heart failure.
Method: This study is literature reviews on online databases using keywords according to the Medical Subject Headings (MeSH). The focused intervention is ketone bodies therapy (sodium-3-OHB) or SGLT2i as ketone inducer. We focused on the result of therapy and any ketosis side effect recorded.

Address: Aisya Ayu Shafira, MD, Faculty of Medicine, Airlangga University, Surabaya, Indonesia, e-mail: aisyaayushafira@gmail.com
DOI: 10.33678/cor.2024.104

Please cite this article as: Hermawan HO, Harsoyo PM, Anandita FA, et al. Ketone Body in Heart Failure Patients with Diabetes: Pathophysiology and the Potential Therapeutic Benefit: a Literature Review. Cor Vasa 2025;67:402–407.

Results: A total of 14 studies (6 human studies and 8 animal studies) related on the therapeutic effects of ketone bodies was selected. A total of 8,742 (8 healthy participants) participants was involved in ketone bodies therapy (sodium-3-OHB) or SGLT2i intervention.
Conclusion: Ketogenic therapy and systemic ketosis regulation show promise based on metabolic changes in the hearts of patients with diabetes and heart failure. This study may provide a literature basis for further research to determine the safety and efficacious limitations of long-term ketone body therapy.

Introduction

Heart failure is a global phenomenon due to its high incidence in developing countries.[1] According to Lam (2015), heart failure is more common in Southeast Asia than it is worldwide. It is thought to affect 1% to 2% of adults in developing countries. The lack of statistics on the prevalence of heart failure may cause this estimate to rise.[2] Additionally, patients with heart failure in Southeast Asia are more likely to have more severe symptoms, require mechanical ventilation more frequently, have longer hospital stays, and have higher hospital mortality.[3]

As an essential organ that works continuously, the heart consumes adenosine triphosphate (ATP) more than seven times its weight per day. The majority of the metabolic resources (50–75%) needed by adult cardiac muscle cells to produce ATP are fatty acids, with 25–50% of the energy used by mitochondria for metabolism comes from glucose.[4] The heart may also use lactic acid, ketone bodies, and amino acids in small amounts as energy sources in addition to fatty acids and glucose. The percentage of these metabolic sources that are used may differ depending on the state of nutrition and the heart's function. For instance, the heart uses glucose primarily during the fetal stage and switches to using fatty acids as a source of ATP generation during the postnatal stage.[5,6] Failure to meet energy requirements will result in cardiac failure. Increasing ATP production in the heart in a bioenergy--efficient way might be the solution.

The heart's use of its metabolic fuel sources could change. These metabolic changes, which include an initial disruption in the oxidation of fatty acid followed by a change in the oxidation of glucose, may occur during the pathophysiological transition to heart failure. This process occurs at the early-stage pathogenesis of heart failure, such as the cardiac muscle hypertrophy creation phase in chronic hypertension patients or the ischemia phase in coronary heart disease patients. Cardiomyocyte mitochondria may be reprogrammed, resulting in decreased fatty acid oxidizing capacity and increased glucose oxidation and glycolysis. Due to the fatty acids as the primary fuel for a healthy heart, the mentioned metabolic reprogramming event causes a decrease in ATP production.[5,7]

There may be additional processes involved in concomitant heart failure and diabetic mellitus (DM). Because of their insulin resistance, diabetic patients' hearts are unable to use glucose as their primary energy source. Due to this circumstance, there is a forced metabolic shift whereby fatty acid sources become the only source of ATP generation. This alteration results in the formation of oxidative stress, which raises the oxygen demand of the heart tissue and ultimately lowers the heart's activity efficiency. This may occur because the oxidation of fatty acids requires more oxygen per mole than the oxidation of glucose. These factors suggest that specific management and greater attention are needed for heart failure with DM comorbidity.[8] The use of alternative energy sources to meet the metabolic requirement for the heart's activity could be one of the targets for heart failure management, especially with DM comorbid.

Evidence suggests that increasing the metabolism of additional energy sources, such as ketone bodies, in adequate quantities can improve energy metabolism efficiency and minimize oxidative stress. Composed of 4-carbon molecules synthesized by the ketogenesis process, ketone bodies can be broken down and utilized in tissues via the ketolysis pathway, forming acetone, acetoacetate, and beta-hydroxybutyrate as ketone molecules. Beta-hydroxybutyrate (-OHB) is the most prevalent ketone body in blood circulation. An adequate level of -OHB in blood circulation has been shown to improve hemodynamics in heart failure patients.[9]

Various preclinical and clinical researches have shown that ketone bodies have a therapeutic effect on heart failure. Exogenous ketone body administration may improve circulatory function and avoid pathological remodeling in the process leading to heart failure. These investigations could point to novel intervention targets for the pharmaceutical therapy of heart failure. The discovery of changes in metabolism and the utility of the ketone body in heart failure patients with diabetes led to a more in-depth and wide debate about the ketone body's therapeutic potential.[10] In order to lower the risk of HF hospitalization and death, SGLT2i have been suggested for patients with HFrEF based on the 2021 ESC guideline.[11] Both individuals with and without diabetes may benefit from SGLT2i's potential mode of action in HF.[12] This raise question on why ketone body treatment is not advised in guidelines similar to SGLT2i.

This review aims to give a thorough overview of the correlation between DM and heart failure, as well as an analysis of the metabolism and utilization of ketone bodies in physiological conditions and how these relate to changes in heart failure and DM conditions. Additionally, it reviews a number of recent studies on the therapeutic effects of ketone bodies in both preclinical and clinical settings.

Methods

This study is a literature review related to the use of ketone body therapy on heart failure. The literature search was carried out on the PUBMED and SCIENCEDIRECT databases using keywords according to the Medical Heading

Subject (MeHS), namely "(Keton) AND (Bodies) AND (Ketosis) AND (Heart failure) AND (Diabetes mellitus) AND (Left ventricular dysfunction)". The population of related study could be human or animal without specific limitation. The intervention is ketone bodies therapy (sodium--3-OHB) or SGLT2i as ketone inducer. The comparison of the ketone therapy could be placebo, other HF agents, or no comparison. We focused on the result of therapy and any ketosis side effect recorded.

Results

A total of 14 studies (six human studies and eight animal studies) related on the therapeutic effects of ketone bodies was selected. A total of 8,742 (eight healthy participants) participants was involved in ketone bodies therapy (sodium-3-OHB) or SGLT2i intervention. From the total six of human studies, empagliflozin was used in two studies, dapagliflozin in two studies, and ketone infusion of sodium-3-OHB also in two studies. While in animal studies, empagliflozin was used in four studies, dapagliflozin in two studies, and ketone infusion of sodium-3-OHB also in two studies. **Table 1** shows the result of the search.

Discussion

1. Correlation of heart failure and diabetes mellitus

Epidemiology of DM and heart failure

Heart failure and diabetes mellitus (DM) are two diseases that could co-exist in a patient. Heart failure is one of DM comorbidities and vice versa. Diabetes affects the elderly (60 years) at a rate ranging from 10 to 47% in patients with heart failure who require hospitalization. The percentage of diabetic patients with heart failure ranges from 9 to 22%, which is four times greater than the healthy population. A study showed that heart failure patients with DM have worse clinical symptoms and prognosis, and significantly increased mortality risk.

As a result, DM is regarded as a significant independent risk for determining the mortality risk in patients with heart failure. The American Heart Association (AHA) and the European Society of Cardiology (ESC) developed management guidelines for heart failure and diabetes mellitus (DM) based on these findings.[24]

Pathophysiology of DM and heart failure

Diabetes mellitus contributes to the pathogenesis of heart failure through systemic, myocardial, and cellular pathways. According to another study, vasculo-myocardial damage – which includes tissue fibrosis, higher risk of thrombosis, vasculopathy, and myocardial hypertrophy – is what causes heart failure brought on by diabetes. These processes are thought to be all brought on by lipotoxicity and glucotoxicity.[24,25]

Diabetes mellitus can cause structural heart damage through the ischemia/infarction mechanism. Hyperglycemia and hyperinsulinemia are known to accelerate the establishment of atherosclerosis by increasing the proliferation of vascular smooth muscle, then followed by inflammation and oxidative stress. This causes endothelial dysfunction leading to vasculopathy. Endothelial dysfunction, combined with high levels of low-density lipoprotein (LDL), will trigger leukocyte and platelet adhesion, resulting in thrombosis, inflammation, and atherosclerotic plaque formation in coronary arteries.[24,25]

In the absence of ischemia/infarction related to coronary heart disease (CHD), diabetes mellitus may produce myocardial abnormalities. Diabetic cardiomyopathy is the medical term for this illness. Rubler et al. coined this phrase in 1972 after discovering cardiomegaly in DM patients without severe CHD. "Diabetic cardiomyopathy" term has been used to describe systolic and/or diastolic dysfunction in diabetic patients, who have no other known cardiomyopathy causes, such as CHD, hypertension, or valvular heart disease, for a long. In diabetic cardiomyopathy, left ventricular hypertrophy in imaging studies accompanied by hyperinsulinemia or insulin resistance is a significant diagnostic criterion.[24] Hyperglycemia can cause myocardial hypertrophy by causing the production of advanced glycation end products (AGEs). AGEs have been shown to limit collagen turnover, increasing the production of fibrotic tissue and interfering with myocardial relaxation function.

In addition to these mechanisms, hyperglycemia stimulates the renin-angiotensin-aldosterone (RAS) system, resulting in angiotensin II and aldosterone overproduction, which has been linked to myocardial hypertrophy via the transforming growth factor beta (TGF-) pathway. Insulin causes mitosis and increases the lifespan of cardiac cells, therefore hyperinsulinemia contributes to myocardial hypertrophy.[26]

The mechanism of heart failure in DM patients is also linked to the "energy-starvation" hypothesis, which states that the heart muscle cannot use glucose as an energy source due to poor glucose metabolism. As a result, the heart undergoes a forced metabolic shift in which all of its energy production is assigned to a fatty acid source. Excessive fatty acid oxidation causes fat accumulation in cardiomyocytes, which triggers lipo-toxicity that damages contractile proteins and causes apoptosis in cardiomyocytes. These mechanisms are associated with DM conditions with lipid accumulation in heart tissue based on studies using cardiac magnetic resonance imaging. Analysis of myocardial tissue in DM patients showed an increase in the number of cardiomyocytes undergoing apoptosis.[24,25]

2. Ketone body and its metabolism

Ketone body metabolism in normal heart

Ketone substances consist of four carbon molecules, including acetone, acetoacetate, and beta-hydroxybutyrate (β-OHB). The liver produces β-OHB, the most common type in the circulation (78%), through a process called ketogenesis. This process, which results in the transformation of fatty acids and some ketogenic amino acids into ketone bodies, is triggered during fasting when the insulin-to-glucagon ratio drops. They provide 5–20% of daily energy requirements from the 300 grams produced, and are used as an energy source during fasting, low-carb diets, and after vigorous exercise.[9,23] Keto-

Table 1 – Studies related on the therapeutic effects of ketone bodies

Author	Population	Intervention	Main findings
Human study			
Verma, 2016[13]	10 people with cardiovascular disease and diabetes mellitus	Pre- and post-empagliflozin study	Empagliflozin enhances echocardiographic parameters and decreases left ventricular mass.
Gormsen, 2017[14]	Eight healthy participants	Randomized crossover experiment comparing saline infusion to sodium-3-OHB	The infusion of ketone reduces the absorption of glucose while increasing myocardial blood flow by 75%
Nielsen, 2019[15]	Sixteen patients with lower ejection fraction because of heart failure	Randomized crossover study comparing isotonic saline to 3-OHB infusion	A ketone application increases cardiac blood flow by 75% while decreasing glucose absorption
McMurray, 2019[16]	4744 people with a lower ejection fraction who suffer from cardiac failure	Randomised crossover study comparing placebo with dapagliflozin	Dapagliflozin is not linked to underlying diabetes mellitus and lowers the risk of cardiovascular death or worsening heart failure
Packer, 2020[17]	3730 people with with class II, III, or IV heart failure and an ejection fraction of 40% or less	Double-blind trial study by comparing placebo with empagliflozin (10 mg once daily) in addition to recommended therapy	Empagliflozin group had a lower risk of cardiovascular death or hospitalization for heart failure than those in the placebo group, regardless of the presence or absence of diabetes
Selvaraj, 2022[18]	234 people with HFrEF	Targeted metabolomics in a placebo-controlled trial of sodium-glucose cotransporter-2 inhibitors in HFrEF	Dapagliflozin increased ketone-related components compared with placebo. However, only physiologic levels of ketosis were observed.
Animal study			
Joubert, 2017[19]	Mice with lipodystrophies	Dapagliflozin only	In patients with heart hypertrophy, dapagliflozin treatment markedly improves diastolic function
Lee, 2017[20]	Wistar male rats undergoing coronary ligation had normoglycemia	Dapagliflozin and control	In cardiac fibrosis, dapagliflozin decreases
Verma, 2018[21]	Diabetes mellitus in mice	Empagliflozin and control	Cardiac ATP generation is increased by empagliflozin, but not by ketone oxidation
Abdurrachim, 2019[6]	Mice suffering from heart failure, hypertension, diabetes, and obesity	Empagliflozin and control	Empagliflozin lowers the quantity of ketone the heart uses, however, it has little effect on fibrosis or hypertrophy of the left ventricle
Horton, 2019[5]	Rats with transaortic constriction/myocardial infarction and dogs with cardiomyopathy induced by tachycardia	Mice given a ketogenic and regular diet; dogs with heart failure receiving 3-OHB infusion against not being given it	In a dog model, 3-OHB infusion dramatically reduced systolic dysfunction and left ventricular remodeling, while a ketogenic diet reduced left ventricular remodeling in mice
Santos-Gallego, 2019[22]	Heart failure following LAD artery ligation in pigs without diabetes	Empagliflozin and control	Pigs given empagliflozin alternate between using branched-chain amino acids, ketones, and fatty acids as substrates
Yurista, 2019[23]	Mice model following myocardial infarction without developing diabetic mellitus	Empagliflozin and control	After myocardial infarction, empagliflozin dramatically increases ejection fraction, reduces hypertrophy, gets rid of fibrosis, and lessens oxidative stress. In the heart, empagliflozin stimulates the expression of ketogenic enzymes and ketone body transporters.
Thai, 2021[9]	Diabetes mellitus model mice	Administration of ketone esters and control	Ketone esters enhance heart systolic and diastolic function, mitochondrial biogenesis, oxygen consumption efficiency, and cell tolerance to oxidative stress

ne molecules are transported into tissues by monocarboxylate transporters (MCTs), where they undergo ketolysis in mitochondria. β-OHB and acetoacetate are converted by essential enzymes such as Bdh1 and SCOT into Acetyl-CoA, which then proceeds to the tricarboxylic acid cycle (TCA) to create ATP. Genetic deficiencies affecting the SCOT, ACAT, and MCT1 enzymes can cause recurrent ketoacidosis.[4,23,27]

Ketone consumption is increased in heart failure and diabetes to maintain metabolic balance. Mice lacking the SCOT or Bdh1 genes exhibit cardiac abnormalities due to loss of ketone metabolism.

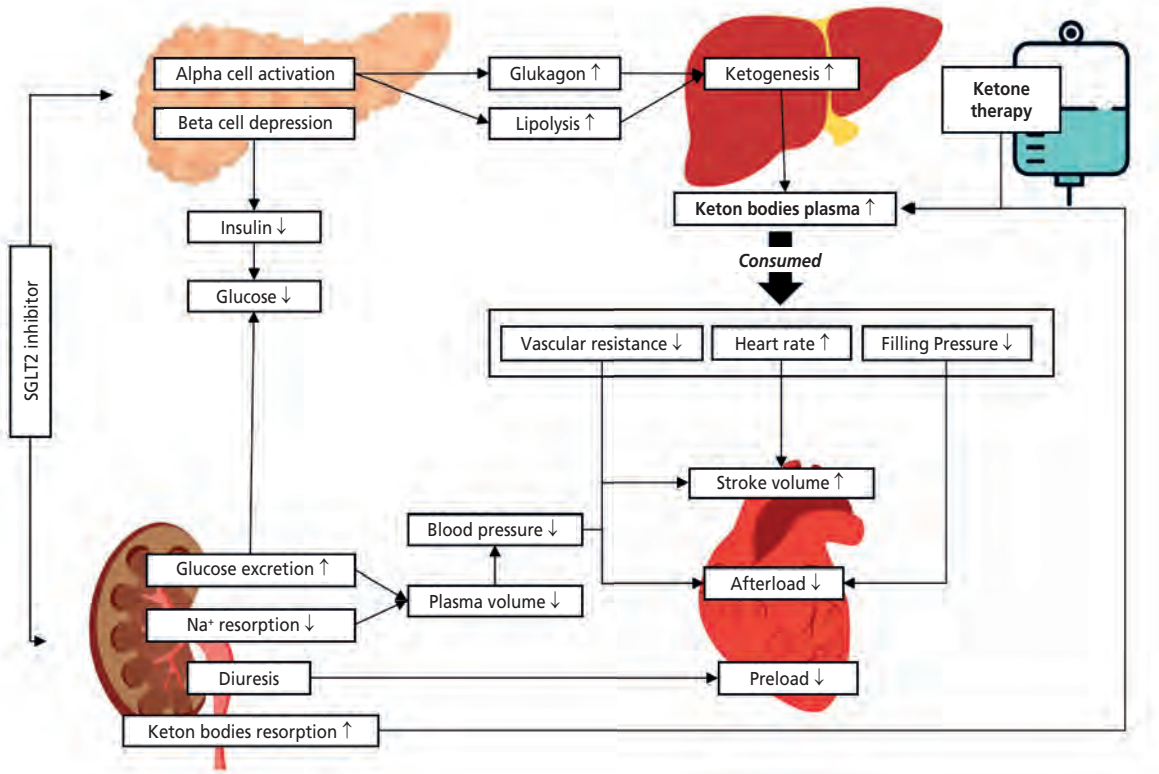


Fig. 1 – Schematic diagram mechanisms of action of SGLT2i related to ketogenesis and the potential ketone therapy

3. Heart failure-related changes in ketone body metabolism

Cardiac changes are characteristic of early heart failure, starting with myocardial hypertrophy, which reduces fatty acid oxidation capacity. Reliance switches to less effective glycolysis in cardiac failure. Hypertrophied hearts compensate for reduced fatty acid oxidation with increased glycolysis at lower workloads. Insulin resistance and other variables may cause changes in glucose utilization over time, which can result in energy deficiency and decreased heart failure glucose and fatty acid utilization.[5]

Ketone body metabolism in diabetic patient with heart failure

Type 1 diabetes and type 2 diabetes can both have major effects on the ketogenic body. In those with type 1 diabetes, routine glucose, and ketone testing is essential to preventing ketonemia, which can quickly worsen in the absence of insulin therapy. Elevated blood ketone levels in type 2 diabetes are associated with impaired glucose management because of low insulin and high glucagon levels, which promote the breakdown of fat in the liver to produce hepatic ketogenesis.[10,27] Diabetic hearts rely less on oxidizing glucose and more on oxidizing fatty acids.[9,27,28]

The potential benefits of ketone body therapy for diabetes and heart failure

Ketone supplementation has the potential to treat heart failure, particularly in patients with a low ejection fraction (HFrEF). According to one study, giving 3-hydroxybutyrate ketone bodies increased cardiac output by 40%. This rise was associated with decreased vascular resistance, elevated heart rate, enhanced stroke volume, and reduced filling pressure. While the fundamental cause of this effect is still unknown, the study suggests that people with preserved ejection fraction (HFpEF) may reap similar benefits.

This presents intriguing opportunities for improving vasodilator effects and systolic function in HFpEF patients by using ketone therapy.[7] Patients with diabetes and heart failure show changes in their heart's metabolism and ketone body utilization, suggesting that ketone treatment or modifications to systemic ketosis may be beneficial. To optimize this approach, research should focus on establishing the optimum methods for inducing ketosis in heart failure patients, such as dosage, preparation, and delivery (oral or intravenous). To adequately analyze outcomes, a larger study incorporating varied patient groups, including those with diabetes, is required.[4,16]

4. The role of SGLT2i therapy as keton inducer for diabetes and heart failure

In individuals with and without diabetes, SGLT2i has proven treatment causes a slight ketosis, which may be the mechanism of action for its beneficial effects in heart failure.[12] Based on Selvaraj et al, (2022) study, the level of **ßOHB** and associated C4-OH were raised in a placebo-controlled experiment assessing circulating metabolites in HFrEF patients after 12 weeks of SGLT2i therapy. Furthermore, the mentioned study show that Dapagliflozin increased ketone-related components compared with placebo. However, only physiologic levels of ketosis were observed.[18] Moreover, SGLT2i also decreased insulin

attenuated inflammation in diabetes type II. In separated literature study about potential side effect of SGLT2i in inducing euglycemic diabetic ketoacidosis (EDKA), suggesting that in mild hyperketonemia caused by SGLT2i, beta-hydroxybutyrate is freely taken up by the cells as a source of energy, especially by the cardiac muscles. This usage of energy source helps the tissues work efficiently, and reducing cardiovascular (CV) mortality by 38%, hospitalization for heart failure by 35%, and death from any cause by 32%.[29]

Based on some literature,[4,12,30] we try to formulate a simple schematic diagram showing mechanisms of action of SGLT2i related to ketogenesis and the usage of the keton bodies in by the cardiac muscles, as well as the potential ketone therapy which discussed above (**Fig. 1**). However, some literatures suggest that SGLT2i has inconsistent ketosis effect, and mechanisms other than ketosis (enhanced glucose and fatty acid oxidation) may also mediate the cardiometabolic effects of SGLT2i.[12,21]

Conclusion

Ketogenic therapy and systemic ketosis regulation show promise based on metabolic changes in the hearts of patients with diabetes and heart failure. Further research is required to determine the safety and efficacious limitations of long-term ketone body delivery, taking into account the effects on the liver and the acid-base balance. It is critical to determine the most effective method of inducing ketosis in patients with heart failure (dosage, preparation, oral vs. intravenous), as well as the outcomes must be assessed in a range of patient populations, including those with diabetes.

References

1. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. Eur J Heart Fail 2020;22:1342–1356.
2. Lam CSP. Heart failure in Southeast Asia: facts and numbers. ESC Heart Fail 2015;2:46–49.
3. Bozkurt B, Coats AJS, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. Eur J Heart Fail 2021;23:352–380.
4. Selvaraj S, Kelly DP, Margulies KB. Implications of Altered Ketone Metabolism and Therapeutic Ketosis in Heart Failure. Circulation 2020;141:1800–1812.
5. Horton JL, Davidson MT, Kurishima C, et al. The failing heart utilizes 3-hydroxybutyrate as a metabolic stress defense. JCI Insight 2019;4:e124079.
6. Abdul Kadir A, Clarke K, Evans RD. Cardiac ketone body metabolism. Biochim Biophys Acta Mol Basis Dis 2020;1866:165739.
7. Selvaraj S, Kelly DP, Margulies KB. Implications of Altered Ketone Metabolism and Therapeutic Ketosis in Heart Failure. Circulation 2020;141:1800–1812.
8. Mizuno Y, Harada E, Nakagawa H, et al. The diabetic heart utilizes ketone bodies as an energy source. Metabolism 2017;77:65–72.
9. Thai PN, Miller CV, King MT, et al. Ketone Ester D-β-Hydroxybutyrate-(R)-1,3 Butanediol Prevents Decline in Cardiac Function in Type 2 Diabetic Mice. J Am Heart Assoc 2021;10:e020729.
10. Selvaraj S, Kelly DP, Margulies KB. Implications of Altered Ketone Metabolism and Therapeutic Ketosis in Heart Failure. Circulation 2020;141:1800–1812.
11. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599–3726.
12. Matsuura TR, Puchalska P, Crawford PA, Kelly DP. Ketones and the Heart: Metabolic Principles and Therapeutic Implications. Circ Res 2023;132:882–898.
13. Verma S, et al. Effect of Empagliflozin on Left Ventricular Mass and Diastolic Function in Individuals With Diabetes: An Important Clue to the EMPA-REG OUTCOME Trial? Diabet Care 2016;39:e212–e213.
14. Gormsen LC, et al. Ketone Body Infusion With 3□ Hydroxybutyrate Reduces Myocardial Glucose Uptake and Increases Blood Flow in Humans: A Positron Emission Tomography Study. J Am Heart Assoc 2017;6:e005066.
15. Nielsen R, Møller N, Gormsen LC, et al. Cardiovascular Effects of Treatment With the Ketone Body 3-Hydroxybutyrate in Chronic Heart Failure Patients. Circulation 2019;139:2129–2141.
16. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med 2019;381:1995–2008.
17. Packer M, Anker SD, Butler J, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med 2020;383:1413–1424.
18. Selvaraj S, Fu Z, Jones P, et al. Metabolomic Profiling of the Effects of Dapagliflozin in Heart Failure With Reduced Ejection Fraction: DEFINE-HF. Circulation 2022;146:808–818.
19. Joubert M, Jagu B, Montaigne D, et al. The Sodium–Glucose Cotransporter 2 Inhibitor Dapagliflozin Prevents Cardiomyopathy in a Diabetic Lipodystrophic Mouse Model. Diabetes 2017;66:1030–1040.
20. Lee TM, Chang NC, Lin SZ. Dapagliflozin, a selective SGLT2 Inhibitor, attenuated cardiac fibrosis by regulating the macrophage polarization via STAT3 signaling in infarcted rat hearts. Free Radic Biol Med 2017;104:298–310.
21. Verma S, Rawat S, Ho KL, et al. Empagliflozin Increases Cardiac Energy Production in Diabetes. JACC Basic Transl Sci 2018;3:575–587.
22. Santos-Gallego CG, Requena-Ibanez JA, San Antonio R, et al. Empagliflozin Ameliorates Adverse Left Ventricular Remodeling in Nondiabetic Heart Failure by Enhancing Myocardial Energetics. J Am Coll Cardiol 2019;73:1931–1944.
23. Yurista SR, Chong CR, Badimon JJ, et al. Therapeutic Potential of Ketone Bodies for Patients With Cardiovascular Disease. J Am Coll Cardiol 2021;77:1660–1669.
24. Bando YK, Murohara T. Diabetes-related heart failure. Circ J 2014;78:576–583.
25. Dunlay SM, Givertz MM, Aguilar D, et al. Type 2 Diabetes Mellitus and Heart Failure: A Scientific Statement From the American Heart Association and the Heart Failure Society of America: This statement does not represent an update of the 2017 ACC/AHA/HFSA heart failure guideline update. Circulation 2019;140:E294–E324.
26. Waddingham MT. Contractile apparatus dysfunction early in the pathophysiology of diabetic cardiomyopathy. World J Diabetes 2015;6:943.
27. Kolwicz SC Jr. Ketone Body Metabolism in the Ischemic Heart. Front Cardiovasc Med 2021;8:789458.
28. Mizuno Y, Harada E, Nakagawa H, et al. The diabetic heart utilizes ketone bodies as an energy source. Metabolism 2017;77:65–72.
29. Somagutta MR, Agadi K, Hange N, et al. Euglycemic Diabetic Ketoacidosis and Sodium-Glucose Cotransporter-2 Inhibitors: A Focused Review of Pathophysiology, Risk Factors, and Triggers. Cureus 2021;13:e13665.

A Rare Case of Acute Limb Ischemia due to Left Ventricular Thrombus in Ischemic Heart Disease: Different Approaches to Long-Term Anticoagulant and Antiplatelet Therapy

Meity Ardiana[a], Ovin Nada Saputri[b], Muhammad Surya Tiyantara[a], Michael Jonatan[a], Andrianto[a], Anudya Kartika Ratri[a]

[a] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Airlangga University – Dr. Soetomo Academic General Hospital, Surabaya, Indonesia*
[b] *Faculty of Medicine, Airlangga University, Surabaya, Indonesia*

ARTICLE INFO

Article history:
Submitted: 28. 3. 2024
Revised: 8. 5. 2024
Accepted: 24. 5. 2024
Available online: 5. 12. 2024

Klíčová slova:
Akutní končetinová ischemie
Antiagregační
Antikoagulační
Ischemická kardiomyopatie
Trombus v levé komoře

SOUHRN

Trombus v levé komoře (left ventricular thrombus, LVT) se může vytvořit v důsledku progrese ischemické choroby srdeční (ICHS), která může ve vzácných případech migrovat do nějaké periferní tepny. V tomto článku popisujeme případ 58letého muže přijatého do naší nemocnice s náhlým nástupem bolesti a necitlivostí pravé dolní končetiny; byla stanovena diagnóza akutní ischemie dolní končetiny. Nečekaně se ukázalo, že muž trpí i němou a rozsáhlou ICHS vedoucí k srdečnímu selhání se sníženou ejekční frakcí (heart failure with reduced ejection fraction, HFrEF) a ke vzniku LVT. Jako příčina akutní ischemie dolní končetiny byla u tohoto pacienta stanovena periferní embolizace trombem. Ke snížení možnosti rozvoje kardiovaskulární příhody a progrese onemocnění bylo třeba zahájit účinnou antitrombotickou léčbu. Pacienti s akutní ischemií dolní končetiny a komplexní ICHS a LVT mohou vyžadovat kombinaci antikoagulační a antiagregační léčby. Proto je třeba zvolit individualizovaný přístup, který je založen na stanovení rizika ischemie a krvácení u pacienta s cílem více omezit možnost ischemických příhod a současně zabránit vzniku významných krvácivých příhod.

Keywords:
Acute limb ischemia
Anticoagulant
Antiplatelet
Ischemic cardiomyopathy
Left ventricular thrombus

ABSTRACT

Left ventricular thrombus (LVT) may develop from the progression of coronary artery disease (CAD), which can rarely embolise and migrate to the peripheral artery. Here, we report the case of a 58-year-old man admitted to our hospital with a sudden onset of pain and numbness in his right lower limb, diagnosed as ALI. Unexpectedly, he also had silent and extensive CAD leading to heart failure with reduced ejection fraction (HFrEF) and LVT formation. LVT embolization in the peripheral artery was identified as the cause of ALI in this patient. Effective long-term antithrombotic therapy was necessary to reduce cardiovascular adverse events and disease progression. Patients with ALI coexisting with complex CAD and LVT may require a combination of anticoagulant and antiplatelet therapy. Therefore, an individualised approach is warranted. This approach is based on the evaluation of the ischemic and bleeding risks of the patient to achieve a greater reduction in ischemic events while avoiding significant bleeding events.

Introduction

Left ventricular thrombus (LVT) is often associated with myocardial infarction (MI).[1] LVT can also lead to peripheral embolization causing limb ischaemia which is very rare.[2] Currently, LVT treatment remains debatable. The consideration of anticoagulant and antiplatelet combination therapy is often challenging in this complicated case.

Case report

A 58-year-old man with a history of heavy smoking was admitted to our hospital because of 12 hours of right lower leg pain and numbness. There were no reports of chest pain, tightness, palpitations or history of leg pain were recorded. On physical examination, he had hypertension with an initial blood pressure of 144/92 mmHg.

Address: Dr. Meity Ardiana, MD, 47 Mayjend. Prof. Moestopo, 60285 Surabaya, Indonesia, e-mail: meityardiana@fk.unair.ac.id
DOI: 10.33678/cor.2024.044

Please cite this article as: Ardiana M, Saputri ON, Tiyantara MS, et al. A Rare Case of Acute Limb Ischemia due to Left Ventricular Thrombus in Ischemic Heart Disease: Different Approaches to Long-Term Anticoagulant and Antiplatelet Therapy. Cor Vasa 2025;67:408–411.

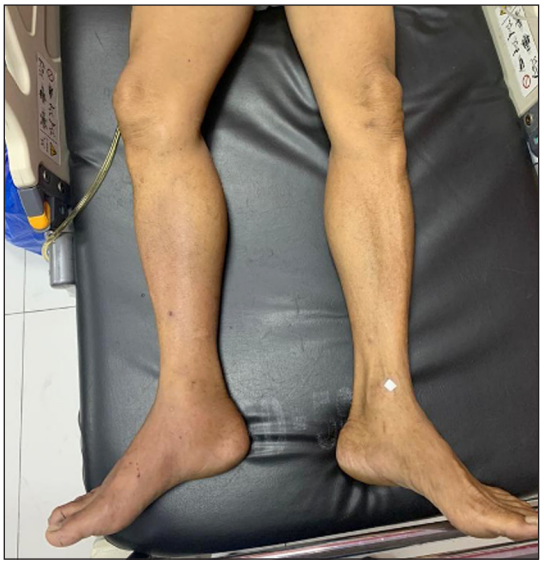


Fig. 1 – Clinical manifestation showed slightly mottled appearance and red discoloration of right lower extremity, highly concerning of acute limb ischemia.

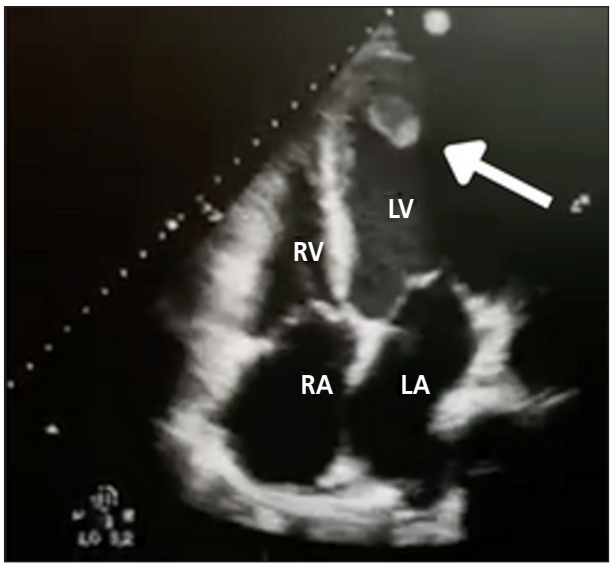


Fig. 4 – Transthoracic echocardiography (TTE) showed LV dilatation with severe systolic dysfunction markedly LV ejection fraction (EF) reduction of 28%. Abnormalities of regional wall motion were present with akinesis of anteroseptal wall and hypokinesis.

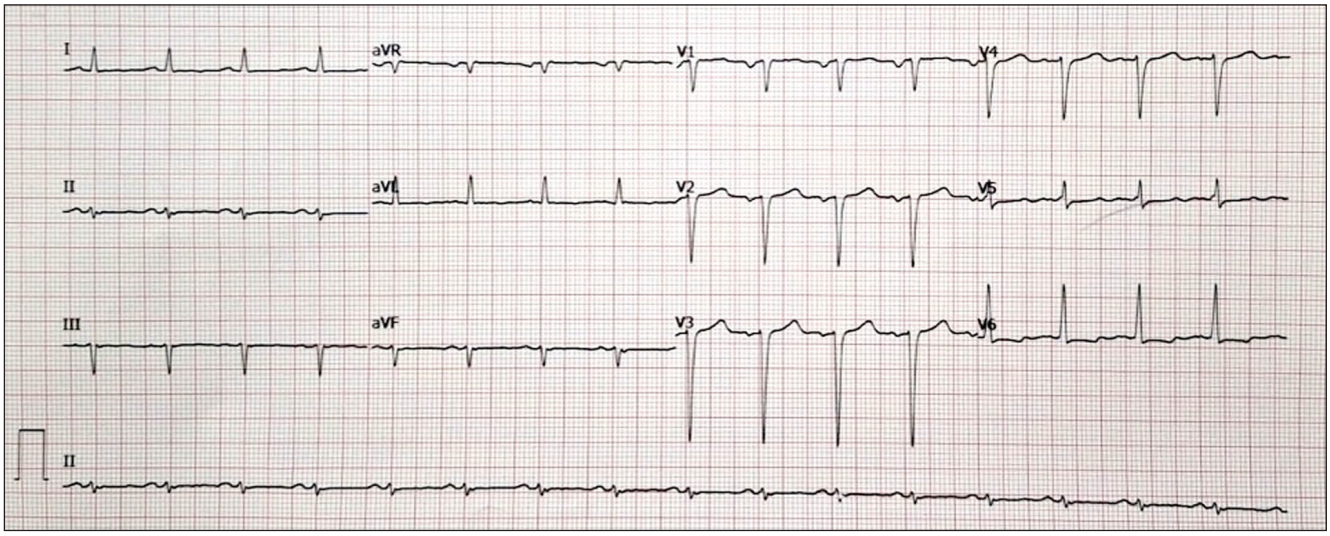


Fig. 2 – The electrocardiogram (ECG) showing a sinus rhythm, normal frontal axis, clockwise rotation, QS pattern in V_1–V_3, poor R wave progression in V_1–V_4.

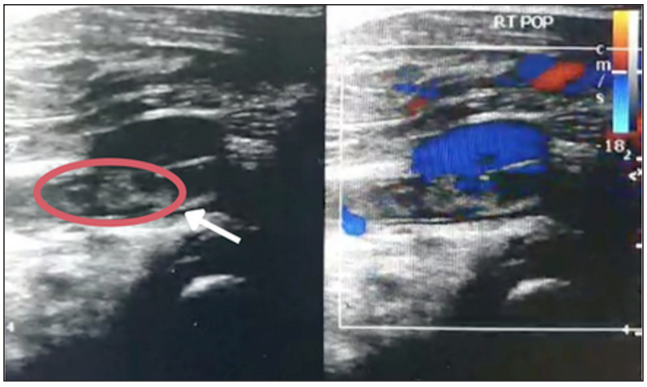


Fig. 3 – DUS showed a partially thrombosed popliteal artery in the right limb, which occluded 80–90% of the ostium, leading to difficulty in evaluating arterial flow towards the distal end.

The right limb assessment revealed cold and pale digits (**Fig. 1**). No pulse was palpated at the artery of the right popliteal, posterior tibial and dorsalis pedis of the right limb. Oxygen saturation was undetectable in all right toes. Electrocardiogram (ECG) showed findings of OMI anteroseptal whereas the presence of QS pattern in V_1–V_3 and poor R wave progression in V_1–V_4 (**Fig. 2**). Routine hematologic examinations were carried out, which revealed a platelet count of 601 × 10^9/L, an HbA_{1c} of 10.1%, and an albumin level of 3.21 g/L, while other routine blood profiles were within normal limits. Chest x-ray imaging showed cardiomegaly. Duplex ultrasonography (DUS) of the right limb showed subtotal-total occlusion of the thrombus in the popliteal artery (**Fig. 3**). Transthoracic echocardiography (TTE) showed LV dilatation, reduced systolic function with an ejection

fraction (EF) of 28%, anteroseptal-anterior akinesis, lateral-inferior hypokinesis. A 2.6 × 1.5 cm apical LVT was noted (**Fig. 4**). Unexpectedly, CT-coronary-angiography revealed an extensive coronary artery occlusion resulting in triple vessel coronary artery disease (CAD) (TVD) without any typical MI symptoms has been reported in this patient. The patient has been diagnosed with ALI classified to Rutherford as IIB, in concomitance with heart failure with reduced ejection fraction (HFrEF) with underlying CAD.

Intravenous heparin and analgesics were administered. An emergency thrombectomy was performed by the cardiothoracic surgeon. After the procedure, the clinician considered administering a combination of warfarin as an oral anticoagulant (OAC) and aspirin as single antiplatelet therapy (SAPT) for three months. Additionally, the patient was prescribed a beta-blocker, mineralocorticoid receptor antagonist (MRA), ACEI and high-intensity statin. In the future, this patient was scheduled to undergo coronary arteriography (CAG) to determine the need of revascularization. Additionally, the use of implantable cardioverter-defibrillators (ICD) was proposed as a means of preventing sudden cardiac death. One week after discharge, the patient assessment in the outpatient clinic showed a good clinical outcome without any bleeding events.

Discussion

Atherosclerosis is a systemic disease that affects several vascular beds, such as coronary artery disease (CAD), cerebrovascular disease and peripheral artery disease (PAD). The possibility of previous MI should be addressed in CAD patients despite presenting with asymptomatic manifestation.[3] An asymptomatic MI may lead to a delay in diagnosis and worsening complications, such as LVT and HFrEF. The patient in this case presented with a history of MI and HFrEF. In this clinical context, we did not perform testing for acute coronary syndrome biomarkers, such as high-sensitivity cardiac troponin (hs-cTn), as there were no clinical findings and the ECG was suggestive of acute cardiac ischemia. The hs-cTn is a biomarker that is widely used in the diagnosis, risk stratification, and management of patients with suspected ACS. It indicates cardiomyocyte injury and is used as a marker of MI.[4]

LVT is defined by Virchow's triad mechanism due to left ventricular wall akinesia and dyskinesia resulting in blood stasis, endocardial injury, and hypercoagulable state.[5] LVT was detected in 15% of patients with ST-elevation MI and 25% of patients with anterior MI. TTE is used as the screening modality for LVT, with or without ultrasound enhancement [1]. A mobile, protruding and apical LVT is associated with a thrombo-embolic event which occurs in 10–15% of patients who are untreated with anticoagulants.[6] Rarely, the thrombus embolization is targeted to peripheral arteries, such as ALI.[5]

ALI is a critical vascular emergency presenting with a sudden decrease in limb perfusion due to arterial occlusion. ALI in this patient was believed to be caused by embolic rather than thrombotic as there were no pre-existing arterial occlusive symptoms. The classic manifestations of ALI are classified into a mnemonic known as the "6 Ps": pain, pallor, pulselessness, poikilothermia, paraesthesia, and paralysis.[7] DUS is a primary modality for screening and diagnosing PAD and has detected arterial occlusions in this case.[8] The severity of ALI has been described by the Rutherford classification based on sensory and motor function in the affected limb. It has an important role in clinician decision-making and in predicting the future prognosis of ALI.[9] Despite good viability, the presence of neurological deficit in the right lower limb in this patient was indicated for urgent revascularization.[8]

Antiplatelet therapy is typically given in MI to prevent the activation and aggregation of platelet in coronary arteries.[10] Furthermore, the discovery of LVT as a complication of MI indicates a patient with a significantly increased ischemic risk. Distant MI followed by LVT should be treated by OAC for 3 to 6 months.[1,10,11] PAD with indication for OAC and high-risk ischemic may be considered for OAC and SAPT for beyond one month.[11] Our clinician decided to treat this patient with a combination of OAC and antiplatelet for three months. A cross-sectional study has reported no thromboembolic events in 35 patients with LVT post-MI treated with aspirin and warfarin as a prophylaxis.[12] Despite the efficacy in ischemic risk prevention, the combination of anti-thrombotic drugs may increase the major bleeding risk that may be life-threatening which the clinician should be aware of. Multiple strategies were needed to reduce the bleeding event in many clinical contexts.[13]

In patients with heart failure, sudden cardiac death often occurs immediately. The use of an ICD has been proposed for patients with a history of coronary artery disease and a low ejection fraction (EF) below 35%. The etiology of mortality in these patients can be attributed to various electrical disturbances, including ventricular arrhythmia, bradycardia, and asystole. However, some cases may be caused by acute vascular events.[14]

Conclusion

Early recognition of MI is important in reducing complications such as LVT formation. Various manifestations of LVT require an individual approach to treatment. This approach is based on weighing the ischemic and bleeding risk of the patient to a greater reduction of the ischemic event without producing a significant bleeding event. A further clinical trial of an anticoagulant and antiplatelet combination is needed to manage thrombosis in various contexts.

Conflict of interest
There is nothing to disclose.

Funding
No funding.

References

1. McCarthy CP, Vaduganathan M, McCarthy KJ, et al. Left Ventricular Thrombus After Acute Myocardial Infarction: Screening, Prevention, and Treatment. JAMA Cardiol 2018;3:642–649.

2. Agarwal KK, Douedi S, Alshami A, et al. Peripheral Embolization of Left Ventricular Thrombus Leading to Acute Bilateral Critical Limb Ischemia: A Rare Phenomenon. Cardiol Res 2020;11:134–137.
3. Khan IA, Karim HMR, Panda CK, et al. Atypical Presentations of Myocardial Infarction: A Systematic Review of Case Reports. Cureus 2023;15:e35492.
4. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes [published correction appears in Eur Heart J 2024;45:1145]. Eur Heart J 2023;44:3720–3826.
5. Delewi R, Zijlstra F, Piek JJ. Left ventricular thrombus formation after acute myocardial infarction. Heart 2012;98:1743–1749.
6. Stratton J R, Resnick A D. Increased embolic risk in patients with left ventricular thrombi ALI to Essential Thrombocytosis. Circulation 1987;75:1004–1011.
7. Callum K, Bradbury A. ABC of arterial and venous disease: Acute limb ischaemia. BMJ 2000;320:764–767.
8. Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). Eur Heart J 2018;39:763–816.
9. Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. J Vasc Surg 1997;26:517–538.
10. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes [published correction appears in Eur Heart J 2020;41:4242]. Eur Heart J 2020;41:407–477.
11. Levine GN, McEvoy JW, Fang JC, et al. Management of Patients at Risk for and With Left Ventricular Thrombus: A Scientific Statement From the American Heart Association. Circulation 2022;146:e205–e223.
12. Ebrahimi M, Fazlinezhad A, Alvandi-Azari M, Abdar Esfahani M. Long-term clinical outcomes of the left ventricular thrombus in patients with ST elevation anterior myocardial infarction. ARYA Atheroscler 2015;11:1–4.
13. Barnes GD. Combining antiplatelet and anticoagulant therapy in cardiovascular disease. Hematology Am Soc Hematol Educ Program 2020;2020:642–648.
14. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599–3726.

ČESKÁ KARDIOLOGICKÁ SPOLEČNOST
THE CZECH SOCIETY OF CARDIOLOGY

ČESKÁ SPOLEČNOST
KARDIOVASKULÁRNÍ
CHIRURGIE

Kardio

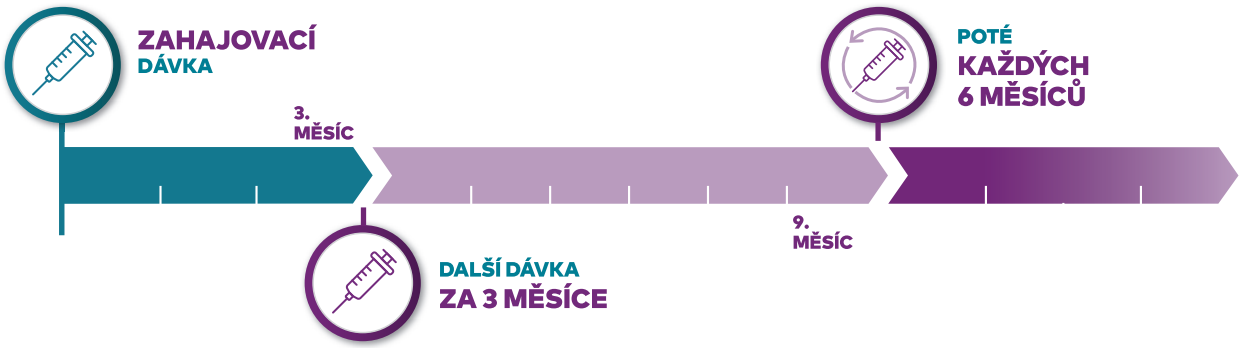
Zprávy o knize

LEQVIO®

(inklisiran) 284 mg injekční roztok v předplněné injekční stříkačce

- Jediné hypolipidemikum ve vaší ambulanci s dávkováním **2× ročně**[1,2,*]
- Efektivní a dlouhodobé snížení LDL-C **o 50-55 %**[1]
- **Příznivý** bezpečnostní profil[1]

VÍCE NEŽ **6 LET** ZKUŠENOSTÍ[3]



*Po počáteční dávce je další dávka za 3 měsíce a další vždy po 6 měsících.

Pro více informací o LEQVIO® naskenujte QR kód:

▼ Tento léčivý přípravek podléhá dalšímu sledování. To umožní rychlé získání nových informací o bezpečnosti. Žádáme zdravotnické pracovníky, aby hlásili jakákoli podezření na nežádoucí účinky. Podrobnosti o hlášení nežádoucích účinků viz SPC bod 4.8.

Zkrácená informace o přípravku LEQVIO 284 mg injekční roztok v předplněné injekční stříkačce

Složení: Jedna předplněná injekční stříkačka obsahuje inclisiranum natricum odpovídající inclisiranum 284 mg v 1,5 ml roztoku. **Indikace:** Přípravek Leqvio je indikován u dospělých s primární hypercholesterolemií (heterozygotní familiární a nefamiliární) nebo smíšenou dyslipidemií jako doplněk k dietním opatřením: v kombinaci se statinem nebo statinem v kombinaci s jinými přípravky snižujícími hladinu lipidů u pacientů neschopných dosáhnout cílů pro LDL-C při maximální tolerované dávce statinu, nebo samostatně nebo v kombinaci s jinými přípravky snižujícími hladinu lipidů u pacientů trpících nesnášenlivostí statinu nebo u nichž je statin kontraindikován. **Dávkování:** Doporučená dávka je 284 mg inklisiranu podávaná jako jednorázová subkutánní injekce: počáteční dávka, další po 3 měsících a poté každých 6 měsíců. Pokud je plánovaná dávka opožděna o méně než 3 měsíce, má být inklisiran podán a dávkování má pokračovat podle pacientova původního schématu. Pokud je plánovaná dávka opožděna o více než 3 měsíce, má být zahájen nový dávkovací režim – má být podána počáteční dávka inklisiranu, další po 3 měsících a poté každých 6 měsíců. Inklisiran lze podávat okamžitě po poslední dávce monoklonální protilátky inhibující PCSK9. Pro udržení snížení LDL-C se doporučuje, aby byl inklisiran podán do 2 týdnů po poslední dávce monoklonální protilátky inhibující PCSK9. **Kontraindikace:** Hypersenzitivita na léčivou látku nebo na kteroukoli pomocnou látku. **Zvláštní upozornění/varování:** Účinek hemodialýzy na farmakokinetiku inklisiranu nebyl studován. Vzhledem k tomu, že inklisiran je vylučován ledvinami, nemá se hemodialýza provádět po dobu nejméně 72 hodin od podání inklisiranu. **Interakce:** Inklisiran není substrátem pro běžné transportéry léčiv, a přestože nebyly provedeny studie *in vitro*, nepředpokládá se, že bude substrátem pro cytochrom P450. Inklisiran není inhibitorem nebo induktorem enzymů cytochromu P450 nebo běžných transportérů léčiv. Proto se neočekává, že by inklisiran měl klinicky významné interakce s jinými léčivými přípravky. Na základě omezených dostupných údajů nejsou očekávány klinicky významné interakce s atorvastatinem, rosuvastatinem nebo jinými statiny. **Těhotenství a kojení:** Údaje o podávání inklisiranu těhotným ženám jsou omezené nebo nejsou k dispozici. Podávání inklisiranu v těhotenství se z preventivních důvodů nedoporučuje. Není známo, zda se inklisiran vylučuje do lidského mateřského mléka. Riziko pro kojené novorozence/děti nelze vyloučit. **Nežádoucí účinky:** *Časté:* Reakce v místě vpichu. **Podmínky uchovávání:** Chraňte před mrazem. **Dostupné lékové formy/velikosti balení:** Předplněná injekční stříkačka s ochranným pouzdrem jehly: 1,5 ml roztoku v předplněné injekční stříkačce (sklo třídy I) s pístovou zátkou (brombutyl, fluorotekem potažená pryž) s jehlou, pevným krytem jehly a s ochranným pouzdrem jehly. Velikost balení jedna předplněná injekční stříkačka s ochranným pouzdrem jehly. **Poznámka:** Dříve než lék předepíšete, přečtěte si pečlivě úplnou informaci o přípravku. **Reg. č.:** EU/1/20/1494/002 **Datum registrace:** 9.12.2020. **Datum poslední revize textu SPC:** 24.03.2022. **Držitel rozhodnutí o registraci:** Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, Dublin 4, Irsko. *Výdej přípravku je vázán na lékařský předpis, přípravek je hrazen z prostředků veřejného zdravotního pojištění.*

Reference: 1. SPC Leqvio 284 mg injekční roztok v předplněné injekční stříkačce, datum poslední revize 24.3.2022. **2.** SÚKL, www.sukl.cz. **3.** Wright R.S., Raal F.J., Koenig W., Landmesser U., Leiter L.A., Vikarunnessa S., et al.: Inclisiran administration potently and durably lowers LDL-C over an extended-term follow-up: the ORION-8 trial. Cardiovasc Res. 2024;cvae109.

NOVARTIS | Reimagining Medicine

Novartis s.r.o., Na Pankráci 1724/129, 140 00 Praha 4, tel.: +420 225 775 111, info.cz@novartis.com, **www.novartis.cz**

CZ/FA-11275429/09/2024

Miroslav Souček, Bohuslav Kianička, editoři: Vnitřní lékařství 1. díl, 2. díl.

**Praha, Grada Publishing a.s., 2025. 1. díl: 616 stran, 2. díl: 860 stran.
Druhé, zcela přepracované vydání, formát 205 × 295 mm,
barevný výtisk, vázaná vazba.
ISBN: 978-80-271-7820-9 (pdf).
ISBN: 978-80-271-5142-4 (print).
Cena obou dílů v e-shopu 2 999 Kč (1 786 Kč + 1 796 Kč).**

První vydání této rozsáhlé monografie vyšlo již v roce 2011 (ISBN 13-978-80-247-2110-1) tedy před 14 lety. Od té doby došlo, zvláště v některých oborech, k velmi významným pokrokům jak v diagnostice, tak v léčbě. To byl také hlavní důvod k napsání nového, zcela přepracovaného vydání. Kniha byla žádaná, v současné době již není v žádném knihkupectví dostupná. Výbor České internistické společnosti ČLS J. E. Purkyně ji v roce 2011 ocenil první cenou za nejlepší monografii vydanou toho roku. U prvního vydání byl jediným editorem Miroslav Souček. Odborný text byl rozdělen do dvou dílů, rejstříky a zkratky do třetí, úzké knihy (128 stran). Publikace byla dvoubarevná.

Referovaná současná monografie je tvořena 20 kapitolami prezentujícími kromě základních oborů vnitřního lékařství (kardiologie, pneumologie, gastroenterologie, nefrologie, endokrinologie, poruchy metabolismu, geriatrie) i tzv. blízké obory (neurologie, psychiatrie, medicína akutních stavů). Kniha má dva hlavní autory, kteří jsou i editory, profesora MUDr. Miroslava Součka, CSc., a profesora MUDr. Bohuslava Kianičku, Ph.D, oba z II. interní kliniky Lékařské fakulty Masarykovy univerzity v Brně a Fakultní nemocnice u svaté Anny v Brně. Psalo ji 250 autorů (!). Je dvoudílná, má rozsah 1 560 stran, (první díl 666 stran, druhý díl 866 stran). Rozsáhlý autorský kolektiv (s jedinou výjimkou) tvoří výhradně pracovníci klinik a ústavů Lékařské fakulty Masarykovy univerzity v Brně.

Text prvního i druhého dílu uvádějí shodně jmenný seznam kolektivu autorů (strany V–XII), obsah 1. dílu (strany XIII–XXIX), obsah 2. dílu (strany XXXI–XLVII) a Úvodní slovo (1. strana). Jednotlivé odborné kapitoly obou dílů jsou číslovány. Byly zařazeny v tomto pořadí: 1. Úvod do vnitřního lékařství, obecná problematika (strany 1–4), 2. Kardiovaskulární onemocnění (strany 5–186), 3. Bronchopulmonální onemocnění (strany 187–34), 4. Onemocnění trávicího ústrojí (strany 235–344), 5. Onemocnění ledvin a močových cest (strany 345–435), 6. Onkologie, hematoonkologie a hematologie (strany 437–615).

Počátek obsahu druhého dílu je shodný s dílem prvním. Odborný text uvádí 7. kapitola, jíž je Revmatologie (strany 617–716), pokračují další kapitoly: 8. Onemocnění imunitního systému (strany 717–756), 9. Endokrinologická a metabolická onemocnění (strany 757–894), 10. Medicína akutních stavů (strany 895–956), 11. Infekční onemocnění (strany 957–1092), 12. Neurologická onemocnění (strany 1093–1152), (výtisk recenzované knihy měl strany 1142 a 1143 vytištěny tučně), 13. Psychiatrická onemocnění a psychiatrické poruchy (strany 1153–1172), 14. Geriatrie (strany 1173–1207), 15. Otravy a předávkování (strany 1209–1256), 16. Bolest (strany 1257–1284), 17. Výživa nemocných z pohledu vnitřního lékařství (strany 1285–1312), 18. Genetika v interní medicíně (strany 1313–1348), 19. Paliativní medicína a péče o pacienta v závěru života (strany 1349–1358). Kapitola 20 Multimorbidní pacient ve vnitřním lékařství (strany 1359–1373) odbornou textovou část knihy uzavírá. Následuje seznam zkratek (1375–1402), dvousloupcový rejstřík (1403–1433) a český a anglický souhrn (1434). Nejrozsáhlejší kapitolou jsou (stejně jako v jiných učebnicích vnitřního lékařství) kardiovaskulární onemocnění (178 stran), nejkratší je úvod a obecná problematika (3 strany).

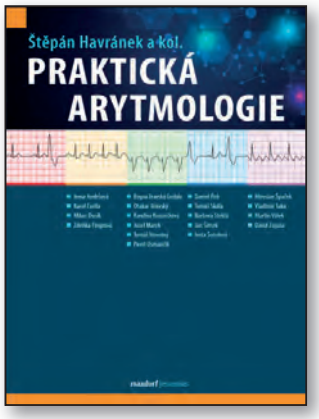
Obsahovou náplní přesahuje odborný text hranice interny a zasahuje do příbuzných oborů (neurologie, psychiatrie, geriatrie, genetika ad.), uvádí i několik významných příznaků (bolest, multimorbidita ad.) nebo léčebných postupů (předávkování, výživa ad.). Text všech kapitol je bohatě ilustrován velkým počtem většinou barevných obrázků, tabulek a schémat. Převážná část reprodukcí rentgenogramů i scanů výpočetní tomografie, magnetické rezonance je výborné kvality. Elektrokardiogramům prospěla reálná reprodukce originálů. Protože texty psal velký počet autorů (250!), některé informace se opakují, ale neprotiřečí si. Formální úroveň textů kapitol závisí na publikační zkušenosti jednotlivých autorů. Ale odborně je text na vysoké úrovni, je aktuální, respektuje doporučení (guidelines) odborných společností, pokud je k danému tématu vydaly.

Rozsáhlou knihu vydalo nakladatelství Grada Publishing (stejně jako její první vydání v roce 2011). I když bylo zpracování velkého množství rukopisů a obrazových ilustrací náročné, odevzdalo nakladatelství velmi kvalitní a bezchybnou redakční práci.

Komu knihu doporučit?

Ve shodě s editory ji doporučují (citace) „všem čtenářům, aby se bezpečně orientovali v široké problematice vnitřního lékařství“ a věřím, „že bude přínosem nejen pro internisty, ale i pro lékaře jiných oborů“. Její pedagogická funkce se uplatní v předatestačním studiu.

Prof. MUDr. Jan Petrášek, DrSc.,
III. interní klinika, 1. lékařská fakulta
Univerzity Karlovy a Všeobecná fakultní nemocnice
v Praze, e-mail: petrjanv@email.cz



Štěpán Havránek a kol. Praktická arytmologie

Praha, Maxdorf s.r.o, 2024.
První vydání, formát 212×273 mm, barevný výtisk, vázaná vazba.
ISBN: 978-80-7345-789-1.

Na monografii se podílelo celkem 20 lékařů, editorem je profesor MUDr. Štěpán Havránek, Ph.D., spoluautory jsou: MUDr. Irena Andršová, Ph.D.; doc. MUDr. Karol Čurila, Ph.D.; MUDr. Milan Dusík, Ph.D.; Ing. Zdeňka Fingrová, Ph.D.; MUDr. Bogna Jiravská Godula, MBA; MUDr. Otakar Jiravský, Ph.D., MBA; MUDr. Karolína Kvasničková; MUDr. Josef Marek, Ph.D.; prof. MUDr. Tomáš Novotný, Ph.D.; prof. MUDr. Pavel Osmančík, Ph.D.; MUDr. Daniel Rob, Ph.D.; prof. MUDr. Tomáš Skála, Ph.D., FESC; MUDr. Barbora Steklá; MUDr. Jan Šimek, Ph.D.; MUDr. Iveta Šotolová; doc. MUDr. Miroslav Špaček, Ph.D.; doc. MUDr. Vladimír Tuka, Ph.D.; MUDr. Martin Válek, Ph.D.; doc. MUDr. David Zogala, Ph.D. Recenzovali prof. MUDr. Miloš Táborský, CSc., MBA, FACC, FESC, a doc. MUDr. Petr Němec, DrSc., MBA.

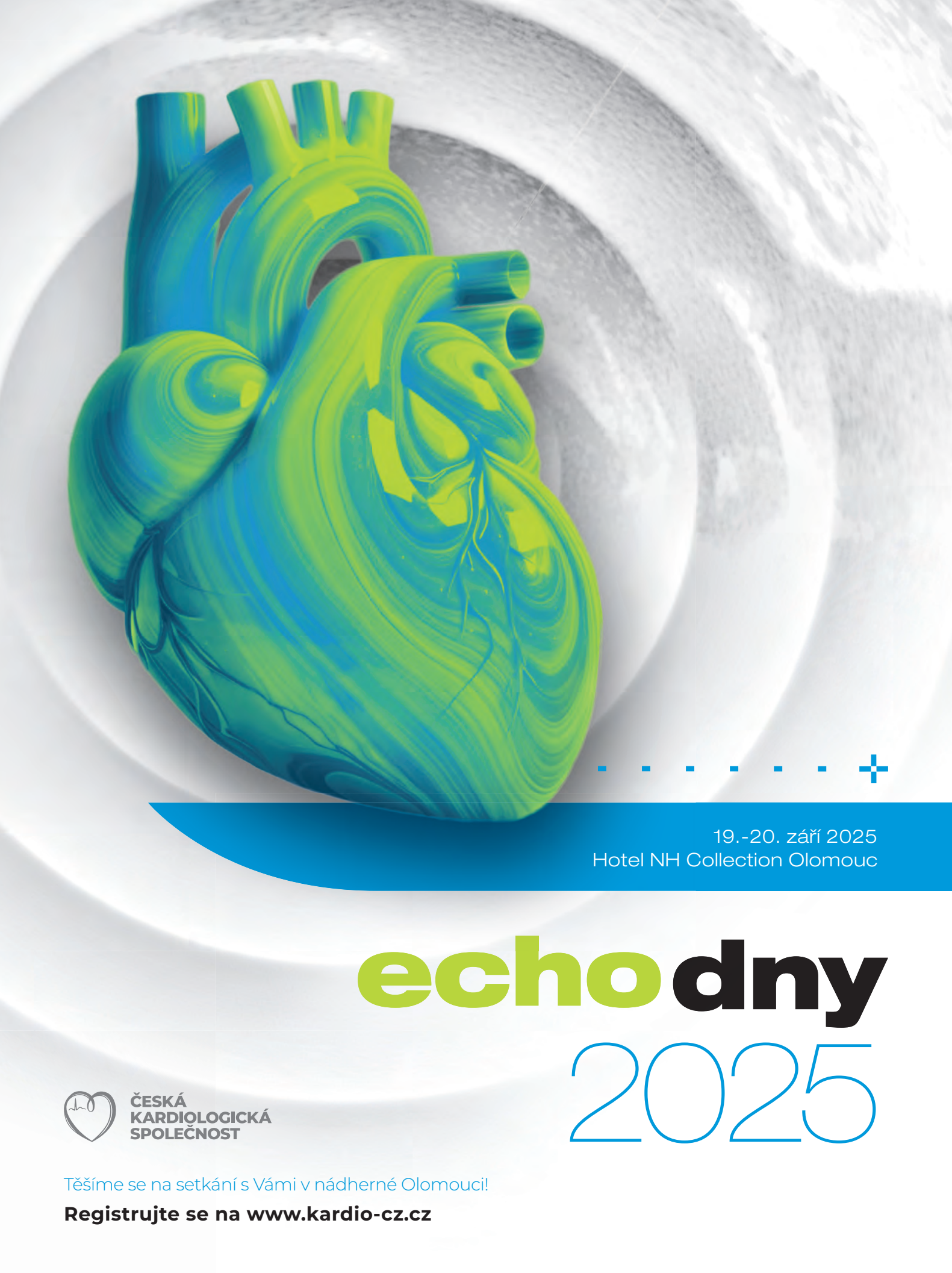
Monografie má 375 stran, text je rozdělen do 14 kapitol:

1. Základní přístup k pacientovi s poruchou rytmu;
2. Symptomatologie poruch srdečního rytmu a náhlá smrt;
3. Rizika poruch srdečního rytmu a riziková stratifikace;
4. Praktický přístup k vyšetřovacím metodám v arytmologii;
5. Základy léčby arytmií;
6. Klasifikace arytmií;
7. Diferenciální diagnostika arytmií;
8. Fibrilace síní;
9. Flutter síní a ostatní reentrantní tachykardie, síňové tachykardie;
10. Paroxysmální supraventrikulární tachykardie;
11. Poruchy komorového rytmu;
12. Bradyarytmie;
13. Synkopa;
14. Specifické situace v arytmologii.

Každá kapitola má v úvodu krátký souhrn minima pro praxi a obsahuje velké množství velmi pěkných EKG záznamů ke všem referovaným arytmiím. Obrazová dokumentace představuje jednu z předností této monografie, k dalším pak patří přehledné algoritmy shrnující diagnostiku i léčbu arytmií. Také tabulky s přehledem farmakoterapie jsou vhodným doplňkem velmi kvalitního textu celé knihy. Literatura je uváděna za jednotlivými kapitolami, nechybí přehled použitých zkratek a rejstřík. Pochvalu zaslouží vydavatelství Maxdorf pod vedením MUDr. Jana Huga, které odvedlo výbornou práci a celá monografie je i po této stránce pěkné dílo.

Monografie představuje mimořádné dílo, které v roce 2025 přináší komplexní a ucelený přehled arytmologie, přístupem zaměřeným na praktické postupy jak v diagnostice, tak v léčbě poruch srdečního rytmu. Souhrn této problematiky je nesmírně přínosný především proto, že arytmologie se v posledních desítkách let stala postupně velmi specifickou oblastí kardiologie s ohromným rozvojem diagnostiky i léčby a vedla k specializaci, ve které je orientace obecného kardiologa náročná. Právě fakt, že přední odborníci české arytmologie připravili praktický souhrn této problematiky, je důležitou předností této monografie. Srozumitelným způsobem podávají přehled jednotlivých poruch srdečního rytmu, jejich diagnostiky a léčby jak farmakologické, tak intervenční a přístrojové, současně jsou všechny postupy podložené doporučeními odborných společností. Nechybějí ani kapitoly o přístupu k těhotným ženám s poruchou srdečního rytmu nebo nemocným po korekci vrozených vad. Rozebrána je i problematika arytmií u sportovců. Na závěr knihy je zařazeno i velice aktuální téma problematiky řízení motorových vozidel. Kniha je určena jak pro kardiology, tak pro řadu dalších oborů, včetně praktických lékařů, neboť setkání s arytmiemi je dnes velmi časté, přivádí pacienty do našich ambulancí každý den.

Prof. MUDr. Michael Aschermann, DrSc., FACC, FESC,
II. interní klinika kardiologie a angiologie, 1. lékařská fakulta Univerzity Karlovy a Všeobecná fakultní nemocnice v Praze, Praha,
e-mail: aschermann@seznam.cz



19.-20. září 2025
Hotel NH Collection Olomouc

echo dny 2025

ČESKÁ KARDIOLOGICKÁ SPOLEČNOST

Těšíme se na setkání s Vámi v nádherné Olomouci!

Registrujte se na www.kardio-cz.cz

ČASR
ČESKÁ ASOCIACE PRO SRDEČNÍ RYTMUS

ČESKÁ KARDIOLOGICKÁ SPOLEČNOST

SASA

KardioTech
PS ČESKÉ KARDIOLOGICKÉ SPOLEČNOSTI

9.–11. listopadu 2025
Clarion Hotel Olomouc

XXII.

ČESKÉ A SLOVENSKÉ SYMPOZIUM O ARYTMIÍCH A KARDIOSTIMULACI

WWW.KARDIO-CZ.CZ | WWW.ARYTMIE.SK