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THE CZECH SOCIETY OF CARDIOLOGY



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KARDIOVASKULÁRNÍ
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Cor et Vasa

**Cardiovascular Risk and DXA Changes
Post-Sleeve Gastrectomy**

**Comparison of the endocardial radiofrequency
ablation of septal hypertrophy and alcohol
septal ablation**

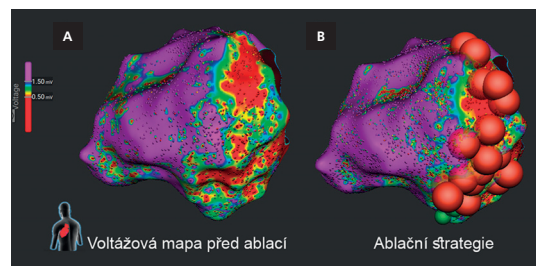
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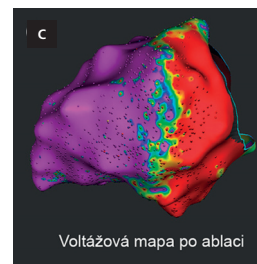
Cardiac sequelae after COVID-19

**Nefarmakologická léčba komorových tachykardií
v komplexním kardiovaskulárním centru**

Izolovaná disekcia arteria carotis interna



Ukázka ablační strategie
u pacienta po infarktu
myokardu.
(Schlosser F, Peichl P, Kautzner
J. Nefarmakologická
lčba komorových
tachykardií v komplexním
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Přehledový článek,
str. 620–630).



Cor et Vasa

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Cardiovascular Risk Factors and DXA-Assessed Body Composition Changes after Laparoscopic Sleeve Gastrectomy: A One-Year Retrospective Study

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Dyslipidemie

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HDL cholesterol

Kardiovaskulární riziko

Rukávová resekce žaludku

Složení těla

SOUHRN

Úvod: Laparoskopická rukávová resekce žaludku (LSG) se ukázala jako účinný zákrok při léčbě těžké obezity, avšak její vliv na kardiovaskulární rizika přes změny tělesného složení dává prostor k bližšímu zkoumání.

Metody: Tato retrospektivní studie hodnotila 98 pacientů, kteří podstoupili LSG, analyzovali jsme tělesné složení pomocí duální rentgenové absorpciometrie (DXA) a metabolické parametry před operací a 12 měsíců po operaci. Byly hodnoceny změny hmotnosti, tukové hmoty, netukové hmoty, lipidového profilu a glukózoového metabolismu, včetně jejich vzájemných vztahů.

Výsledky: Dvanáct měsíců po operaci byly pozorovány významné redukce celkové tělesné hmotnosti, tukové hmoty a netukové hmoty (všechny $p < 0,001$). Metabolické parametry vykazovaly výrazné zlepšení, s významným poklesem glykemie nalačno, glykovaného hemoglobinu (HbA_{1c}) a triglyceridů, spolu se zvýšením HDL cholesterolu (všechny $p < 0,001$). LDL/HDL poměr se zlepšil z mediánu (interkvartilové rozpětí [IQR]) 2,79 (1,59) na 2,20 (0,91) ($p < 0,001$). Aterogenní index plazmy se snížil z 0,23 (0,30) na -0,10 (0,29) ($p < 0,001$), což představuje posun ze zvýšeného na nízké kardiovaskulární riziko. Byla zjištěna střední negativní korelace mezi změnami netukové hmoty a HDL cholesterolu ($r = -0,331$, $p < 0,001$), zatímco slabé, ale významné korelace byly nalezeny mezi změnami poměru pas/boky a glykemickými parametry.

Závěr: LSG vede k významnému zlepšení kardiovaskulárního rizika jeden rok po operaci s pozitivním ovlivněním lipidových parametrů a složení těla. Nově objevená korelace mezi ztrátou netukové hmoty a změnami HDL cholesterolu naznačuje, že zachování netukové hmoty by mohlo být klíčové pro optimalizaci metabolických benefitů po bariatrické operaci.

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ABSTRACT

Background: While laparoscopic sleeve gastrectomy (LSG) is known to reduce weight, its impact on cardiovascular risk profile through changes in body composition remains unclear.

Methods: This retrospective study evaluated 98 patients who underwent LSG, analyzing body composition via dual-energy X-ray absorptiometry (DXA) and cardiovascular risk parameters at baseline and 12 months post-surgery. Changes in weight, fat mass, lean mass, atherogenic lipid profile, and glucose metabolism were assessed, along with their interrelationships.

Results: Significant reductions were observed in total body weight, fat mass, and lean mass at 12 months post-surgery (all $p < 0.001$). Metabolic parameters showed marked improvements, with significant decreases in fasting glucose, HbA_{1c} , and triglycerides, alongside an increase in HDL cholesterol (all $p < 0.001$). The LDL/

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HDL ratio improved from median (IQR) 2.79 (1.59) to 2.20 (0.91) ($p < 0.001$). The atherogenic index of plasma decreased from 0.23 (0.30) to -0.10 (0.29) ($p < 0.001$), representing a shift from increased to low cardiovascular risk. A moderate negative correlation was identified between changes in lean mass and HDL cholesterol ($r = -0.331$, $p < 0.001$), while weak but significant correlations were found between changes in waist-to-hip ratio and glycemic parameters.

Conclusions: LSG results in significant improvements in cardiovascular risk profile at one year post-surgery, with favorable changes in atherogenic lipid parameters and body composition. The novel correlation between lean mass preservation and HDL cholesterol suggests that maintaining muscle mass might be crucial for optimizing cardiovascular benefits following bariatric surgery.

Introduction

Obesity has emerged as one of the most pressing public health challenges of the 21st century, with its prevalence reaching epidemic proportions worldwide.¹ Beyond its direct health implications, obesity represents a major modifiable risk factor for cardiovascular disease, the leading cause of mortality worldwide.² The pathophysiological relationship between obesity and cardiovascular risk is complex and multifaceted, involving various metabolic perturbations including dyslipidemia, insulin resistance, and chronic inflammation.³ Of particular concern is the impact of excess adiposity on lipid metabolism, specifically its association with decreased high-density lipoprotein (HDL) cholesterol levels and elevated triglycerides, both independent risk factors for cardiovascular disease.⁴

In cases of severe obesity, bariatric surgery has demonstrated superior efficacy compared to conventional weight loss approaches, not only in achieving sustained weight reduction but also in improving cardiovascular risk factors.^{5,6} Among various bariatric procedures, laparoscopic sleeve gastrectomy (LSG) has gained prominence due to its favourable risk-benefit profile and significant metabolic effects.⁷ LSG induces weight loss through both restrictive and hormonal mechanisms, leading to substantial improvements in obesity-related comorbidities. However, the procedure's impact extends beyond simple weight reduction, affecting body composition and metabolic parameters in ways that are not fully understood.

Traditional methods of assessing post-bariatric outcomes have primarily focused on total weight loss and basic anthropometric measurements. However, these metrics fail to capture crucial changes in body composition, particularly the relative loss of fat versus lean mass.⁸ Dual-energy X-ray absorptiometry (DXA) has emerged as a valuable tool in this context, offering precise quantification of body composition components.⁹ This technology enables detailed analysis of fat distribution and lean mass changes, providing insights that may be more relevant to cardiovascular risk assessment than total weight loss alone.

The preservation of lean mass during weight loss has gained increasing attention in bariatric medicine, as skeletal muscle plays a crucial role in metabolic health.⁹ Emerging evidence suggests that muscle tissue functions as an endocrine organ, secreting myokines that influence lipid metabolism and insulin sensitivity.¹⁰ However, the specific relationship between post-operative lean mass preservation and improvements in cardiovascular risk factors, particularly lipid profiles, remains inadequately characterized. This knowledge gap is especially relevant

given that excessive loss of lean mass might potentially attenuate the metabolic benefits of bariatric surgery.

Furthermore, the dynamic interplay between body composition changes and metabolic parameters following LSG warrants investigation within the context of cardiovascular risk modification. While improvements in traditional cardiovascular risk factors after bariatric surgery are well-documented, current research is establishing precise body composition targets to optimize these cardiovascular benefits.⁶ Understanding these relationships could inform post-operative care strategies and potentially enhance cardiovascular outcomes in bariatric patients.

Therefore, this retrospective study aimed to evaluate comprehensive changes in body composition via DXA and their correlation with metabolic parameters one year after LSG. Our investigation focused particularly on the relationship between lean mass preservation and metabolic improvements, with special attention to lipid profile changes. By elucidating these associations, we sought to provide insights that could guide post-operative care strategies and optimize metabolic outcomes in patients undergoing bariatric surgery.

Material and methods

Study design and population

The study retrospectively enrolled 98 patients who underwent laparoscopic sleeve gastrectomy (LSG) at two centers (Hospital 1 [Hospital AGEL Ostrava-Vítkovice]: 71 [72%] and Hospital 2 [University Hospital Ostrava]: 27 [28%] of patients) between the years 2010–2019. There were no significant differences in patient characteristics, surgical techniques, and protocols or outcomes between the two centers. Inclusion criteria followed the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) guidelines: body mass index (BMI) ≥ 40 kg/m² or BMI ≥ 35 kg/m² with obesity-related comorbidities. Exclusion criteria included active malignancy, and inability to complete follow-up visits. The study was approved by the institutional ethics committee.

Clinical assessments and measurements

Comprehensive evaluations were conducted at baseline and 12 months post-surgery. Anthropometric measurements included weight, height, waist circumference, and hip circumference, performed using standardized protocols. Body composition analysis was performed using DXA (Discovery A; Hologic, Waltham, MA, USA), which provided measurements of total body mass, fat mass, and lean

Table 1 – Baseline demographic and clinical characteristics

Characteristics	Value
Total participants, n	98
Age (years), mean $\pm$ SD	43.8 $\pm$ 9.6
Sex, n (%)	
Male	25 (25.5 %)
Female	73 (74.5 %)
Height (cm), mean $\pm$ SD	169.5 $\pm$ 8.4

Baseline demographic and clinical characteristics of 98 patients undergoing laparoscopic sleeve gastrectomy. Data presented as mean $\pm$ standard deviation (SD) or number (percentage).

mass. Blood samples were collected after overnight fasting for analysis of lipid profile (triglycerides, high-density lipoprotein cholesterol, total cholesterol, and low-density lipoprotein cholesterol) and glucose metabolism (fasting glucose and glycated hemoglobin).

Statistical analysis

Statistical analyses were performed using IBM SPSS version 30.0.0. The Shapiro–Wilk test was used to assess data normality. For non-normally distributed variables (weight, DXA total mass, fat mass, lean mass, glycemia, triglycerides, HbA_{1c}, LDL/HDL ratio, atherogenic index and waist-to-hip ratios), the Wilcoxon signed-rank test was applied to compare baseline and 12-month values. Paired t-tests were used for normally distributed variables. Only parameters showing significant changes ($p < 0.05$) were included in the subsequent correlation analysis. Relationships between changes in body composition and metabolic parameters were evaluated using Spearman's correlation coefficient. Correlation strength was categorized as weak ($r = 0.2$ – 0.3), moderate ($r = 0.3$ – 0.5), or strong ($r > 0.5$).

Results

Patient demographics

The study cohort comprised 98 Caucasian patients (25 men, 73 women) with a mean age of 43.8 ± 9.6 years and

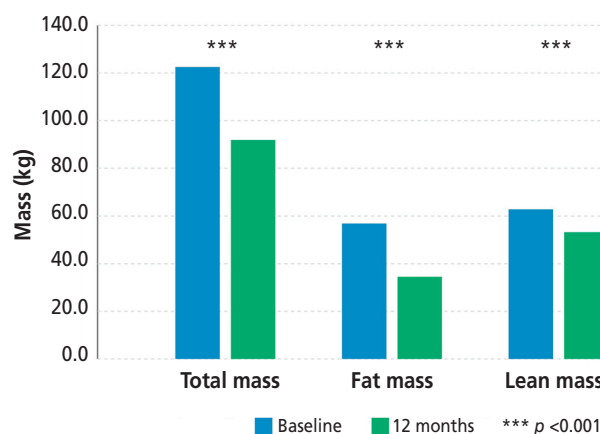


Fig. 1 – Body composition changes 12 months after laparoscopic sleeve gastrectomy.

Changes in body composition parameters measured by dual-energy X-ray absorptiometry (DXA) at baseline (blue bars) and 12 months post-surgery (green bars). Values are presented as medians. Total mass decreased from 122.5 kg to 91.8 kg, fat mass from 56.9 kg to 34.6 kg, and lean mass from 62.8 kg to 53.2 kg. *** indicates statistical significance at $p < 0.001$ for all comparisons.

mean height of 169.5 ± 8.4 cm (Table 1). Pre-existing comorbidities included hypertension in 49 patients (50%) and type 2 diabetes mellitus in 25 patients (25.5%). 26 patients (26.5%) were current smokers at the time of surgery. All patients completed the 12-month follow-up period.

Changes in body composition

Significant reductions were observed in all anthropometric measurements at 12 months post-surgery (Table 2, Fig. 1). Median body weight decreased by 31.7 kg, from 122.4 kg (IQR: 13.2) at baseline to 90.7 kg (IQR: 26.3) at 12 months ($p < 0.001$). DXA analysis revealed substantial changes in body composition. Total body mass decreased from a median of 122.5 kg (IQR: 34.8) to 91.8 kg (IQR: 26.9) ($p < 0.001$). Fat mass showed a median reduction of 22.3 kg, from 56.9 kg (IQR: 19.6) to 34.6 kg (IQR: 16.0) ($p < 0.001$). Lean mass also decreased significantly, from 62.8 kg (IQR: 17.2) to 53.2 kg (IQR: 17.1) ($p < 0.001$).

Table 2 – Changes in body composition and anthropometric parameters

Parameter	Baseline	12 months
Weight (kg), median (IQR)	122.4 (13.2)	90.7 (26.3)
DXA total mass (kg), median (IQR)	122.5 (34.9)	91.8 (26.9)
DXA fat mass (kg), median (IQR)	56.9 (19.6)	34.6 (16.0)
DXA lean mass (kg), median (IQR)	62.8 (17.2)	53.2 (17.1)
Waist 1 (cm), mean $\pm$ SD	120.4 $\pm$ 14.5	97.3 $\pm$ 13.3
Waist 2 (cm), mean $\pm$ SD	129.7 $\pm$ 15.9	104.6 $\pm$ 14.1
Hip circumference (cm), mean $\pm$ SD	132.9 $\pm$ 13.5	112.00 $\pm$ 11.6
Waist 1-to-hip ratio, mean $\pm$ SD	0.91 $\pm$ 0.11	0.87 $\pm$ 0.10
Waist 2-to-hip ratio, mean $\pm$ SD	0.98 $\pm$ 0.10	0.93 $\pm$ 0.09

Body composition and anthropometric measurements at baseline and 12 months post-surgery ($n = 98$). Waist 1 measured at midpoint between 10th rib and iliac crest. Waist 2 measured at umbilicus level. All changes were statistically significant ($p < 0.001$). Data presented as median (interquartile range, IQR) or mean $\pm$ standard deviation (SD).

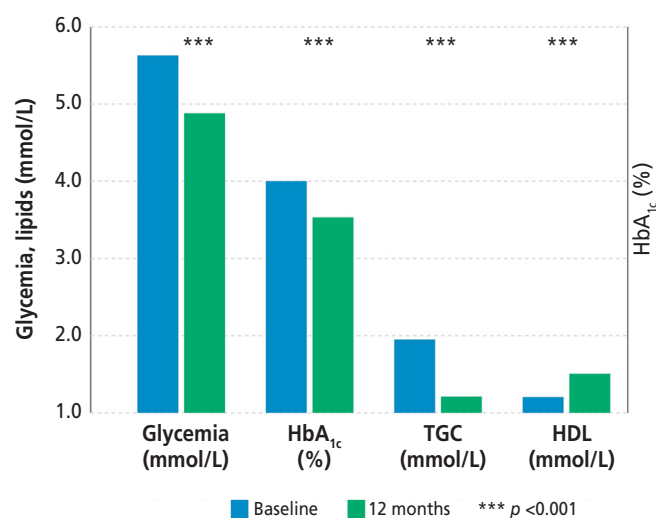


Fig. 2 – Changes in metabolic parameters 12 months after laparoscopic sleeve gastrectomy. Changes in metabolic parameters at baseline (blue bars) and 12 months post-surgery (green bars). Values are shown for glycemia (mmol/L), glycated hemoglobin (HbA_{1c} %), triglycerides (TGC, mmol/L), and HDL cholesterol (mmol/L). Significant improvements were observed in all parameters, with decreases in glycemia (5.63 to 4.88 mmol/L), HbA_{1c} (4.0 to 3.6%), and TGC (1.95 to 1.21 mmol/L), while HDL cholesterol increased (1.20 to 1.51 mmol/L). *** indicates statistical significance at $p < 0.001$ for all comparisons.

Metabolic outcomes

Glucose metabolism markers showed significant improvements (Table 3, Fig. 2). Median fasting glucose levels decreased from 5.63 mmol/L (IQR: 1.75) to 4.88 mmol/L (IQR: 0.75) ($p < 0.001$). HbA_{1c} levels reduced from a median of

4.0% (IQR: 1.4) to 3.6% (IQR: 0.6) ($p < 0.001$). The lipid profile demonstrated favourable changes, with median triglyceride levels decreasing from 1.95 mmol/L (IQR: 0.99) to 1.21 mmol/L (IQR: 0.64) ($p < 0.001$). Mean HDL cholesterol increased from 1.20 ± 0.30 mmol/L to 1.51 ± 0.32 mmol/L ($p < 0.001$). Total cholesterol and LDL cholesterol did not show statistically significant changes over the study period.

Correlation analysis

Analysis of the relationships between changes in body composition and metabolic parameters revealed several significant correlations (Table 4). The most notable was a moderate negative correlation between changes in lean mass and HDL cholesterol ($r = -0.331$, $p < 0.001$). Weak but significant correlations were observed between changes in hip circumference and HbA_{1c} ($r = -0.258$), between changes in glycemia and waist-to-hip ratio (first measurement: $r = 0.235$; second measurement: $r = 0.250$), and between changes in HbA_{1c} and waist-to-hip ratio (first measurement: $r = 0.224$; second measurement: $r = 0.245$).

Additional analysis of atherogenic profile

The comprehensive analysis of cardiovascular risk markers revealed significant improvements in the atherogenic profile (Table 5). The LDL/HDL ratio decreased from median (IQR) 2.79 (1.59) to 2.20 (0.91) ($p < 0.001$). Analysis of the atherogenic index of plasma (AIP), calculated as $\log_{10}(\text{triglycerides}/\text{HDL cholesterol})$, showed significant improvement from baseline to 12-month follow-up. The median (IQR) AIP decreased from 0.23 (0.30) at baseline, indicating increased cardiovascular risk, to -0.10 (0.29) at 12 months, representing low cardiovascular risk ($p < 0.001$).

Table 3 – Changes in metabolic parameters

Parameter	Baseline	12 months	p-value
Glycemia (mmol/L), median (IQR)	5.63 (1.75)	4.88 (0.75)	<0.001
HbA _{1c} (%), median (IQR)	4.0 (1.4)	3.6 (0.6)	<0.001
TGC (mmol/L), median (IQR)	1.95 (0.99)	1.21 (0.64)	<0.001
HDL cholesterol (mmol/L), mean $\pm$ SD	1.20 ± 0.30	1.51 ± 0.32	<0.001
Total cholesterol	Not significant change		NS
LDL cholesterol	Not significant change		NS

Changes in metabolic parameters from baseline to 12 months post-surgery (n = 98). Data presented as median (IQR) or mean $\pm$ SD. NS – not significant; TGC – triglycerides.

Table 4 – Correlation analysis of changes in body composition and metabolic parameters

Parameters	Correlation coefficient (R)	Strength
Δ DXA lean mass vs. Δ HDL	-0.331	Moderate
Δ Hip circumference vs. Δ HbA _{1c}	-0.258	Weak
Δ Glycemia vs. waist 1-to-hip ratio	0.235	Weak
Δ Glycemia vs. waist 2-to-hip ratio	0.250	Weak
Δ HbA _{1c} vs. waist 1-to-hip ratio	0.224	Weak
Δ HbA _{1c} vs. waist 2-to-hip ratio	0.245	Weak

Correlation analysis between changes in body composition and metabolic parameters over 12-month follow-up. All correlations significant at $p < 0.05$. Correlation strength: weak ($r = 0.2$ – 0.3), moderate ($r = 0.3$ – 0.5), strong ($r > 0.5$).

Table 5 – Changes in atherogenic profile after laparoscopic sleeve gastrectomy

Parameter	Baseline	12 months	p-value
LDL/HDL ratio, median (IQR)	2.79 (1.59)	2.20 (0.91)	<0.001
Atherogenic index of plasma, median (IQR)	0.23 (0.30)	−0.10 (0.29)	<0.001

AIP was calculated as $\log_{10}(\text{triglycerides}/\text{HDL cholesterol})$

Cardiovascular risk interpretation:

- AIP >0.21 increased risk; AIP 0.11–0.21 intermediate risk; AIP <0.11 low risk;
- LDL/HDL ratio interpretation: Ideal: <2.0; good: <5.0; poor: >5.0

Discussion

This retrospective study demonstrates significant improvements in both body composition and cardiovascular risk factors one year after laparoscopic sleeve gastrectomy, with several notable findings regarding the interrelationship between these changes. The median weight loss of 31.7 kg observed in our cohort aligns with previous studies,¹¹ which reported mean excess weight loss ranging from 60–70% at one year post-LSG. This weight loss represents substantial cardiovascular risk reduction, particularly considering established evidence that each 10 kg of weight loss associates with a 6 mmHg reduction in systolic blood pressure and improved insulin sensitivity.¹²

The comprehensive body composition analysis via DXA revealed substantial reductions in both fat mass (median reduction 22.3 kg) and lean mass (median reduction 9.6 kg). These findings are comparable to those reported by previous studies.¹³ However, our study extends beyond these observations by examining the metabolic implications of these compositional changes.

Our analysis revealed clinically significant improvements in cardiovascular risk markers. The marked increase in HDL cholesterol and substantial decrease in triglycerides, combined with the improvement in LDL/HDL ratio, represent meaningful reductions in cardiovascular risk. The magnitude of HDL increase (0.31 mmol/L) is particularly noteworthy, given that previous studies have associated each 0.03 mmol/L increase in HDL with a 2–3% reduction in cardiovascular events.¹⁴

The most significant finding of our study was the moderate negative correlation ($r = -0.331$, $p < 0.001$) between changes in lean mass and HDL cholesterol levels. This novel observation suggests that excessive lean mass loss may attenuate improvements in this cardioprotective lipoprotein. This relationship likely reflects the role of skeletal muscle as an endocrine organ,¹⁰ through myokine secretion. Our findings add to this body of knowledge by suggesting that lean mass preservation during post-bariatric weight loss might be crucial for optimizing cardiovascular risk reduction.

The marked reduction in atherogenic index of plasma represents a clinically significant shift from high to low cardiovascular risk category. This improvement in AIP, which is considered a sensitive predictor of cardiovascular risk, particularly in obesity, suggests that the beneficial ef-

fects of sleeve gastrectomy extend beyond simple weight reduction to fundamental improvements in lipoprotein metabolism. The magnitude of AIP reduction shows that bariatric surgery can lead to substantial improvements in cardiovascular risk markers, even before maximal weight loss is achieved.

The improvements in glycemic parameters (median fasting glucose reduction from 5.63 to 4.88 mmol/L) and lipid profile (triglycerides reduction from 1.95 to 1.21 mmol/L) are consistent with previous research.⁶ However, our study uniquely demonstrates weak but significant correlations between changes in waist-to-hip ratio and both glycemia ($r = 0.235$ – 0.250) and HbA_{1c} ($r = 0.224$ – 0.245), suggesting that improvements in body fat distribution contribute to enhanced glucose metabolism. These changes in glycemic parameters contribute to cardiovascular risk reduction through reduced glycation end-products, improved endothelial function, decreased inflammatory markers, and enhanced insulin sensitivity.

These findings have important implications for cardiovascular risk management. The significant improvements in cardiovascular risk factors support considering LSG in high-risk cardiovascular patients with obesity who have failed conservative management. When monitoring these patients, careful attention should be paid to exercise testing protocols and safety measures, particularly in times of increased infectious disease risk.¹⁵ The inverse relationship between lean mass loss and HDL improvement suggests that muscle preservation strategies should be integrated into post-operative cardiovascular risk management. This aligns with recent guidelines by major bariatric societies recommending structured resistance training and adequate protein intake post-operatively.^{16–19} Furthermore, regular monitoring of lipid parameters is essential for optimizing cardioprotective medication regimens.

Several limitations warrant consideration. The absence of inflammatory marker data limits our understanding of inflammation-mediated cardiovascular risk reduction. We also lack endothelial function measurements and direct assessment of cardiovascular events. While our one-year follow-up provides valuable insights, longer-term studies are needed to evaluate the durability of these relationships.

Future research directions should explore three critical areas: determining the optimal fat-to-lean mass reduction ratio for maximal metabolic benefits, evaluating post-operative protocols focused on lean mass preservation through prospective studies, and developing personalized strategies based on individual body composition profiles. These investigations would help establish evidence-based guidelines for optimizing metabolic outcomes after bariatric surgery.

Conclusions

This study demonstrates that laparoscopic sleeve gastrectomy leads to significant improvements in cardiovascular risk factors at one year post-surgery, characterized by favourable changes in atherogenic lipid profile and body composition. The novel finding of a relationship between lean mass preservation and HDL cholesterol levels suggests that maintaining muscle mass might be crucial for

optimizing cardiovascular benefits. These results support the role of LSG in cardiovascular risk reduction strategies for patients with severe obesity.

Conflict of interest

The authors declare no conflict of interest.

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Ethical statement

This study was approved by the local Ethics Committee (Hospital AGEL Ostrava-Vítkovice, EK/94/2024). Due to the retrospective nature of the study, the requirement for informed consent was waived by the local Ethics Committee.

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Endocardial radiofrequency ablation of septal hypertrophy in the interventional treatment of the hypertrophic obstructive cardiomyopathy; comparison with the alcohol septal ablation, pilot data of the randomized trial

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Gradient ve výtokovém traktu levé komory

Hypertrofická obstrukční

kardiomyopatie

Zlepšení funkční třídy NYHA

SOUHRN

Úvod: Hypertrofická obstrukční kardiomyopatie (HOCM) je charakterizována dynamickou obstrukcí výtokového traktu levé komory (LVOT) způsobenou asymetrickou hypertrofií septa a systolickým anteriorním pohybem (SAM) předního cípu mitrální chlopně. U pacientů s přetrvávajícími symptomy navzdory optimalizované farmakoterapii je indikována intervenční metoda redukce septální hypertrofie. Zatímco alkoholová septální ablace (ASA) je dlouhodobě zavedenou metodou, endokardiální radiofrekvenční ablace septální hypertrofie (ERASH) se v poslední době jeví jako slibná alternativní strategie. Cílem naší práce je ukázat pilotní výsledky randomizované studie srovnávající účinnost a bezpečnost ERASH a ASA.

Metodika: Cílem této prospektivní, randomizované pilotní studie bylo srovnat účinnost a bezpečnost ERASH a ASA u symptomatických pacientů s obstrukční HOCM refrakterní na medikamentózní terapii. ERASH byla provedena pomocí katérové radiofrekvenční ablace septální hypertrofie za použití 3D elektroanatomického mapování, přítlačových katétrů a intrakardiální echokardiografie (ICE). ASA spočívala v aplikaci 96% alkoholu do septální větve levé koronární arterie a v následném kontrolovaném infarktu této tepny, který vedl k fibróze septa a jeho ztenčení s následnou redukcí obstrukce výtokového traktu. Gradienty v LVOT byly invazivně měřeny před výkonem a bezprostředně po výkonu. Sledování pacientů probíhalo v 3., 6. a 12. měsíci a zahrnovalo kontrolu echokardiografických parametrů a klinického stavu pacientů.

Výsledky: Celkem bylo randomizováno 19 pacientů k výkonu ERASH ($n = 10$) nebo ASA ($n = 9$) od května 2021 do prosince 2023. Doba výkonu byla signifikantně delší ve skupině ERASH (medián 180 vs. 30 minut, $p < 0,001$), zatímco čas a dávka rtg záření byly srovnatelné (6,24 min/11 000 mGy/cm² ERASH vs. 7,18 min/11 151 mGy/cm² ASA, $p = 0,391/0,967$). Obě skupiny dosáhly výrazného bezprostředního poklesu gradientu ve výtokovém traktu levé komory (LVOTG). Ve skupině ERASH se klidový gradient snížil z mediánu 103 mm Hg na 22,5 mm Hg a provokovaný gradient z 205 mm Hg na 67 mm Hg. Ve skupině ASA došlo ke snížení klidového gradientu ze 72 mm Hg na 20 mm Hg a provokovaného ze 155 mm Hg na 54,5 mm Hg. Při 12měsíčním sledování zůstávaly klidové gradienty nízké (17,5 mm Hg ve skupině ERASH vs. 15,5 mm Hg ve skupině ASA) a došlo ke zlepšení funkční třídy NYHA na 2,25 a 1,75. Také došlo k zlepšení testu šestiminutovou chůzí (395,9 m vs. 311,9 m, $p = 0,264$).

Periprocedurální komplikace byly čtenější ve skupině ERASH, včetně dvou případů perikardiálního výpotku a jedné trvalé atrioventrikulární (AV) blokády, převážně u pacientů s předchozími poruchami převodního systému.

Závěr: V této randomizované pilotní studii prokázala metoda ERASH srovnatelnou účinnost jako ASA při redukcí LVOTG a zlepšení symptomů pacientů. Vyšší výskyt komplikací ve skupině ERASH může souviset s učební křivkou a rizikovým profilem pacientů. ERASH může do budoucna představovat alternativní metodu septální redukce u pacientů s nevhodnou anatomií koronárních tepen nebo jinými kontraindikacemi k ASA. K potvrzení těchto výsledků a upřesnění indikačních kritérií jsou zapotřebí rozsáhlejší multicentrické studie.

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ABSTRACT

Introduction: Hypertrophic obstructive cardiomyopathy (HOCM) is characterized by dynamic left ventricular outflow tract (LVOT) obstruction due to asymmetric septal hypertrophy and systolic anterior motion (SAM) of the mitral valve. In patients with persistent symptoms despite optimized medical therapy, septal reduction therapy is indicated. While alcohol septal ablation (ASA) is a well-established catheter-based treatment, endocardial radiofrequency ablation of septal hypertrophy (ERASH) has recently emerged as a promising alternative. Aim of our study is to report the pilot data of the randomized study comparing efficacy and safety of ERASH versus ASA.

Methods: This single-center, prospective, randomized pilot study compared the efficacy and safety of ERASH versus ASA in symptomatic patients with obstructive HOCM refractory to medical therapy. ERASH procedure is catheter radiofrequency ablation of septal hypertrophy using contact force-sensing irrigated ablation catheters guided by 3D electroanatomical mapping with use of intracardiac echocardiography. ASA is based on injection of 96% alcohol into the septal branch of the left coronary artery to induce a small, controlled infarction of the hypertrophic septum and consequently abolishes the dynamic outflow obstruction. LVOT gradients were measured invasively at baseline and immediately post-procedure, and patients were followed at 3, 6, and 12 months for clinical and echocardiographic reassessment.

Results: Nineteen patients were randomized to undergo ERASH ($n = 10$) or ASA ($n = 9$) from May 2021 to February 2023. Procedural duration was significantly longer in the ERASH group (median 180 vs. 30 minutes, $p < 0.001$), while fluoroscopy time and dose (6,24 min/11000 mGy/cm² ERASH group vs 7,18 min/11151 mGy/cm² ASA group, $p = 0.391/0.967$) were comparable. Both groups achieved substantial immediate reductions in LVOT gradients. In the ERASH group, resting LVOT gradient decreased from a median of 103 mmHg to 22.5 mmHg, and provokable gradient from 205 mmHg to 67 mmHg. In the ASA group, resting gradient decreased from 72 mmHg to 20 mmHg, and provokable gradient from 155 mmHg to 54.5 mmHg. At 12-month follow-up, resting gradients remained low (17.5 mmHg in ERASH vs. 15.5 mmHg in ASA), and NYHA functional class improved to 2.25 and 1.75, respectively. ERASH patients showed a greater improvement in 6-minute walk distance (395.9 m vs. 311.9 m, $p = 0.264$). Periprocedural complications were more frequent in the ERASH group, including two pericardial effusions and one permanent atrioventricular (AV) block, mostly occurring in patients with pre-existing conduction disorders.

Conclusion: In this randomized pilot study, ERASH demonstrated comparable clinical and hemodynamic efficacy to ASA in reducing LVOT gradients and improving symptoms. While the complication rate was higher with ERASH, it may reflect procedural learning curve and baseline patient risk. ERASH may offer an alternative in patients with unsuitable coronary anatomy or different contraindications to ASA. Larger studies are needed to confirm these results and optimize patient selection.

Keywords:

Alcohol septal ablation
Endocardial radiofrequency
ablation of septal hypertrophy
Functional NYHA class
improvement
Hypertrophic obstructive
cardiomyopathy
Left ventricle outflow tract
gradient

Introduction

Hypertrophic obstructive cardiomyopathy (HOCMP) is characterized by abnormal thickening of the left ventricular myocardium not explained by abnormal hemodynamic conditions.¹ HOCMP is a common inherited cardiomyopathy, typically autosomal dominant, caused by >1,500 mutations across ≥ 15 sarcomeric genes,² with a prevalence of approximately 1 : 500 in adults.³

In adults, hypertrophic cardiomyopathy (HCM) is defined by a maximal wall thickness ≥ 15 mm in one or more left ventricle (LV) segments, as measured by any imaging modality, in the absence of other causes.¹ The obstructive form is characterized by left ventricular outflow tract (LVOT) obstruction with a maximal LVOT gradient (LVOTG) ≥ 30 mmHg at rest and/or after provocation.⁴ Hemodynamically significant obstruction occurs in up to ~25% of patients with HCM⁵ and is frequently associated with systolic anterior motion (SAM) of the anterior mitral leaflet.

Symptomatic pharmacological treatment is the basis of HOCMP therapy. Treatment choice is guided by symptoms and the severity of LVOT obstruction.⁶ Agents with negative inotropic effects (e.g. betablockers and verapamil) reduce myocardial oxygen demand, prolong diastolic filling and decrease LVOT gradient and symptoms. Mavacamten, the first representative of a new drug group of

selective allosteric myosin inhibitors that reduce myocardial oxygen demand and prolong diastolic filling, reduces actin-myosin cross-bridge formation and lowers LVOT gradients with functional improvement (EXPLORER-HCM; VALOR-HCM).^{7,8} However, pharmacological treatment has limited efficacy with risk of adverse effects.^{9,10} Contemporary guidelines recommend invasive septal reduction therapy for persistently symptomatic patients, typically New York Heart Association III–IV (NYHA III–IV) with resting or provoked LVOTG ≥ 50 mmHg despite guideline-directed medical therapy.^{6,11} Some centers consider earlier intervention in highly symptomatic NYHA II with marked provokable gradients and SAM-related mitral regurgitation.¹¹ Reducing LVOTG is strongly associated with improved survival compared to healthy population.¹²

The oldest method to reduce LVOTG is surgical septal myectomy (Morrow procedure), introduced in the 1960s and still considered the gold standard in many centers, especially in the United States. The principle is resection of the hypertrophic basal interventricular septum (IVS) to the papillary muscle bases with selective mobilization.¹³ Concomitant mitral valve surgery is required in ~11–20% of patients.¹⁴ In experienced centers, operative mortality is ~1–2%, and permanent pacemaker (PPM) dependency is ~4% after septal myectomy.¹⁵

Less invasive strategies such as dual-chamber pacing were explored in the 1970s,¹⁶ aiming to alter activation and lessen dynamic obstruction. The principal is the api-

cal preexcitation effect, which is the shortening of the atrioventricular conduction interval. First, contraction of the apex and apical part of the IVS is present, while the basal parts of the IVS participate in LVOT narrowing and contract at the end of systole, which leads to improved ejection fraction of the left ventricle, however, it is not longer recommended for LVOTG reduction.

Alcohol septal ablation (ASA) was first reported by Sigwart in 1994.¹⁷ This catheter-based intervention relies on the injection of 96% alcohol into the septal branch of the left coronary artery to induce a small, controlled infarction of the hypertrophic septum and consequently abolishes the dynamic outflow obstruction (in the case of a suitable coronary artery anatomy). LVOTG decrease was correlated with a significant clinical improvement in the patient's symptomatology and left ventricular remodeling. Periprocedural mortality is <1% in tertiary centers, and survival approaches that of the general population.¹⁸ Atrioventricular (AV) block is the principal complication (temporary or permanent ~20–50%) with a need of pacemaker implant rates 7–20%, especially with pre-existing LBBB or larger alcohol volumes.¹⁹ A total volume of 2 ml is generally safe. Higher doses of alcohol are slightly more effective in reducing LV obstruction and result in a higher incidence of peri-procedural complete heart block,²⁰ and other severe risks are potential developing defects of the interventricular septum. Therefore, ASA should be indicated in cases of IVS thickness >15 mm as recommended by American guidelines in 2011²¹ and >16 mm as recommended by European guidelines in 2014.¹ After the procedure, reduction of LVOTG significantly decreased total mortality, which is likely comparable to the healthy population.²² However, in 10–15% of patients, ASA could not be performed because of unsuitable coronary artery anatomy.⁶

Endocardial radiofrequency ablation of septal hypertrophy (ERASH) seems to be a new method to reduce septal hypertrophy. Principally, this is catheter-based ablation procedure that targets the hypertrophied basal interventricular septum to reduce LVOT obstruction.²³ Using retrograde transaortic or transseptal access, an irrigated RF catheter delivers focal lesions at the mitral-septal contact zone under fluoroscopy plus electroanatomic mapping with intracardiac echocardiography guidance. The aim is to create localized hypokinesis and lessen SAM-mediated obstruction, lowering resting and provokable gradients. ERASH is repeatable, avoids coronary injury, and – when guided by 3 D mapping/ICE – can be performed with low risk of complications; the principal safety concerns are conduction block (occasionally requiring pacing) and, less commonly, pericardial effusion.

ERASH first emerged in the early 2000s as a catheter-based alternative to surgical myectomy and alcohol septal ablation for obstructive HCM. The first clinical experience, reported by Lawrenz and colleagues in 2004, demonstrated technical feasibility: after two inconclusive transseptal attempts, a stable retrograde approach with an irrigated catheter achieved a substantial decrease in resting and provokable LVOT gradients.²⁴ Larger retrospective series from the same group six years later were made on 19 patients using electroanatomic mapping and irrigated RF energy via right- or left-ventricular approaches, showing

consistent reductions in resting and provokable gradients and improvement in NYHA class, while also revealing the main deal – conduction injury (complete AV block in ~21% requiring pacing) and a small risk of pericardial effusion.²⁵

Parallel pediatric work from Emmel et al. described two children with meaningful gradient reduction,²⁶ and Sreeram et al. subsequently reported a 32-patient pediatric cohort with sustained hemodynamic improvement over long follow-up, tempered by rare serious events including one death from paradoxical obstruction and occasional pacemaker implantation for AV block.²⁷

By 2016, a transseptal series from Crossen et al. ($n = 11$) demonstrated a decrease in the gradient and symptomatic benefits, again with a measurable risk of permanent pacing.²⁸ Beaser et al. explored ERASH against pharmacologic comparators such as disopyramide, showing substantial early gradient reduction.²⁹

Taken together, these studies trace ERASH's evolution to focused, image-guided therapy: a repeatable option that consistently reduces LVOT gradients and improves symptoms. However, conduction system injury stays as the principal periprocedural risk to be avoided.²⁹

Despite of these studies, there still remains a lack of randomized studies directly comparing the two approaches. Our study reports pilot data from a prospective randomized trial designed to evaluate and compare the efficacy and safety of ERASH versus ASA in patients with symptomatic hypertrophic obstructive cardiomyopathy who remained refractory to optimal medical therapy.

Methods

Study design

The primary aim of our study was to conduct a comparative evaluation of the efficacy and safety of endocardial radiofrequency ablation of septal hypertrophy (ERASH) versus alcohol septal ablation (ASA) in patients with symptomatic hypertrophic obstructive cardiomyopathy (HOCM) who remained refractory to optimal medical therapy. Specifically, we sought to determine whether ERASH, as a catheter-based alternative to ASA, could achieve comparable reduction in LVOTG, symptom relief, and functional capacity, while maintaining an acceptable procedural risk profile. The study was a single-center, open-label, prospective, randomized pilot comparison.

Patient population

Eligible patients had symptomatic obstructive HCM with resting or provokable LVOTG ≥ 50 mmHg despite optimized medical therapy; IVS thickness ≥ 16 mm; and NYHA class $\geq$ III or progressive class II with significant daily-life limitation.

All patients were evaluated in a specialized heart-failure outpatients clinic. Baseline assessment included transthoracic echocardiography (TTE), clinical status, and optimization of pharmacotherapy. Cardiac MRI, genetic testing, 24-h Holter monitoring, and sudden cardiac death risk stratification were done.

Each patient had TTE performed at screening (pre-randomization) and at 3-, 6-, and 12-month follow-up. LV

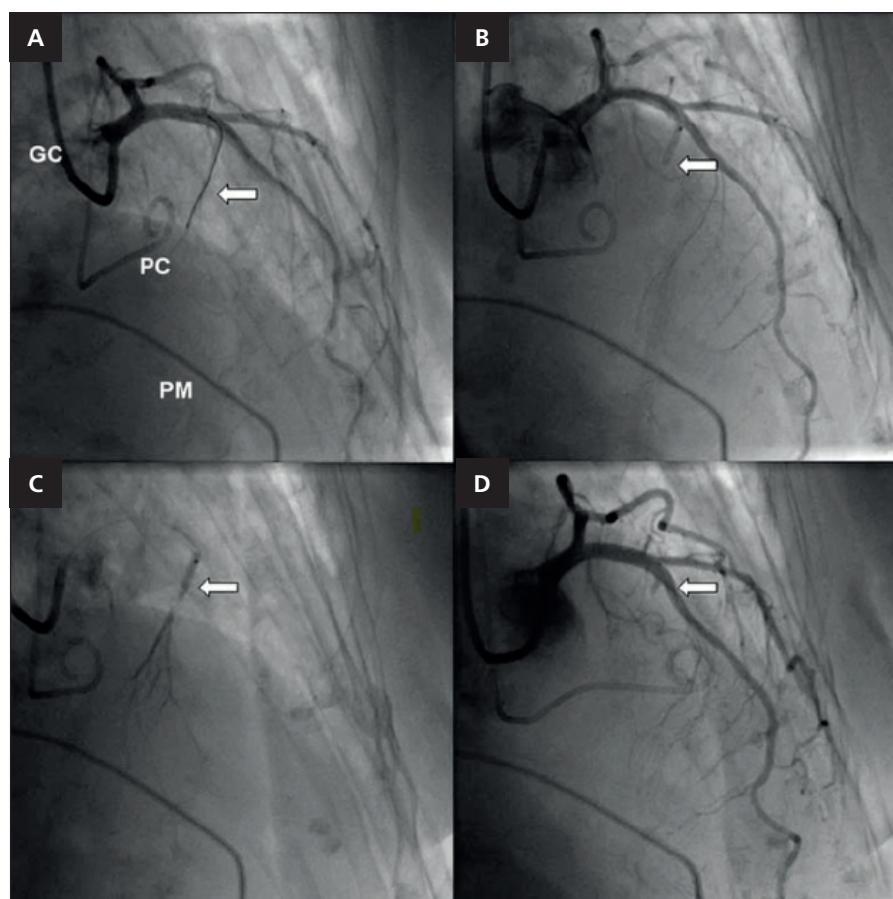


Fig. 1 – Principle of the alcohol septal ablation. (A) Introduction of the guidewire to ramus septalis, (B) occlusion of the artery with balloon, (C) introduction of the alcohol, (D) obstruction of artery, artificial infarction.

dimensions, IVS thickness, left atrial diameter, left ventricle ejection fraction (LVEF), presence of SAM, and diastolic parameters were obtained from standard parasternal long-axis and apical four-chamber views. LVOTG was measured by continuous-wave Doppler at rest and during Valsalva maneuver.

Patients who agreed with interventional method of treatment underwent coronary angiography due to check anatomy of coronary arteries. That was a part of screening protocol.

After we checked inclusion criteria and informed consent was signed, patients were randomized to ASA or ERASH group

Alcohol septal ablation

A temporary RV pacing lead was placed before ASA for brady-arrhythmia backup. Left coronary angiography delineated septal branches. A pigtail catheter recorded LV-to-aortic gradients at rest and with provocation (Valsalva maneuver). An over-the-wire balloon catheter was positioned in the target septal branch; echocontrast injection confirmed myocardial territory (echo-guided approach). Ethanol (96%) was administered, approximately 2 mL, followed by 10-min balloon occlusion and repeat gradient assessment. Final angiography excluded non-target injury/no-reflow. Temporary pacing remained *in situ* for ~24 h; telemetry monitoring continued for ≥48 h in in-

tensive Care Unite (ICU) up to 5 days total. Alcohol dose limits and pacemaker thresholds followed center protocol (Fig. 1).

Endocardial radiofrequency ablation of septal hypertrophy

Procedure was performed in a standard electrophysiology laboratory. For ablation, via v. femoralis l. dx., Agilis steerable sheath for transeptal approach was introduced and for retrograde approach 9F standard sheath to the right femoral artery was introduced. An 8F standard ablation catheter with irrigation tip and contact force technology TactiCath™ SE (Abbott, Chicago, IL, USA), or THERMOCOOL SMARTTOUCH® (Biosense Webster, Diamond Bar, CA, USA) were used for ablation. The rest of catheters: decapolar 7F catheter to coronary sinus, quadripolar catheter on His and intracardiac ultrasound probe was inserted via left femoral vein. Electroanatomy map of the left ventricle was created with 3D electroanatomical mapping system EnSite Precision™ Mapping System (Abbott, Chicago, IL, USA) or CARTO®3 System, (Biosense Webster, Diamond Bar, CA, USA). The whole procedure was performed with multichannel electrophysiology diagnostic system LabSystem PRO EP Recording System (Boston Scientific, Marlborough, MA, USA) and intracardiac ultrasound (ICE) AcuNav® (Siemens, Biosense-Webster) (Fig. 2). Measurements of LVOTG in rest and after Valsal-

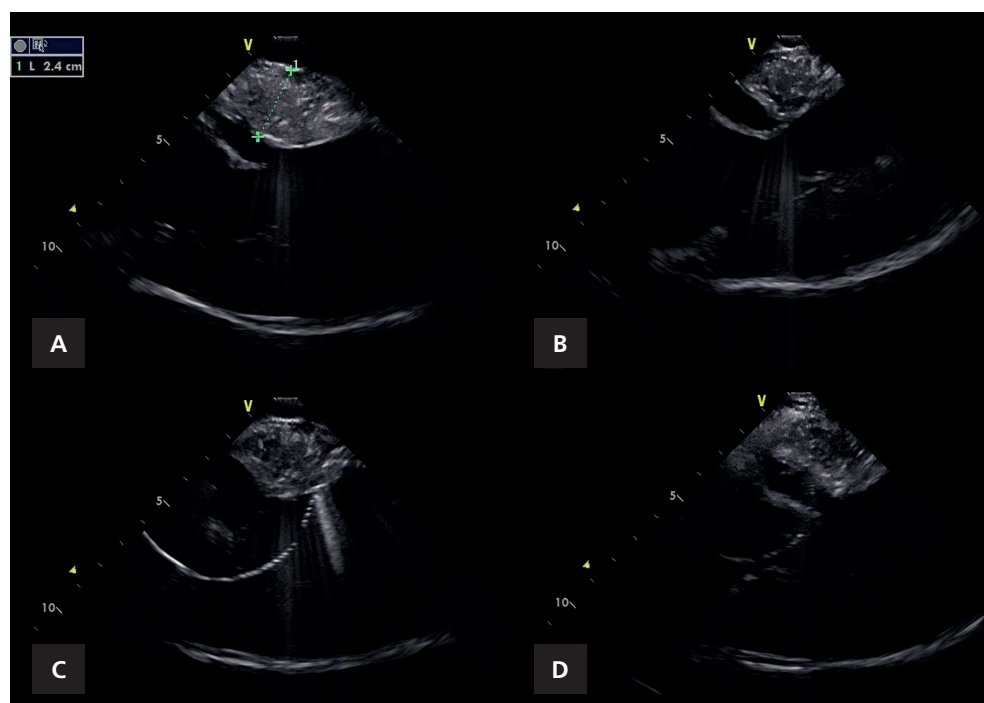


Fig. 2 – Endocardial radiofrequency ablation of septal hypertrophy, images from intracardiac ultrasound. (A) Hypertrophic septum, (B) contact of catheter with myocardium, (C, D) creating ablation lesions.

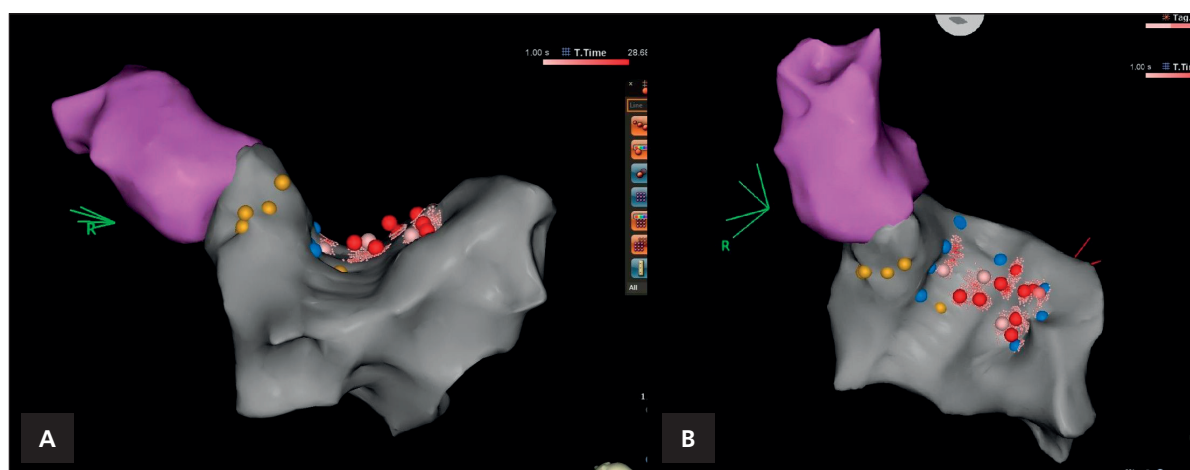


Fig. 3 – Three dimensional electroanatomical map of the left ventricle (grey) and ascending aorta (violet) created during ERASH. (A) The hypertrophic septum is clearly visible as an imprint in the left ventricle model. Blue dots are tags created during mapping of the left ventricle and bordering septal hypertrophy. Yellow points marked conduction system. White and red points marked regions of the radiofrequency ablations. (A) Modified inferior projection, (B) anteroposterior projection.

va maneuver were performed with pigtail catheter. His potentials were marked to the electroanatomy map to avoid damage of the conduction system (Fig. 3). Ablation targeted the basal septum at the mitral–septal contact zone, with iterative reassessment of gradients. Anticoagulation was hold with ACT about 300. Radiofrequency ablation of the sepum was done with power 35–40 W and irrigation 30 ml/min under the ICE and 3D mapping control. After ablation, measurements of gradient were performed with pigtail catheter again. Post-procedure, patients were monitored on the arrhythmology unit for arrhythmias and complications eventually.

Clinical follow-up

Follow-up visits occurred at 3, 6, and 12 months for clinical assessment, TTE, ECG/Holter, and medication adjustment. At 12 months, we obtained 6-minute walk test. Patients continued routine care thereafter.

Statistical analysis

Statistical analysis was performed with the programming language R in the integrated development environment R studio. Results with a p -value below 0.05 were considered statistically significant. Continuous variables are presented as mean $\pm$ standard deviation (SD) or median

(interquartile range). Categorical variables are presented as numbers with percentages. Data were tested for normality using Shapiro-Wilk test and graphically using Q-Q plots and histograms. Mann-Whitney test was used to determine differences in continuous variables between two groups. Chi-square test was used to determine an association in categorical variables.

Results

Baseline patient characteristics

Between May 2021 and February 2023 a total of 19 patients was enrolled and randomized to the ERASH group ($n = 10$) or ASA group ($n = 9$). Baseline characteristics are comparable, only ERASH group had a trend to the higher BMI (29.4 vs. 25.8 kg/m², $p = 0.055$). Most patients were highly symptomatic, with median NYHA class III in both groups at baseline ($p = 0.087$). For details see **Table 1**.

Baseline echocardiographic parameters did not differ significantly between groups. Mean interventricular septal (IVS) thickness was similar (18.5 mm in ERASH vs. 18 mm in ASA, $p = 0.123$), as resting and provokable LVOT gradients were ($p = 0.905$ and $p = 0.252$, respectively). Systolic anterior motion (SAM) of the mitral valve was present in nearly all patients (100 % in ERASH, 88.9% in ASA; $p = 0.957$). Left atrial diameter was significantly larger in the ASA group (50 mm vs. 41.5 mm; $p = 0.037$).

Periprocedural results

Procedural parameters are shown in **Table 2**. Procedure time was significantly longer in the ERASH group (median 180 vs. 30 minutes, $p < 0.001$), reflecting the complexity of 3D mapping and ablation strategy. However, fluoroscopy time (7,18 min for ASA group vs 6,24 min for ERASH group, $p = 0.391$) and radiation dose (11151 mGy/cm² vs 11000 mGy/cm², $p = 0.967$) were similar between groups.

Table 1 – Baseline characteristics of patients

Baseline characteristics	ASA (N = 9)	ERASH (N = 10)	p-value
Male	4 (44.4)	3 (30.0)	0.861
Age	60 (48–70)	67 (61–70)	0.595
BMI (kg/m ²)	29.43 (27.77–30.02)	25.82 (23.51–27.61)	0.055
Initial NYHA	3 (3–3)	2.5 (2.5–3)	0.087
6M walking test (m)	405 (300–462.5)	336 (318.7–404.4)	0.606
Hypertension	4 (44.4)	8 (80.0)	0.259
Diabetes mellitus type 2	2 (22.2)	2 (20.0)	>0.999
Medication			
Calcium blockers	9 (100.0)	10 (100.0)	–
Betablockers	6 (66.7)	8 (80.0)	0.891
Anticoagulant therapy or antiplatelet therapy	5 (55.6)	3 (30.0)	0.508
Echocardiography parameters			
Ejection fraction (%)	65 (65–75)	72.5 (70–75)	0.209
LVOTG in rest before (mmHg)	90 (67–153)	99 (53–133)	0.905
LVOTG Valsalva before (mmHg)	140 (90–200)	105 (72–128)	0.252
SAM	8 (88.9)	10 (100.0)	0.957
IVS thickness (mm)	18 (17–18)	18.5 (17–22)	0.123
LA diameter (mm)	50 (45–54)	41.5 (39–47)	0.037
E (m/s)	0.96 (0.86–1.06)	0.84 (0.62–0.99)	0.230
E' med (m/s)	0.06 (0.05–0.06)	0.05 (0.04–0.05)	0.099
E' lat (m/s)	0.07 (0.06–0.1)	0.06 (0.06–0.07)	0.134
E/E' med	17.22 (15.5–19.5)	17.05 (13–21.25)	0.284
E/E' lat	12.29 (9.45–17.37)	14.83 (10–16.83)	0.633
LV diameter	43 (39–48)	39.5 (37–46)	0.413
Mi regurgitation			
1	1 (11.1)	0 (0.0)	0.409
1.5	4 (44.4)	7 (70.0)	
2	1 (11.1)	0 (0.0)	
2.5	3 (33.3)	2 (20.0)	

Table 2 – Periprocedural parameters

Periprocedural parameters	ASA (N = 9)	ERASH (N = 10)	p-value
Procedure time (minutes)	180 (124–223)	30 (22–35)	<0.001
X ray time (min)	7.18 (5.8–18.8)	6.24 (4–10.51)	0.391
X ray dose (mGy/cm ²)	11151 (8191–21030)	11000 (8000–21500)	0.967
Number of RFA	17 (16–35)	–	–
Time of RFA	577 (483–891)	–	–
LVOTG beginning of procedure / in rest (mmHg)	72 (19–107)	103 (77–113)	0.270
LVOTG beginning of procedure / Valsalva (mmHg)	155 (73–166)	205 (105–250)	0.066
LVOTG end of procedure / rest (mmHg)	20 (7.5–57)	22.5 (8–68)	>0.999
LVOTG end of procedure / Valsalva (mmHg)	54.5 (41–130.5)	67 (49–128)	0.896
LVOTG delta in rest (mmHg)	56.5 (10.1–64.5)	73.5 (33–95)	0.3281
LVOTG delta Valsalva (mmHg)	40.9 (12.5–104)	108.5 (39–131)	0.09121

Table 3 – Periprocedural complications

Periprocedural complications	ASA (N = 9)	ERASH (N = 10)
Hemodynamically significant effusion	0	2
Complete AV block requiring pacemaker implant	0	1
Temporary pacing required	1	0
Onset of LBBB	0	1
Onset of RBBB	5	1
Jugular vein thrombosis	1	0

Table 4 – Follow-up at 3 months

Follow-up at 3 months	ASA (N = 9)	ERASH (N = 10)	p-value
LVOTG rest (mmHg)	22 (8–62)	18 (13–21)	0.682
LVOTG Valsalva (mmHg)	55 (12–111)	44.5 (25–59)	0.967
SAM	7 (77.8)	7 (70.0)	0.567
IVS thickness (mm)	16 (14–17)	15.5 (12–18)	0.967
LVEF (%)	62 (55–65)	66 (60–70)	0.157
LA diameter (mm)	46 (40–51)	43 (41–46)	0.346
E (m/s)	0.83 (0.71–1.43)	0.76 (0.64–0.87)	0.449
E' med (m/s)	0.06 (0.05–0.07)	0.05 (0.04–0.06)	0.218
E' lat (m/s)	0.08 (0.08–0.09)	0.06 (0.05–0.07)	0.020
E/E' med	16.05 (10.44–23.75)	13.65 (12.57–17.75)	0.722
E/E' lat	11.81 (7.94–17.03)	12.7 (8.88–14.5)	0.964
LV diameter (mm)	42 (41–47)	42.5 (38–48)	0.837

Both groups showed substantial reduction in LVOT gradients immediately after the procedure. In the ERASH group, median resting gradient decreased from 103 mmHg to 22.5 mmHg and provokable gradient from 205 mmHg to 67 mmHg. In the ASA group, resting gradient declined from 72 mmHg to 20 mmHg and provokable gradient from 155 mmHg to 54.5 mmHg. Intergroup differences in postprocedural gradients were not statistically significant.

Periprocedural complications were more frequent in the ERASH group. Two patients developed a hemody-

namically significant pericardial effusion requiring drainage. One patient developed a complete AV block necessitating permanent pacemaker implantation, and another required temporary pacing. Notably, both cases of complete AV block occurred in patients with preexisting right bundle branch block. One patient developed new-onset left bundle branch block. In the ASA group, one transient complete AV block resolved during hospitalization. Five patients developed new right bundle branch block, and one experienced jugular vein thrombosis associated with temporary pacing. For details see **Table 3**.

Table 5 – Follow-up at 6 months

Follow-up at 6 months	ASA (N = 9)	ERASH (N = 10)	p-value
LVOTG rest (mmHg)	16 (10–24)	20 (17–33)	0.513
LVOTG Valsalva (mmHg)	55 (30–111)	49.5 (34–61)	0.548
SAM	16 (15–17)	12.5 (11–15)	0.032
IVS thickness (mm)	5 (55.6)	3 (30.0)	0.474
LVEF (%)	65 (60–70)	66 (60–70)	>0.999
Diameter left atrium (mm)	50 (39–53)	43.5 (38–46)	0.059
E (m/s)	0.8 (0.64–1.47)	0.79 (0.59–0.91)	0.315
E' med (m/s)	0.06 (0.06–0.06)	0.05 (0.04–0.06)	0.165
E' lat (m/s)	0.07 (0.07–0.07)	0.06 (0.05–0.08)	0.074
E/E' med	10.5 (10–24.83)	15.17 (13.29–18.25)	0.525
E/E' lat	11.43 (9.14–21)	11 (9.83–14.33)	0.489
LV diameter (mm)	44 (44–47)	42.5 (41–45)	0.592

Table 6 – Follow-up at 12 months

Follow-up at 12 months	ASA (N = 9)	ERASH (N = 10)	p-value
Echocardiography parameters			
Ejection fraction (%)	65 (62.5–67.5)	70 (65–70)	0.163
LVOTG in rest (mmHg)	15.5 (9–26)	17.5 (10–25)	0.9291
LVOTG Valsalva before (mmHg)	68.5 (20–90)	41 (28–45)	0.306
SAM	2 (22.2)	7 (70.0)	0.1547
IVS thickness (mm)	15.5 (14–17.5)	15.5 (14–20)	0.9642
Diameter of left atrium (mm)	50 (39–53)	42.5 (39–45)	0.078
E (m/s)	0.67 (0.53–1.11)	0.7 (0.58–1.1)	0.896
E' med (m/s)	0.06 (0.06–0.07)	0.06 (0.05–0.06)	0.059
E' lat (m/s)	0.08 (0.07–0.09)	0.06 (0.05–0.06)	0.002
E/E' med	9.29 (7.17–24.83)	13.4 (9.67–21.33)	0.469
E/E' lat	8.75 (7.46–12.92)	13.5 (9.67–18.33)	0.138
LV diameter (mm)	44.5 (42–48)	46 (41–48)	0.656
Mi regurgitation			
1	4 (44.4)	2 (20.0)	0.171
1,5	3 (33.3)	5 (50.0)	
2	1 (11.1)	0 (0.0)	
Initial NYHA	2.25 (2–2.5)	1.75 (1.5–2)	0.202
6M walking test (metres)	311.95 (255–343.6)	395.9 (381–436)	0.242
Medication			
Ca blockers	5 (55.6)	3 (30.0)	0.508
Betablockers	9 (100.0)	9 (90.0)	>0.999
Anticoagulation therapy or antiplatelet therapy	4 (44.4)	3 (30.0)	0.860

Follow-up

Follow-up at 3 months

At 3 months, both groups maintained lower LVOT gradients. Resting gradients were 18 mmHg (ERASH) vs. 22 mmHg (ASA), and provokable gradients were 44.5 mmHg vs. 55 mmHg, respectively ($p = \text{NS}$). Septal thickness slight-

ly decreased in both groups (15.5 vs. 16 mm, $p = 0.967$), and LVEF remained preserved. For details see **Table 4**.

Follow-up at 6 months

At 6 months, the resting and provokable LVOT gradients remained stable: 20 mmHg (ERASH) vs. 16 mmHg (ASA) at rest; 49.5 mmHg vs. 55 mmHg with Valsalva. Septal thickness and left atrial diameter showed continued

downward trends without significant differences. Diastolic indices remained stable. A significantly lower residual SAM grade was observed in the ERASH group (median 12.5 mm vs. 16 mm; $p = 0.032$). For details see **Table 5**.

Follow-up at 12 months

At 12 months, both groups maintained improved hemodynamic and symptomatic status. Resting LVOT gradients were 17.5 mmHg (ERASH) and 15.5 mmHg (ASA), with provokable gradients 41 mmHg vs. 68.5 mmHg ($p = \text{NS}$). IVS thickness remained similar between groups. NYHA functional class improved from baseline to 2.25 (ERASH) and 1.75 (ASA) ($p = 0.202$). Six-minute walk distance improved in both groups, with a trend to bigger improvement in the ERASH cohort (395.9 m vs. 311.9 m, $p = 0.264$). Mild to moderate mitral regurgitation persisted in several patients, but no progression was noted. Diastolic function parameters (E/E') and LA size showed the modest improvement without statistical significance. For details see **Table 6**.

Discussion

Endocardial radiofrequency ablation is an established therapeutic modality for cardiac arrhythmias; its adaptation for the treatment of obstructive hypertrophic cardiomyopathy (ERASH) represents an innovative catheter-based alternative to traditional septal reduction therapies. ERASH could reduce left ventricular outflow tract gradients reproducibly and improve symptoms in carefully selected patients with hypertrophic obstructive cardiomyopathy.

In this pilot randomized study, we performed a comparison of ERASH and alcohol septal ablation and our findings suggest that both modalities achieved significant periprocedural reductions in LVOT gradients, with comparable fluoroscopy time and radiation exposure. Procedure duration was longer in the ERASH group, likely reflecting the complexity of endocardial mapping and lesion delivery. While both techniques were generally safe, the overall complication rate was higher in the ERASH group – predominantly related to pericardial effusion and conduction system disturbances. Probably also due to learning curve of operators, and notably, the occurrence of complete atrioventricular block was observed primarily in patients with pre-existing right bundle branch block. These findings underscore the importance of a precise conduction system mapping, intracardiac echocardiography guidance, and individualized risk assessment.

Septal myectomy and ASA remain the current standard-of-care options for patients with drug-refractory obstructive HCM. However, the recent introduction of cardiac myosin inhibitors, such as mavacamten, has altered the therapeutic landscape by offering a pharmacologic means of gradient reduction, potentially decreasing the need for septal reduction therapy in selected patients. Despite these new treatment, ERASH may hold distinct value for patients who are not candidates for ASA or myectomy – particularly those with unsuitable septal artery anatomy, or high surgical risk. ERASH reduces LVOT ob-

struction not by extensive septal thinning but through the creation of focal myocardial hypokinesis at the mitral–septal contact point, which disrupts systolic anterior motion of the mitral valve. This effect highlights the importance of accurate lesion depth, and controlled delivery of radiofrequency energy using contact force-sensing catheters and advanced mapping systems.

The safety profile of ERASH must be carefully considered. The risk of high-grade atrioventricular block necessitates detailed mapping of the His-Purkinje system, cautious energy titration. ERASH should be approached with caution in patients with baseline RBBB, given the potential for iatrogenic left bundle branch block to acquire complete heart block. Furthermore, the risk of pericardial effusion, although low, needs real-time imaging with ICE, adherence to anticoagulation protocols, and precise post-procedural observation.

Limitations

This study was limited by a small sample size and potentially, learning curve effects could have influenced outcomes in the ERASH group. Larger, multicenter trials with standardized imaging protocols and long-term follow-up are needed.

Conclusion

In conclusion, this pilot randomized comparison, ERASH and ASA achieved significant reductions in LVOTG with symptomatic improvement at 12 months. Procedure duration was longer with ERASH but fluoroscopy time/dose were similar. Complications were more frequent with ERASH, particularly pericardial effusion. Probably it was associated with standard potential risk and complications of radiofrequency catheter ablation with transseptal approach. Secondly, conduction disturbances in patients with baseline RBBB. Pacemaker implant was needed in one case, in second case just temporary pacing with following restitution of sinus rhythm. This means amount of complete AV block occurred in 11,1 % almost comparable amount to ASA procedure known from registers. Careful patient selection, conduction system mapping, and ICE guidance are essential for this method. Larger, multicenter trials are warranted to define long-term efficacy, safety, and patient selection criteria.

Septal myectomy and ASA remain the current standard-of-care options for patients with drug-refractory obstructive HCM. However, ERASH may represent a valuable and effective option for selected patients, particularly those with challenging anatomy or contraindications to ASA.

Conflict of interest

All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Ethical statement

The study was approved by the Ethics Committee of St. Anne's University Hospital in Brno.

Informed consent

The patients signed informed consent to participate in the study.

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Prophylactic Negative Pressure Therapy in Reducing the Risk of Sternal Wound Infection after Cardiac Surgery

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SOUHRN

Úvod: Pooperační infekce a dehiscence sternální rány jsou závažné komplikace kardiokirurgických operací, které prodlužují délku hospitalizace a zvyšují náklady na zdravotní péči. U vysoce rizikových pacientů je standardní péče o ránu pro prevenci této komplikace nedostatečná. Díky našim rozsáhlým zkušenostem s podtlakovou terapií rány (NPWT) při komplikacích po sternotomii předpokládáme, že okamžité ošetření rány touto technikou může snížit výskyt komplikací rány.

Metody: Provedli jsme prospektivní, randomizovanou, nezaslepenou studii srovnávající účinnost profylaktické NPWT (Prevena) aplikované na uzavřené sternotomii ($n = 40$) oproti standardnímu převazu rány ($n = 40$) u pacientů s vysokým rizikem infekce sternální rány po kardiokirurgickém výkonu. Primární výsledky zahrnovaly výskyt poruch hojení rány a délku hospitalizace. Komplikace rány jsme kontrolovali sedm dní po operaci a poté ve třech měsících.

Výsledky: Studie zahrnovala 80 pacientů (64 mužů, 16 žen; průměrný věk 65,4 roku), kteří byli do studie zařazeni od dubna 2023 do ledna 2024. Mezi komorbiditami patřily diabetes mellitus (82,5 %), obezita (index tělesné hmotnosti [BMI] ≥ 30 ; 82,5 %), chronická obstrukční plicní nemoc (21,3 %), aktivní kouření (20 %), renální insuficience (12,5 %) a užívání kortikosteroidů (13,8 %). Oboustranný odběr vnitřní mamární tepny (BIMA) byl proveden v 18,8 % případů. Po sedmi dnech po operaci se vyskytly komplikace v ráně u čtyř pacientů ve skupině Prevena (10 %) a u sedmi v kontrolní skupině (17,5 %) (hodnota $p = 0,52$). Po třech měsících byla hluboká infekce rány přítomna u jednoho pacienta ve skupině Prevena (2,5 %) a u dvou pacientů v kontrolní skupině (5 %) (hodnota $p = 1,00$). Medián délky hospitalizace byl srovnatelný mezi skupinou Prevena (12 dní) a kontrolní skupinou (11 dní) (hodnota $p = 0,75$).

Závěr: Preventivní podtlaková léčba ran snižuje výskyt komplikací hojení ran u vysoce rizikových pacientů, i když ve studii nebyl statisticky významný. Ačkoli studie neprokázala významný vliv na délku hospitalizace, potenciální snížení výskytu komplikací rány si zaslouží další zkoumání. Ke zjištění účinnosti a nákladové efektivity této preventivní strategie jsou nutné rozsáhlejší studie.

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ABSTRACT

Background: Postoperative sternal wound infections and dehiscence are serious complications of cardiac surgery that increase the length of hospital stay and healthcare costs. Standard wound care may be insufficient for preventing these complications in high-risk patients.

Methods: We conducted a prospective, randomized study comparing the efficacy of closed incisional negative pressure wound therapy (ciNPWT) using Prevena (study group) versus standard wound dressing (control group) in patients at high risk of sternal wound infections following cardiac surgery. Primary outcomes included the incidence of sternal wound infection at seven days and three months postoperatively, and length of hospital stay.

Results: The study cohort comprised 80 patients (64 male, 16 female; mean age 65.4 years) randomized into two groups with 40 patients in each. At 7 days post-operation, there were four patients with sternal wound infection in the study group (10 %) and seven in the control group (17.5%) (p -value=0.52). At 3 months, deep wound infections were present in 1 patient in the study group (2.5%) and 2 in the control group (5%) ($p = 1.00$). Median length of hospital stay was comparable between the study (12 days) and control (11 days) groups (p -value = 0.75).

Conclusions: Preventive negative pressure wound treatment showed a trend towards reducing the incidence of wound healing complications in high-risk patients following cardiac surgery, although the differences were not statistically significant. Further large-scale studies are warranted to establish the efficacy and cost-effectiveness of this preventive strategy.

Keywords:

Closed incisional negative pressure wound therapy

Negative pressure wound therapy

Poststernotomy

Prevena

Sternotomy

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Introduction

Despite all the improvements in modern cardiac surgery, sternal wound infections remain a significant concern. These complications are associated with increased morbidity, mortality, length of hospital stay and cost.^{1,2} They are particularly prevalent in high-risk patient groups, especially obese patients, those with diabetes, chronic obstructive pulmonary disease (COPD), and those undergoing bilateral internal mammary artery (BIMA) harvesting.^{3–7}

Sternal wound infections (SWI) can be classified as superficial sternal wound infection (SSWI) or deep sternal wound infection (DSWI). SSWI involve the skin, subcutaneous tissue, and the pectoralis fascia. Sternal wounds with bony involvement and signs of infection in the mediastinum are classified as DSWI.¹ The prevalence of SSWI ranges from 0.5% to 8% with a combined morbidity and mortality of 0.5% to 9%.^{1,3} DSWI prevalence ranges from 0.4% to 5% with mortality rates ranging from 19% to as high as 40%.^{1,3,6}

Traditional strategies for preventing sternal wound complications have focused on optimizing patient risk factors, improving surgical technique, and implementing strict perioperative infection control measures.^{1,7} These include preoperative skin preparation, appropriate antibiotic prophylaxis, meticulous surgical technique, and postoperative wound care.^{1,7} Despite these measures, sternal wound infections remain a persistent problem, particularly in high-risk patients.

Negative pressure wound therapy (NPWT) has been widely studied and used for treating postoperative open wound complications. Its application as a prophylactic measure on closed surgical incisions, closed incision negative pressure wound therapy (ciNPWT), is relatively less utilized nor studied. The Prevena™ Incision Management System (KCI USA, Inc., San Antonio, TX) is one such ciNPWT device designed specifically for closed surgical incisions. It provides a sterile, closed environment, maintains wound edge approximation, and reduces tension on the incision, potentially decreasing the incidence of wound complications.⁸ Studies have shown that ciNPWT can significantly reduce the incidence of SWIs in high-risk patients, particularly those with obesity, diabetes, and those undergoing BIMA harvesting.^{3,4}

Given the significant morbidity and mortality associated with sternal wound complications, and the potential benefits suggested by early studies, there is a clear need for further investigation of ciNPWT in high-risk cardiac surgery patients. We hypothesized that immediate application of ciNPWT to closed sternal incisions could decrease the incidence of sternal wound infection in this population.

This study aims to contribute to the growing body of evidence regarding the use of ciNPWT in cardiac surgery and to inform clinical decision-making regarding its use in high-risk patients. By analyzing sternal wound healing outcomes in specific well-defined high-risk patient sub-groups in the study, we hope to provide valuable insights into the potential benefits of ciNPWT for these specific patient groups.

Methods

Study design and patients

We conducted a prospective, randomized study from April 2023 to January 2024 at the Department of Cardiac Surgery, University Hospital in Hradec Králové, Czech Republic. The study protocol was approved by the institutional ethics committee, and all patients gave written informed consent.

Eligible patients were adults undergoing elective cardiac surgery via median sternotomy who had at least two of the following risk factors: diabetes mellitus, obesity (BMI ≥ 30 kg/m²), COPD, active smoking, renal insufficiency, corticosteroid use, or planned BIMA harvesting. Exclusion criteria included emergency surgery, redo sternotomy, and known allergy to dressing materials. Eligible patients were randomly assigned in a 1 : 1 ratio to receive either prophylactic ciNPWT using the Prevena™ Incision Management System (study group) or standard wound dressing (control group). Randomization was performed using a computer-generated sequence. In the study group, the Prevena™ dressing was applied to the closed surgical incision immediately after skin closure in the operating room and left in place for 7 days. In the control group, standard sterile wound dressings were applied and changed as per our institution's protocol, usually every 2 to 3 days.

Our primary outcomes were the incidence of sternal wound infection at seven days and three months postoperatively, and length of hospital stay. Sternal wound infections were classified as superficial or deep wound infections based on the Centers for Disease Control and Prevention criteria.⁹ We further compared the outcome of treatment using ciNPWT or standard dressings in specific high-risk patient sub-groups, stratified according to comorbidities.

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation or median (interquartile range), and categorical variables as numbers and percentages. Between-group comparisons were performed using Student's t-test or Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. A *p*-value < 0.05 was considered statistically significant. All analyses were performed using NCSS 2021 Statistical Software 2021 (NCSS, LLC, Kaysville, Utah, USA, [ncss.com/software/ncss](https://www.ncss.com/software/ncss)).

Results

Baseline characteristics

Eighty patients were enrolled and randomized into two groups, 40 patients in each group. Baseline characteristics were generally well-balanced between the groups (Table 1). Eighty percent of the study population were male. Sixty-six patients had diabetes and 66 were obese with BMI ≥ 30 . Patients in the study group were slightly older and had higher BMI. The study group had slightly more comorbidities compared to the control group. The use of BIMA grafting was similar between the groups.

Table 1 – Baseline characteristics of study participants

Characteristic	Study group (n = 40)	Control group (n = 40)	p-value
Age, years (mean ± SD)	66.4 ± 7.4	64.4 ± 10.5	0.58
Male sex, n (%)	31 (77.5)	33 (82.5)	0.58
BMI, kg/m ² (mean ± SD)	34.0 ± 5.1 32.9 (31–36.5)	32.7 ± 3.8 32.5 (30.9–35.1)	0.35
Diabetes mellitus, n (%)	35 (87.5)	31 (77.5)	0.38
COPD, n (%)	12 (30)	5 (12.5)	0.06
Active smoking, n (%)	9 (22.5)	7 (17.5)	0.58
Renal insufficiency, n (%)	7 (17.5)	3 (7.5)	0.31
Corticosteroid use, n (%)	7 (17.5)	4 (10)	0.52
BIMA harvesting, n (%)	7 (17.5)	8 (20)	0.78
EuroSCORE II (mean ± SD)	2.7 ± 2.6	2.3 ± 1.5	0.77

Table 2 – Primary outcomes

Outcome	Study (n = 40)	Control (n = 40)	p-value
Wound defects at 7 days, n (%)	4 (10%)	7 (17.5%)	0.52
- Superficial wound infection	3 (7.5%)	5 (12.5%)	0.61
- Deep wound infection	1 (2.5%)	2 (5%)	
Deep wound infection at 3 months, n (%)	1 (2.5%)	2 (5%)	1.00
Length of hospital stay, days (mean ± SD) (IQR)	13.4 ± 6.3 12 (9–15)	13.7 ± 8.4 11 (9–16)	0.75

Primary outcomes

At 7 days post-surgery, 13.75% of the study population developed wound complications (11 patients) (Table 2). Three had deep wound infections and eight developed superficial wound infections. We observed fewer patients with wound complications in the study group (four patients, 10%) compared to the control group (seven patients, 17.5%). Three patients in the study group had superficial wound infection and one had deep wound infection compared to five superficial and two deep wound infections in the control group. This difference though did not reach statistical significance ($p = 0.52$).

At the 3-month follow-up, only deep wound complications were observed (3 patients). One patient had deep wound infections the study group (2.5%) compared to two patients in the control group (5%) (p -value = 1.00).

The median length of hospital stay was comparable between the study (12 days, IQR 9–15) and the control group (11 days, IQR 9–16) ($p = 0.75$).

Analyses of specific patient sub-groups

Our study included several predefined patient populations based on specific risk factors for sternal wound complications.

In the BIMA harvesting group ($n = 15$; 7 in the study group vs 8 in the control group), there was a notable trend towards fewer wound complications in the study group compared to the control group. At 7 days post-operation, there was 1 superficial wound infection in the study group (14.3%) and no deep wound infection whilst there were 4 superficial and 1 deep wound infection in

the control group (62.5%) ($p = 0.184$). At 3 months, no deep infections were present in the study group, while 1 deep infection (12.5%) occurred in the control group (p -value = 1.00).

In obese patients (BMI ≥ 30 ; $n = 66$, 33 patients in each group), we observed a lower incidence of wound complications in the study group. In the study group, 3 patients had superficial wound infection (9.1%) and 1 patient had deep wound infection (3.0%) at 7 days compared to 4 patients with superficial wound infections (12.1%) and 2 deep wound infections (6.1%) in the control group (p -value = 0.78). At 3 months, both groups had 1 patient with deep wound infection.

Similar trends were observed in other high-risk patient populations, including patients with diabetes mellitus, renal insufficiency, corticosteroid use, active smoking, obesity and COPD. The differences however, did not reach statistical significance due to limited sample sizes.

Discussion

In this prospective, randomized study of high-risk patients undergoing cardiac surgery, we found that prophylactic ciNPWT using the Prevena™ system showed a trend towards reducing the incidence of sternal wound infections compared to standard wound dressing. Although the differences did not reach statistical significance, the potential clinical importance of these findings warrant further investigation.

Our results are consistent with previous studies that have suggested a benefit of ciNPWT in reducing surgical

site infections. A large multicentre propensity matched study by Suelo-Calanao et al. consisting of 1532 patients (766 per group) with high risk of sternal wound infection comparing ciNPWT and standard dressings found that ciNPWT reduced the incidence of sternal wound infection (6% vs 16%, p -value= 0.0001). However, length of hospital stay was not reduced.¹⁰

Grauhan et al. compared patients prospectively receiving ciNPWT with standard dressings retrospectively and reported lower infection rate in the group with ciNPWT compared to the control within 30 days (1.3% in the study group, 1 patient out of 237 vs 3.4% in the control group, 119 patients out of 3508, p -value = 0.05).¹¹ Witt-Majchrzak et al. reported a reduction in superficial sternal wound infections with the use of ciNPWT (PICO™) in a similar high-risk population undergoing cardiac surgery.¹² A retrospective study conducted by Jennings et al. demonstrated a statistically significant reduction in sternal wound infections in patients treated with ciNPWT compared to a predicted rate.⁴ Similarly, Grauhan et al. found a significant reduction in wound infections in obese patients receiving ciNPWT after cardiac surgery.³ A recent systematic review and meta-analysis of ten studies by Biancari et al. showed ciNPWT was associated with lower risk of developing sternal wound infection (both superficial and deep). However, the difference was not statistically significant for superficial sternal wound infection.¹³

The analysis of specific patient populations, while exploratory in nature and limited by small sample sizes, provide valuable insights into the potential benefits of ciNPWT in specific high-risk patient groups. The trend towards reduced wound complications in our BIMA harvesting subgroup is particularly noteworthy. Although these differences did not reach statistical significance, the magnitude of the effect is clinically relevant. This finding is particularly important given that BIMA harvesting is a known risk factor for sternal wound complications.^{14,15} BIMA grafting has been associated with improved long-term outcomes in coronary artery bypass surgery but is often avoided due to concerns about sternal wound complications.¹⁶ Should our findings be confirmed in a larger study focused on use of ciNPWT in patients after BIMA harvesting, it could potentially increase the utilization of BIMA grafting and improve long-term patient outcomes.

Even after developing deep sternal wound infection, Lo Torto et al. demonstrated the benefit of using ciNPWT (Prevena™) combined with monolateral pectoralis major muscle flap (MPMF) compared to a control group using standard dressings with MPMF in improving patient outcomes, with few patients in the study group developing wound complications compared to the control group.¹⁷ A similar outcome was observed by Gabriel et al. who used ciNPWT to improve healing outcomes in patients who developed deep sternal wound infection.¹⁸

Length of hospital stay was comparable between the study and control group. This finding was unexpected, given the trend towards fewer wound complications in the ciNPWT group. Several factors may explain this result. With only a small number of wound complications in both groups, the impact on overall length of stay may

have been limited. Our institution's standardized care protocols for postoperative cardiac surgery patients may have mitigated the impact of wound infections on discharge timing. Factors unrelated to wound healing, such as cardiac rehabilitation protocols or social factors affecting discharge planning, may have played a more significant role in determining length of stay.

Though cost-effectiveness was not analysed in our study, a study by Hawkins et al. found that ciNPWT was cost-effective for the prevention of deep but not superficial wound infection, and as such recommend using ciNPWT only in patients with a high risk of deep sternal wound infection.¹⁹

According to Hyldig et al.'s meta-analysis, ciNPWT is related with a considerable reduction in surgical site infections across various surgical specialties.²⁰ This implies that the benefits of ciNPWT may go beyond cardiac surgery and have broader uses in high-risk surgical groups.

What distinguishes this study from previous studies is its prospective and randomized design, which compared the use of ciNPWT and standard dressings on sternal wound healing outcomes in a well-defined high-risk patient cohort. While many prior studies on closed incisional negative pressure wound therapy (ciNPWT) have been retrospective or observational, this trial randomly assigned patients and monitored them for both early (7-day) and late (3-month) outcomes. This study design decreases bias and other confounding variables and as such makes the results more reliable. Furthermore, we analyzed specific high risk patient sub-groups providing a more granular insight into the effectiveness of ciNPWT in these patient groups. This helps determine which patient sub-groups might benefit the most from this therapy and aiding in providing patient tailored postoperative treatment strategies. The trend towards reduced wound infections in the BIMA harvesting sub-group suggests a potential clinical significance that could influence future surgical protocols and increase the use of BIMA grafts.

Although our findings were not statistically significant even in the sub-group analysis, the trend towards reduced sternal wound infections in high-risk cardiac surgery patients receiving ciNPWT merits larger studies to confirm these findings and assess its cost-effectiveness. These results if validated, could influence future clinical and surgical practices.

Conclusion

In conclusion, our findings indicate that ciNPWT may help minimize sternal wound complications in high-risk patients undergoing cardiac surgery, however, the differences were not statistically significant. Larger, multicenter trials are required to determine the efficacy and cost-effectiveness of this preventive method. Such studies should also seek to identify specific patient categories who may benefit the most from preventive ciNPWT, enabling for more tailored delivery of this resource-intensive strategy. Future study should include longer-term follow-up, economic evaluations, and patient-reported outcomes to gain a more complete picture of the impact of prophylactic ciNPWT in cardiac surgery.

Conflict of interest

None.

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Ethical statement

The study was approved by the Faculty of Medicine in Hradec Králové institutional ethics committee and complied with the Declaration of Helsinki.

Informed consent

All patients gave written informed consent for the conduction and publication of the study.

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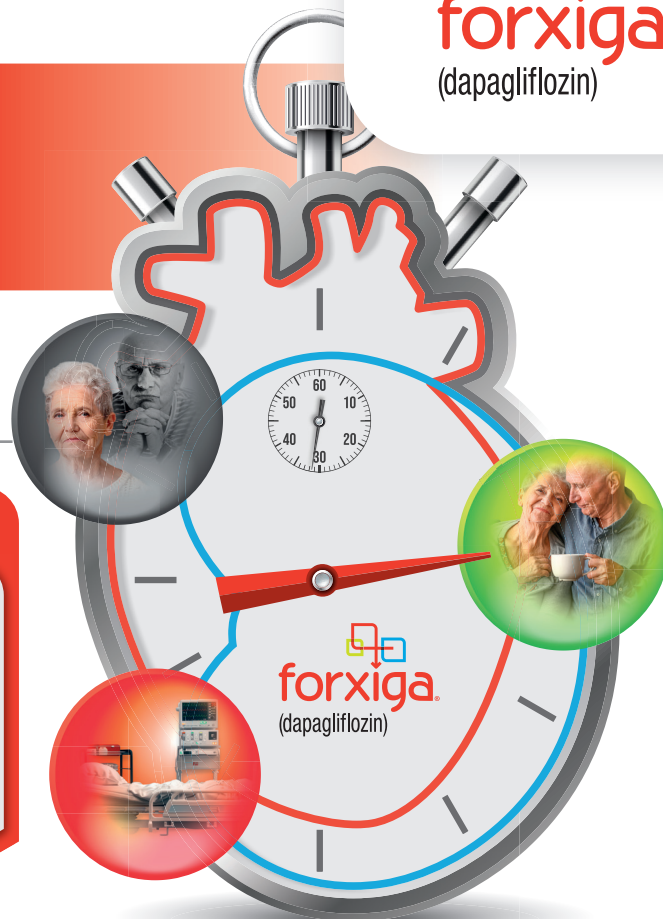
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DM2

SNÍŽENÍ
KV ÚMRTÍ¹

45 %
RRR

Subanalýza studie
DECLARE u pacientů s HFREF⁺

HR 0,55
(95% CI; 0,34-0,90)
p = 0,02

CKD

SNÍŽENÍ CELKOVÉ
MORTALITY vs placebo²

31 %
RRR

Sekundární cíl
studie DAPA-CKD³

HR 0,69
(95% CI; 0,53-0,88)
p = 0,004

HF

SNÍŽENÍ
KV ÚMRTÍ³

14 %
RRR

Metaanalýza studií
DAPA-HF a DELIVER⁴

HR 0,86
(95% CI; 0,76-0,97)
p < 0,01

+ Studie DECLARE: multicentrická, randomizovaná, dvojitě zaslepená, placebem kontrovaná studie fáze 3, hodnotící bezpečnost a účinnost dapagliflozinu 10 mg/1x denně oproti placebu u 17 160 pacientů s DM2 optimálně léčených farmakologickou léčbou. Medián sledování 4,2 roku. 40 % pacientů mělo při vstupu do studie KV onemocnění (sekundární prevence), 60 % pacientů mělo pouze KV rizikové faktory (primární prevence). Primárním bezpečnostním ukazatelem byl MACE (KV úmrtí, nefatální infarkt myokardu nebo nefatální ischemická cévní mozková příhoda). Primárním účinným cílem byly MACE a složený výsledek KV úmrtí nebo hospitalizace pro HF. Studie DECLARE splnila primární bezpečnostní cíl – noninferiorita MACE [HR 0,93 (95% CI; 0,84–1,03), p < 0,001]. Kompozitní cíl snížení KV mortality a hospitalizace pro srdeční selhání byl snížen o 17 % (95% CI; 0,73–0,95; p = 0,005). Diabetická ketoacidóza byla častější u dapagliflozinu (0,3 % vs 0,1 %, p = 0,02), stejně jako výskyt genitálních infekcí (0,9 % vs 0,1 %, p < 0,001). Nebyl pozorován rozdíl ve výskytu amputací, fraktur či Fournierovy gangrény mezi sledovanými skupinami.

* Studie DAPA-CKD: multicentrická, randomizovaná, dvojitě zaslepená, placebem kontrovaná studie, která hodnotila efekt léčby dapagliflozinem v dávce 1x 10 mg/den oproti placebu na snížení rizika renálních a KV příhod u 4 304 pacientů s chronickým onemocněním ledvin (s nebo bez DM2), s eGFR ≥ 25 až ≤ 75 ml/min/1,73m² a poměrem albumin/kreatininu v moči (UACR) ≥ 200 až ≤ 5000 mg/g, kteří byli na standardní léčbě (včetně maximálně tolerovaných dávek ACEi nebo ARB). Primárním složeným cílem studie: ≥ 50% setrvalé snížení eGFR, ESKD nebo renální úmrtí, složený cíl pro KV onemocnění (hospitalizace pro srdeční selhání nebo kardiovaskulární úmrtí) a úmrtí z jakékoliv příčiny. Dapagliflozin snížil riziko primárního složeného cíle o 39 % [HR 0,61 (95% CI; 0,51–0,72, p < 0,000000028)]. Četnost výskytu nežádoucích účinků a závažných nežádoucích účinků se mezi léčebnými skupinami nelišila.

Metaanalýza studií DAPA-HF a DELIVER: ve společně předem specifikované metaanalýze na úrovni pacienta (n=11007) pokrývající celý rozsah ejekčních frakcí u pacientů se srdečním selháním, která vycházela ze studií DAPA-HF a DELIVER, dapagliflozin významně snížil riziko úmrtí s příčinou o 14 % (HR 0,86; 95% CI 0,76–0,97; p = 0,01), riziko celkové mortality o 10 % (HR 0,90; 95% CI 0,82–0,99; p = 0,03), riziko hospitalizací pro srdeční selhání o 29 % (rate ratio 0,71; 95% CI 0,65–0,78; P < 0,001) a MACE (složený cíl z KV úmrtí, infarktu myokardu nebo mozkové příhody) o 10 % (HR 0,90; 95% CI 0,81–1,00; p = 0,045). Dapagliflozin byl účinný napříč ejekční frakcí.

CI – konfidenční interval; CKD – chronické onemocnění ledvin; DM2 – diabetes mellitus 2. typu; HF – srdeční selhání; HFREF – srdeční selhání s redukcí ejekční frakcí; HR – Hazard Ratio; KV – kardiovaskulární; RRR – relativní redukce rizika.

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Zkrácená informace o léčivém přípravku FORXIGA® 10 mg potahované tablety

Kvalitativní a kvantitativní složení: Dapagliflozinum propandiolium monohydricum odpovídající dapagliflozinu 10 mg v 1 potahované tabletě. Jedna 10 mg tableta obsahuje 50 mg laktosy. **Terapeutické indikace:** Diabetes mellitus 2. typu (DM2) – u dospělých pacientů a dětí ve věku 10 let a starších – jako přídatná léčba k dietě a fyzické aktivitě ke zlepšení kontroly glykémie – jako monoterapie, pokud je podávání metforminu nevhodné v důsledku intolerance; – jako přídatná léčba k jiným léčivým přípravkům k léčbě DM2. Výsledky studií ve vztahu ke kombinované léčbě s jinými léčivými přípravky, vlivy na kontrolu glykémie a kardiovaskulární příhody a studované populace viz SPC. **Srdeční selhání (SS)** – k léčbě dospělých pacientů se symptomatickým chronickým srdečním selháním. **Chronické onemocnění ledvin (CKD)** – k léčbě dospělých pacientů s chronickým onemocněním ledvin. **Dávkování a způsob podání:** Doporučená dávka je 10 mg dapagliflozinu jednou denně. Pokud je dapagliflozin podáván v kombinaci s inzulínem nebo inzulínovými sekretagogy, lze uvažovat o jejich snížení dávce, aby se snížilo riziko hypoglykémie. Přípravek se podává perorálně, jednou denně, kdykoli v průběhu dne, s jídlem nebo mimo jídlo. Tablety se polykají celé. **Kontraindikace:** Hypersenzitivita na léčivou látku nebo na kteroukoli pomocnou látku. **Zvláštní upozornění a opatření pro použití:** Není nutná úprava dávky s ohledem na funkci ledvin. Nedoporučuje se zahájit léčbu dapagliflozinem u pacientů s eGFR < 25 ml/min. Účinnost dapagliflozinu na snížení glukózy závisí na funkci ledvin, a je snížena u pacientů s eGFR < 45 ml/min a pravděpodobně chybí u pacientů s těžkou poruchou funkce ledvin a je třeba zvážit další léčbu snižující hladinu glukózy, pokud je nutná další kontrola glykémie. Dapagliflozin se nemá používat k léčbě pacientů s diabetem 1. typu. U pacientů s těžkou poruchou funkce jater je zvýšená expozice dapagliflozinu. Nedoporučuje se upravovat dávku dle věku. V důsledku mechanismu účinku zvyšuje dapagliflozin diurézu, která může vést k mírnému snížení krevního tlaku. Opatnosti je zapotřebí u pacientů, u kterých může pokles krevního tlaku vyvolat dapagliflozinem představovat riziko. U pacientů léčených inhibitory společného transportéru pro sodík a glukózu (SGLT2i), byly vzácně hlášeny případy diabetické ketoacidózy (DKA), u rizikových pacientů je nutno užívat SGLT2i opatrně. Před zahájením léčby mají být pacienti vyšetřeni s ohledem na riziko DKA. Více informací viz SPC. Pokud se vyskytnou známky nebo symptomy ketoacidózy, mají být pacienti poučeni, aby si změnili hladiny ketonů. Po uvedení přípravku SGLT2i na trh byly u pacientů hlášeny případy nekrotizující fasciitidy perineu (Fournierova gangréna) – jde o vzácnou, ale závažnou a potenciálně život ohrožující příhodu, která vyžaduje neodkladnou léčbu a je třeba poučit pacienta. Vylučování glukózy močí může být spojeno se zvýšeným rizikem infekcí močových cest. Zkušenosti s dapagliflozinem u pacientů se SS ve třídě IV podle NHA jsou omezené. Nejsou žádné zkušenosti s dapagliflozinem v léčbě CKD u pacientů bez diabetu, kteří nemají albuminurii. Pacienti s albuminurií mohou mít z léčby dapagliflozinu větší prospěch. Ve studiích pacientů s DM2 s SGLT2i byl pozorován zvýšený výskyt amputací na dolních končetinách a není známo, zda jde o skupinový účinek. Je důležité poučit pacienty o pravidelné preventivní péči o nohy. Starší pacienti (≥ 65 let) mohou být rizikovější z pohledu objemové deplece. Pacienti léčení dapagliflozinem budou mít pozitivní výsledek testu na glukózu v moči, což je dáno mechanismem účinku léčivé látky. V průběhu léčby dapagliflozinem byly pozorovány zvýšené hodnoty hematokritu. Pacienti s výrazným zvýšením hodnoty hematokritu mají být sledováni a vyšetřeni pro vyloučení hematologického onemocnění. **Interakce s jinými léčivými přípravky a jiné formy interakce:** Dapagliflozin může zvyšovat diuretický účinek thiazidů a kličkových diuretik a může zvyšovat riziko dehydratace a hypotenze. Nedoporučuje se monitorovat glykémii metodou stanovení 1,5-AG, neboť měření není u pacientů užívajících SGLT2i spolehlivé. Dapagliflozin může zvyšovat renální exkreci lithia a hladina lithia v krvi se může snížit, koncentrace lithia v séru se má kontrolovat častěji. **Těhotenství a kojení:** Nejsou dostupné údaje o použití dapagliflozinu u těhotných žen. Jakmile je zjištěno těhotenství, musí se léčba dapagliflozinem přerušit. Není známo, zda se dapagliflozin a/nebo jeho metabolity vylučují do lidského mateřského mléka. **Účinky na schopnost řídit a obsluhovat stroje:** Přípravek Forxiga nemá žádný vliv nebo má zanedbatelný vliv na schopnost řídit nebo obsluhovat stroje. Pacienti mají být upozorněni na riziko hypoglykémie, pokud je dapagliflozin podáván souběžně s deriváty sulfonylmočoviny nebo s inzulínem. **Nežádoucí účinky:** Nejčastěji hlášenými nežádoucími účinky v klinických studiích byly infekce pohlavních orgánů, byly popsány případy fimózy, výskyt hypoglykémie byl srovnatelný s placebem, jejich frekvence se zvýšila při kombinaci se SU či inzulínem. Dalšími častými nežádoucími účinky byly infekce močových cest, závrata, dysurie, polyurie, bolest zad, zvýšený hematokrit, snížená renální clearance kreatininu během zahájení léčby, dyslipidemie a vyrážka. Méně časté jsou plísňové infekce, objemová deplece, žízeň, zácpa, sucho v ústech, nykturie, vulvovaginální pruritus, pruritus genitálu, zvýšený kreatinin či zvýšená močovina v krvi, snížená tělesná hmotnost, vzácně DKA (při použití u DM2), velmi vzácně angioedém, tubulointersticiální nefritida. U pacientů užívajících inhibitory SGLT2, včetně dapagliflozinu, byly velmi vzácně hlášeny případy Fournierovy gangrény. Celkový bezpečnostní profil dapagliflozinu u pacientů s SS a CKD odpovídal známému bezpečnostnímu profilu dapagliflozinu. **Zvláštní opatření pro uchovávání:** Nevýžaduje se. **Druh obalu a velikost balení:** AluAl blister, 28 a 98 potahovaných tablet v neperforovaných kalendářních blistrech; 30x1 a 90x1 potahovaná tableta v perforovaných jednodávkových blistrech. **Držitel rozhodnutí o registraci:** AstraZeneca AB, SE 151 85 Södertälje, Švédsko. **Registrační čísla:** EU/112/795/007-008, EU/112/795/009-010. **Datum revize textu:** 9. 8. 2024.

*Všimněte si, prosím, změny v informacích o léčivém přípravku.

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Adherence to treatment in the elderly with chronic heart failure

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Chronické srdeční selhání

Seniori

SOUHRN

Cíl: Cílem této studie bylo prozkoumat a zhodnotit adherenci k léčbě u seniorů s chronickým srdečním selháním a význam faktorů, které ji vysvětlují.

Metodika: Jedná se o průřezovou korelační a deskriptivní kvantitativní studii. Výzkumný vzorek tvořilo 127 seniorů s chronickým srdečním selháním, kteří splnili stanovená kritéria. K posouzení adherence k léčbě u seniorů s chronickým srdečním selháním byla použita česká verze upraveného standardizovaného dotazníku ACDI – Adherence pacientů s chronickým onemocněním. Sběr dat probíhal v letech 2023 až 2024 na kardiologickém oddělení vybraného zdravotnického zařízení se souhlasem jeho náměstkyně pro ošetrovatelskou péči.

Výsledky: Většina seniorů uvedla dobrou adherenci jak k medikaci (99,2 %), tak ke zdravému životnímu stylu (87,4 %). Mezi faktory ovlivňující adherenci k léčbě dosáhla nejvyšší prevalence odpovědnost, a to 97,6 %. Nejsilnějším faktorem souvisejícím s dodržováním medikace byla odpovědnost, zatímco faktorem nejvíce spojeným s dodržováním zdravého životního stylu byla motivace. Jedním z významných prediktivních faktorů adherence k léčbě je edukace o režimových opatřeních.

Závěr: Adherenci k léčbě lze posílit zvýšením motivace pacientů k dodržování léčebných opatření zaměřených na změnu rizikového chování, které negativně ovlivňuje progresi onemocnění. Důraz na edukaci pacientů může také vést ke zlepšení adherence k léčbě u seniorů s chronickým srdečním selháním.

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ABSTRACT

Objective: The objective of this study was to investigate and evaluate adherence to treatment in the elderly with chronic heart failure and the significance of factors explaining it.

Methods: This is cross-sectional correlational and descriptive quantitative study. The research sample consisted of 127 elderly people with chronic heart failure who met the specified criteria. To assess adherence to treatment in the elderly with chronic heart failure, the Czech version of the modified standardized questionnaire ACDI – Adherence of Patients with Chronic Disease Instrument was used. Data collection took place between 2023 and 2024 at the Cardiovascular Department of a selected healthcare facility with the consent of its deputy for nursing care.

Results: Most of the elderly indicated good adherence to both medication (99.2%) and a healthy lifestyle (87.4%). Among the factors affecting adherence to treatment, responsibility reached the highest prevalence, namely 97.6%. The strongest factor related to medication adherence was responsibility, while the factor most strongly linked to adherence to a healthy lifestyle was motivation. One of the significant predictive factors for treatment adherence is education about regimen measures.

Conclusion: Adherence to treatment could be strengthened by increasing patient motivation to follow therapeutic measures aimed at changing risk behaviours that negatively affect disease progression. Emphasizing patient education may also lead to improved adherence to treatment in the elderly with chronic heart failure.

Keywords:

ACDI questionnaire

Adherence to treatment

Factors affecting adherence

Chronic heart failure

The elderly

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Introduction

Heart failure is considered one of the epidemics of the 21st century in developed countries and represents a major public health challenge. Heart failure represents a complex multifactorial syndrome and is the most common cause of hospitalization in patients over 65 years old. It is primarily a disease of older age, with the average age of patients around 75 years.¹ Despite significant advancements in care achieved in recent decades, the prognosis for patients with this condition remains severe and unfavourable. Heart failure is one of the main causes of morbidity and mortality and is responsible for high healthcare costs in developed countries.² It leads to a shortening in life expectancy and a reduced quality of life. Given its complexity, the care provided to patients with heart failure should be organized, systematic, and multidisciplinary.¹

A significant medical and socioeconomic issue is the repeated rehospitalization of patients with this condition. These rehospitalizations are caused not only by the natural progression of the disease but also by poor patient education, inadequate adherence to treatment, and insufficient post-hospitalization management. More than half of rehospitalizations are due to modifiable factors, which could be prevented through appropriate care setting and organization. Epidemiological data indicate that after the first hospitalization, a quarter of patients is rehospitalized within one month, and half of patients within six months.³

Adherence is a complex, multifaceted concept that is a key in nursing practice, influencing patient care and behaviour throughout the healthcare system.⁴ Adherence to the treatment in chronic diseases affects their course significantly. It is crucial for stabilizing or potentially improving the disease, preventing its decompensation and progression, reducing rehospitalizations, lowering mortality, and improving the quality of life for patients. The World Health Organization (WHO) defines adherence to treatment as the extent to which a patient's behaviour (including medication use, diet adherence, and/or lifestyle modifications) aligns with the agreed-upon recommendations of a healthcare provider. Definition of WHO assumes the patient's active participation, cooperation, and perseverance in following the treatment regimen.⁵ Adherence to treatment is of clinical interest due to the widespread nature of non-adherence.⁶ Poor adherence can lead to adverse events such as severe relapses, symptom exacerbation, increased risk of dependency, toxicity, or resistance. Improving patient adherence can enhance the effectiveness of chronic disease treatment, increase patient safety, and reduce healthcare costs.⁷ There are numerous possible methods and interventions to improve patient adherence. Interventions aimed at improving adherence, or rather non-adherence, can be categorized into educational/cognitive, behavioural, psychosocial, financial, and medication-related interventions.⁸ Educational interventions play a significant role in adherence, as they improve adherence to the treatment plan, enhance treatment outcomes, and increase patient satisfaction.^{9,10} Adherence depends on developing a concordant relationship and should be measured using appropriate tools.^{7,11}

Adherence to treatment is a multifactorial behavioural process influenced by numerous interrelated factors.^{11,12} Factors affecting adherence to treatment can be categorized into several groups: patient-related factors, treatment-related factors, healthcare system factors, socioeconomic factors, and disease-related factors.^{6,13} One concept addressing adherence to treatment and its explanatory factors is the Theory of Adherence to Treatment in Patients with Chronic Disease.¹⁴ According to this theory, adherence in individuals with chronic disease is defined as an active, intentional, and responsible care process in which patients with chronic illnesses work collaboratively with healthcare professionals to maintain their health. Adherence involves taking prescribed medications and maintaining a healthy lifestyle, which includes proper nutrition, physical activity, abstaining from smoking, and moderate consumption of alcohol. According to Kyngäs' theory, explanatory factors linked to adherence to treatment in individuals with chronic illness include motivation, responsibility, results of care, cooperation, a sense of normality, support from next of kin, nurse support, physician support, and fear of complications.¹²

The objective of this research was to investigate and evaluate adherence to treatment in the elderly with chronic heart failure, including adherence to medication and adherence to a healthy lifestyle. Additionally, the study aimed to assess the significance of factors explaining adherence to treatment. The explanatory factors included patient motivation, fear of complications, support from next of kin, physicians, and nurses, responsibility, results of care, cooperation with healthcare professionals, and a sense of normality. For all the observed factors, the relationship with selected predictive factors was also examined, which included sociodemographic data (The Mini-Mental State Examination [MMSE], gender, age, education, marital status, cohabitation) and information specific to the disease (NYHA functional classification, number of hospitalizations, education).

Methodology

Design

A cross-sectional, correlational, and descriptive quantitative study was conducted using a questionnaire survey.

Sample

The research sample consisted of 127 elderly people with chronic heart failure who met the specified criteria (age 65 and older, diagnosis of chronic heart failure, knowledge of the Czech language, MMSE score of at least 24 points, consent to participate in the research). The most represented group in the research sample were the elderly with an MMSE cognitive function test score of 27 points ($N = 44$; 34.6%), with an average score of 26.9. Regarding the NYHA functional classification, all four classes were represented, with class III being the most common ($N = 60$; 47.2%), with an average value of 2.6. The sample had a higher representation of men ($N = 79$; 62.2%). The age of respondents ranged from 65 to 94 years, with a mean age of 75.0 years. The elderly divided into three categories corresponding to stages of old age were the

Table 1 – Sociodemographic characteristics and disease-specific information of the sample

Characteristic		N	%
MMSE	24	1	0.8
	25	13	10.2
	26	34	26.8
	27	44	34.6
	28	26	20.5
	29	8	6.3
	30	1	0.8
NYHA	Class I	5	3.9
	Class II	50	39.4
	Class III	60	47.2
	Class IV	12	9.4
Gender	Male	79	62.2
	Female	48	37.8
Age	65–74 years	60	47.2
	75–84 years	52	40.9
	85–94 years	15	11.8
Education	Primary school	11	8.7
	Secondary school without diploma	59	46.5
	Secondary school with diploma	39	30.7
	Higher vocational education	5	3.9
	University	13	10.2
Marital status	Single	9	7.1
	Married	64	50.4
	Widowed	37	29.1
	Divorced	17	13.4
Living situation	Alone	43	33.9
	In a shared household	84	66.1
Hospitalization	0	11	8.7
	1	52	40.9
	2	33	26.0
	3 or more	31	24.4
Education	Yes	96	75.6
	No	31	24.4

N – absolute frequency; % – relative frequency.

most represented age group being 65–74 years (N = 60; 47.2%). The largest proportion of the elderly had a secondary education without a high school diploma (N = 59; 46.5%). Most participants were married (N = 64; 50.4%) and lived in a household with others (N = 84; 66.1%). The number of hospitalizations related to heart issues in the past year ranged from 0 to 11, with an average of 2.0 hospitalizations. The largest portion of respondents had been hospitalized once in the past year (N = 52; 40.9%). Most the elderly reported being educated about regimen measures related to their heart condition by a physician

or nurse (N = 96; 75.6%). Sociodemographic characteristics and specific information related to the disease are provided in **Table 1**.

Data collection

To determine adherence to treatment and the significance of explanatory factors among in the elderly with chronic heart failure, the Czech version of the modified standardized ACIDI (Adherence of Patients with Chronic Disease Instrument) questionnaire was used.¹⁵ This questionnaire was chosen primarily because it assesses not only adherence to treatment but also other aspects influencing adherence.¹⁶ The study also collected selected sociodemographic data of the elderly (MMSE, gender, age, marital status, cohabitation, education) and information specific to the disease (NYHA classification, number of hospitalizations, education). MMSE is the most commonly used method in cognitive impairment detection in both clinical and research fields. The maximum achievable MMSE score is 30 points, where values of 30–24 indicate a state without cognitive impairment.

The ACIDI questionnaire is established on the theoretical model of adherence in patients with chronic disease of Kyn-gäs,¹⁴ which was originally developed and tested among adolescent patients with diabetes mellitus. This instrument demonstrates high validity and reliability.¹⁵ Originally created in Finnish, the ACIDI questionnaire has been subsequently translated, tested, and successfully used in several studies in English, Japanese, German, Turkish, and Russian. The modified ACIDI questionnaire contains 37 items assessing adherence to treatment, rated on a 5-point Likert scale (1 – strongly disagree; 2 – disagree; 3 – neither agree nor disagree; 4 – agree; 5 – strongly agree). The items are divided into 11 categories. These 11 categories are split into two endogenous mean sum variables: adherence to medication (two items) and adherence to a healthy lifestyle (four items). These two endogenous mean sum variables are explained by nine exogenous mean sum variables: cooperation (three items), responsibility (two items), motivation (two items), sense of normality (seven items), results of care (two items), support from next of kin (five items), support from physicians (four items), support from nurses (four items), and fear of complications (two items).^{16,17} For comparison with previous studies using the same tool,^{17,18} the average composite variables were categorized into two classes. Variables with values from 1 to 3.5 indicate a decreased level of adherence to treatment, while variables with values ranging from 3.51 to 5 represent a good level of adherence to treatment.

Data collection took place in 2023 and 2024 in the Cardiovascular Department of a selected university hospital in the Czech Republic, with the consent of the deputy head for nursing care. The elderly meeting the research criteria were given printed questionnaires during hospitalization or visits to the heart failure clinic. They were informed about how to complete the questionnaire, the voluntary nature of participation, anonymity, and confidentiality.

Translation and validation of the Czech version of the ACIDI questionnaire

First, we obtained the author's official consent to use a modified version of the ACIDI questionnaire for the

purposes of this research. A modified questionnaire for a group of patients with chronic heart disease was received from the authors in English and needed to be translated into Czech. The whole translation and validation process was carried out according to the methodological procedure according to Wild et al.¹⁹

The Czech version of the ACDI questionnaire was tested for validity and reliability. Similar to previous studies,^{17,18} high reliability was found (Cronbach's alpha 0.83). To verify the validity of the Czech version of the ACDI questionnaire, an exploratory factor analysis (EFA) was performed to test the connections between individual items. This analysis produced a factor solution with satisfactory statistical values (factor loadings 0.24–0.97, Cronbach's alpha values for individual factors 0.46–0.98) and its results were similar to the study with the modified English-language ACDI questionnaire.¹⁷

Data analysis

Exploratory factor analysis (EFA) was conducted to verify the validity of the tool. Structural equation modelling (SEM) was used to determine the relationship between adherence to treatment and its explanatory factors. Model adequacy was evaluated using the CFI (Comparative Fit Index; a model with a CFI value ≥ 0.90 is considered a sufficiently good), RMSEA (Root Mean Square Error of Approximation; a model with a RMSEA value <0.06 is considered a sufficiently good), and the Chi-square test. In order to find relationships between independent predictive factors (sociodemographic data and disease-specific information) and dependent factors explaining adherence to treatment contingency tables and the Chi-square test were first used. In the next phase, independent factors predicting adherence to treatment were identified using multivariate logistic regression (all statistically significant relationships from the univariate model were verified). OriginLab software was used for descriptive statistics and contingency tables. SEM was performed using SPSS Amos

26. Logistic regression and EFA were conducted using SPSS Statistics 29. Statistical tests were evaluated at a 5% significance level ($\alpha = 0.05$).

Results

Adherence to treatment in the elderly with chronic heart failure

The majority of the elderly reported good adherence to medication (99.2%) and to a healthy lifestyle (87.4%). Among the factors influencing adherence to treatment, responsibility had the highest prevalence at 97.6%; 94.5% of the elderly experienced good results of care and the same number received high support from next of kin. Slightly fewer respondents mentioned high levels of cooperation with healthcare professionals and high motivation for self-care (92.9%). Support from physicians and nurses was provided to 91.3% and 89.8% of the elderly, respectively. A sense of normality, indicating that the disease and its treatment did not limit their normal daily life, was felt by 69.3% of respondents. Fear of complications was mentioned by 46.5% of respondents. The prevalence of adherence and factors explaining adherence to treatment are shown in Table 2.

Relationships between adherence to treatment and explanatory factors

Initially, direct positive relationships between factors associated with adherence to medication and adherence to a healthy lifestyle was tested (Fig. 1). SEM excluded direct positive associations between sense of normality, fear of complications, results of care, cooperation, support from next of kin, physicians and nurses with adherence to medication, and a healthy lifestyle. Direct, positive associations were revealed between motivation and adherence to medication (standardized regression weight 0.18) and adherence to a healthy lifestyle (0.43), and between

Table 2 – Prevalence of good adherence to treatment and factors explaining adherence

Mean sum variables	Items	Good adherence (%) (n)	$\bar{x}$	Median	SD
Adherence to treatment					
Adherence to medication	1, 2	99.2 (126)	1.99	2	0.09
Adherence to healthy lifestyle	3–6	87.4 (111)	1.87	2	0.33
Factors explaining adherence to treatment					
Responsibility	10, 11	97.6 (124)	1.98	2	0.15
Results of care	21, 22	94.5 (120)	1.94	2	0.23
Support from next of kin	23–27	94.5 (120)	1.94	2	0.23
Cooperation	7–9	92.9 (118)	1.93	2	0.26
Motivation	12, 13	92.9 (118)	1.93	2	0.26
Support from physicians	28–31	91.3 (116)	1.91	2	0.28
Support from nurses	32–35	89.8 (114)	1.90	2	0.30
Sense of normality	14–20	69.3 (88)	1.69	2	0.46
Fear of complications	36, 37	46.5 (59)	1.46	1	0.50

n – frequency; $\bar{x}$ – mean values; SD – standard deviation.

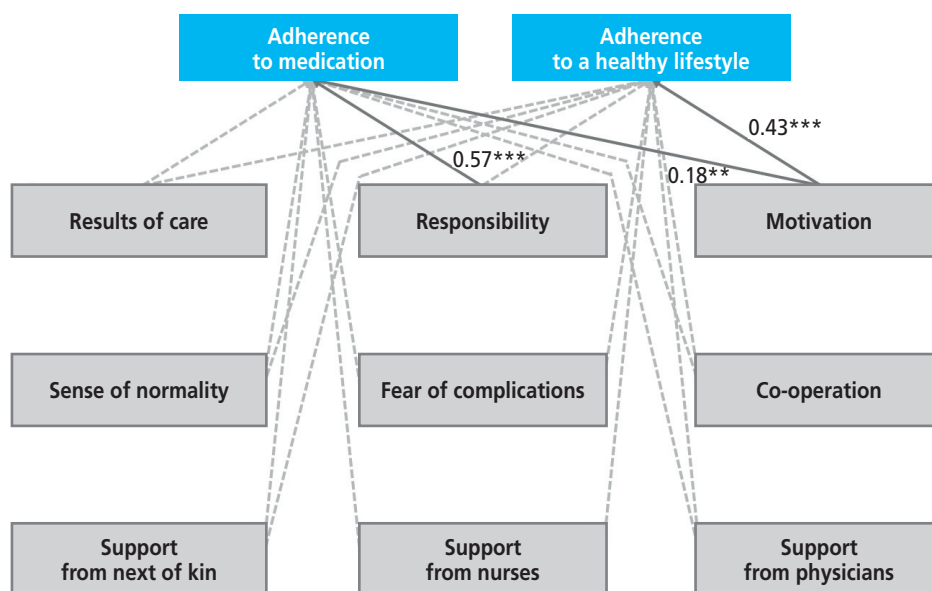


Fig. 1 – Hypothetical Theory of Adherence of People with Chronic Disease among the elderly with Chronic Heart Failure, direct connections. Standardized regression weights are presented, with significance levels indicated as follows: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; p – statistical significance.

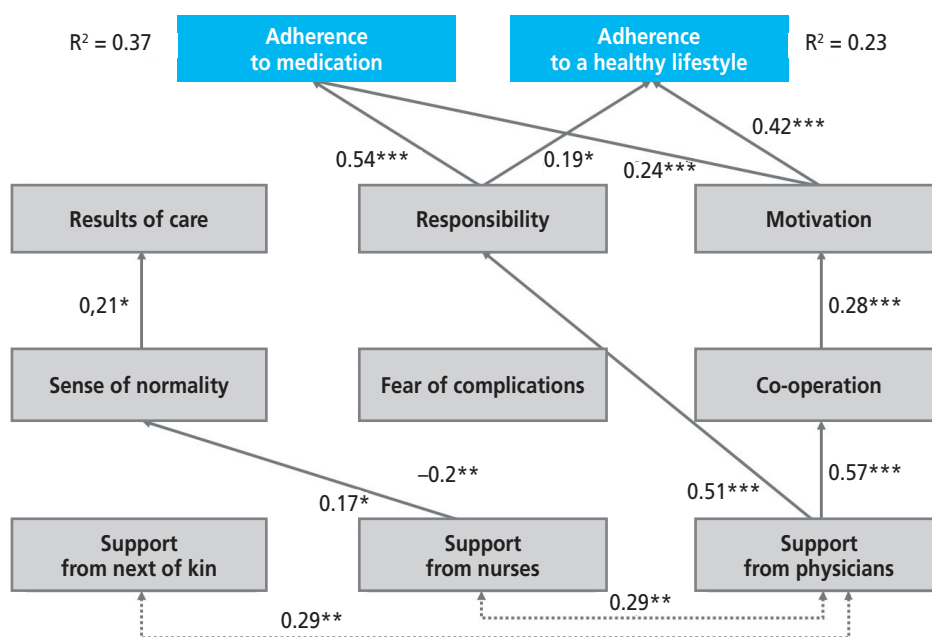


Fig. 2 – Hypothetical Theory of Adherence of People with Chronic Disease among the elderly with chronic heart failure, indirect connections. Standardized regression weights are presented, with significance levels indicated as follows: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; p – statistical significance; R^2 – coefficient of determination.

responsibility and adherence to medication (0.57). However, given the model fit parameters (Chi-square [χ^2] = 196.9; degrees of freedom [df] = 37; χ^2/df ratio = 5.3; CFI = 0.38; and RMSEA = 0.19), it was evident that this model, based on the Theory of Adherence of People with Chronic Disease,¹⁴ was not suitable for the obtained data. Therefore, it was necessary to include indirect associations between individual explanatory factors in the model.

In the second phase, the indirect associations between factors and adherence to medication and a healthy lifestyle were tested (Fig. 2). In the proposed model in Figure 2, solid arrows represent the effect of one explanatory factor on the other, and dashed bidirectional arrows represent covariances between pairs of factors. This model demonstrated that support from physicians was correlated with support from both nurses and next of kin.

The model demonstrated statistically significant ($p < 0.05$) positive relationships between support from nurses and a sense of normality (standardized regression weight 0.17) and between a sense of normality and results of care (standardized regression weight 0.21). Further associations were found between support from doctors and cooperation (standardized regression weight 0.57), support from physicians and responsibility (standardized regression weight 0.51), and between cooperation and motivation (standardized regression weight 0.28). Motivation showed a positive association with adherence to medication and a healthy lifestyle (standardized regression weights 0.24 and 0.42, respectively). Responsibility revealed strong association with adherence to medication (standardized regression weight 0.54) and weaker association with adherence to a healthy lifestyle (standardized regression weight 0.19). This model was able to explain 37% of the variance in the factors linked to adherence to medication and 23% of the variance in the factors linked to adherence to a healthy lifestyle. The parameters used to assess the model's accuracy (Chi-square [χ^2] = 53.4; degrees of freedom [df] = 43; χ^2 /df ratio = 1.24; CFI = 0.96; and RMSEA = 0.044) indicate that the model aligns well with the data.

Sociodemographic factors and disease-specific factors predicting adherence to treatment and its explanatory factors

The relationships between basic variables and factors explaining adherence to treatment in the elderly are shown in Table 3. A connection was found between education and fear of complications, with the educated elderly being approximately four times more likely to be aware of possible complications from non-compliance with regimen measures than the elderly who were not educated. The elderly with an MMSE score of 27–30 and NYHA functional classification I and II had approximately 2.5 and 3.2 times higher chances of living a normal life without limitations than the elderly with an MMSE score of 24–26 and NYHA classification III and IV. The elderly with one or more hospitalizations related to heart failure in the past year had about ten times more support from next of

kin than the elderly without hospitalization. The elderly who were married, widowed, or divorced had about 12.5 times more support from physicians than the elderly who were single.

Discussion

The goal of this study was to assess adherence to treatment among elderly patients with chronic heart failure, focusing on medication adherence and a healthy lifestyle. Additionally, the study aimed to identify the significance of factors explaining adherence to treatment. The relationships between these factors and selected predictive factors, including sociodemographic data and disease-specific information, were also examined.

This study is the first to present results using a self-assessment tool to examine factors explaining adherence and their predictive factors (both sociodemographic and disease-specific) in patients with chronic heart failure. A key finding of this investigation was a high level of adherence to treatment, with 99.2% of respondents reporting good adherence to medication. Previous studies utilizing the ACDI tool also found medication adherence rates exceeding 90%. For instance, a study by Kähkönen et al.¹⁷ investigating predictive factors of adherence to treatment in patients suffering from ischemic heart disease post-percutaneous coronary intervention reported a 95.2% adherence rate using the same modified standardized ACDI questionnaire designed for assessing adherence in patients with chronic heart disease.¹⁵ Medication adherence levels in heart failure patients depend on the definition and measurement method used.²⁰ For example, in a study of 124 respondents in Singapore with chronic heart failure and an average age of 69.1 years using the MARS-5 tool, 73.6% reported good medication adherence.²¹ Generally, adherence tends to decrease over the duration of living with the disease. Studies indicate that older age alone is not associated with reduced medication adherence in patients with chronic heart failure.²²

Regarding adherence to a healthy lifestyle, this study found that 87.4% of respondents reported good adher-

Table 3 – Multivariable logistic regression describing the relationships between primary variables and factors explaining adherence to treatment in the elderly with chronic heart failure

Predictive factors (Negelerke R ²)	Odds ratio (95% confidence interval)	<i>p</i>	χ^2	df	<i>p</i>
Fear of complications (0.100)			9.886	1	0.002
Education: yes	4.05 (1.59/10.30)	0.003			
Sense of normality (0.162)			15.492	4	<0.001
MMSE: 27–30	2.65 (1.18/5.95)	0.015			
NYHA: I a II	3.19 (1.33/7.65)	0.011			
Support from next of kin (0.144)			6.493	5	0.011
Hospitalization: 1 or more	10.50 (2.00/55.22)	0.005			
Support from physicians (0.159)			9.348	3	0.002
Marital status: married, widowed, divorced	12.69 (2.77/58.03)	0.001			

p-value – statistical significance; χ^2 – chi-square; df – degrees of freedom.

ence, comparable to the 89.9% reported in Kähkönen et al.¹⁷ The higher proportion of respondents with reduced adherence to a healthy lifestyle in this study might be attributed to decreased mobility due to advanced age and the presence of comorbidities, leading to inadequate physical activity. Another reason could be the reliance on meals provided by catering services that do not consider dietary restrictions for the disease, limiting the elderly control over their diet. Adherence to a sodium-restricted diet among older patients with heart failure varies from 13% to 75%, depending on data collection methods.²³

Among elderly patients with chronic heart failure, The Theory of Adherence of People with Chronic Disease explained 37% and 23% of the variance in adherence to medication and a healthy lifestyle, respectively. Based on the results of this study, the Theory of Adherence of People with Chronic Disease is an appropriate theoretical framework for planning and implementing nursing interventions for the elderly with chronic heart failure.

Although not all factors explaining adherence to treatment according to the Theory of Adherence of People with Chronic Disease had a direct effect on adherence to medication and healthy lifestyle, several statistically and clinically noteworthy findings emerged. The results showed that responsibility was the strongest factor associated with medication adherence, while motivation proved to be the strongest factor associated with adherence to a healthy lifestyle. These findings are in agreement with previous studies testing the Theory of Adherence of People with Chronic Disease. For example, a significant link between good patient motivation and good adherence was demonstrated in adolescents with diabetes mellitus,¹⁴ epilepsy,²⁴ and chronic illness in general.²⁵ Motivation was also a key factor for adult patients undergoing warfarin therapy,¹⁸ patients at risk of cardiovascular disease,²⁶ and patients with ischemic heart disease post-percutaneous coronary intervention.^{15,27} Similarly to previous studies, motivation appears to be a critical factor for adherence to a healthy lifestyle in the findings of this study. Motivation, a psychosocial factor influencing adherence to treatment, significantly impacts health behaviours and patients' approach to treatment. Therefore, the main challenge in caring for patients with cardiovascular disease is to initiate and maintain necessary changes of health behaviour, i.e. adequate and regular physical activity, abstinence from smoking and alcohol, and adherence to dietary restrictions. Healthcare providers should adopt a motivational approach built on mutual trust and partnership with patients, enhancing mutual communication.^{15,23}

Unlike adherence to a healthy lifestyle, the strongest factor associated with adherence to medication was responsibility. This study also observed relationships between responsibility and healthy lifestyle adherence, and between motivation and medication adherence. Both motivation (through the factor of cooperation) and responsibility are associated with physician support, which covaries with support from nurses and next of kin. These findings confirm the importance of social support for elderly patients with heart failure, known to positively influence adherence to treatment.^{28,29}

The results of this study indicated that education on lifestyle modifications related to heart disease predicted greater fear of complications among the elderly, reflecting an awareness of the risks associated with non-adherence to treatment regimens. Education for heart failure patients focusing on lifestyle modifications, self-care, and symptom management provides patients with information about the nature of the disease, the importance of treatment, self-monitoring, and the consequences of non-adherence. Awareness of the potential risks of inadequate adherence to heart failure treatment can lead to fear of complications among the elderly. The study by Kähkönen et al.²⁷ demonstrated that informational support was indirectly, but statistically significantly, related with adherence to both medication and a healthy lifestyle. In this study, informational support is understood as practical patient education, where patients receive basic and detailed information and recommendations regarding their illness, including feedback. These findings emphasize patient adherence to treatment as a multidimensional concept highlighting the active role and participation of a patient in his own care, which are currently a priority in nursing.¹⁶ To fully engage in self-care and make relevant decisions, patients should have enough knowledge and information about their disease and its treatment. This fact is supported by results from earlier studies indicating that knowledge and information are perceived as the most critical for engaging patients in treatment regimens. It is also essential to emphasize not only information provision but also improving competencies for collaboration between patients and professionals.^{12,16}

Another finding of this study was that the elderly with MMSE scores of 27-30 and NYHA functional classification I and II reported a greater sense of normality compared to those with lower MMSE scores and NYHA functional classification III and IV. Evidence suggests that cognitive function contributes independently to adherence in older adults with heart failure.³⁰ Patients with poor NYHA functional status typically have increased physical limitations, restricting their ability to perform daily activities. Although the elderly with NYHA functional classification III and IV experienced greater limitations in daily life, this study did not observe reduced adherence to treatment in these patients. However, some studies have shown that the severity of symptoms, reflected in worse NYHA functional class, is associated with poorer adherence to treatment.³¹

Furthermore, the study found that hospitalization related to chronic heart failure in the past year predicted better support from next of kin. A plausible explanation might be that hospitalization makes relatives perceive the disease as a severe condition, leading to increased support for the elderly with heart failure.

The final observed relationship between adherence predictors and explanatory factors was the association between marital status and physician support. The elderly who were married, widowed, or divorced had a higher likelihood of receiving strong support from a physician compared to those who were single. This finding aligns with the understanding that socioeconomic status is an important factor influencing adherence to treatment in older patients with heart failure.²³

It is worth noting that, unlike the study by Kähkönen et al.¹⁷ on predictors of adherence to treatment, this study did not find a relationship between motivation and any predictive factors. A possible explanation is that the sample of respondents showed high percentages of good adherence across most factors explaining adherence to treatment (except for the sense of normality and fear of complications), making it more challenging to identify predictors for these factors statistically.

Limitations of the study

Due to the fact that adherence is a multidimensional concept based on different definitions and there is no agreement upon generally accepted definition of adherence, and moreover the terminology has evolved over time, direct comparison with previously published studies is limited. In addition, a large proportion of adherence testing studies are focused only on medication adherence testing. Another limitation is the possible bias of the results due to the use of a self-assessment tool.

Conclusion

The results of this study align with the multifactorial concept of adherence to treatment, emphasizing the importance of assessing adherence not only to medications but also to a healthy lifestyle and all influencing aspects. One of the significant factors affecting adherence to treatment identified in this study is education. Therefore, it is crucial that education is tailored to the specific needs of the patient, considering their age, educational level, health literacy, and is based on professional knowledge. Most studies, including this one, agree that motivation is a key factor for adherence to treatment. Healthcare providers should thus focus on enhancing patient motivation through appropriate interventions, such as setting treatment plans, establishing, and monitoring individual goals, individual consultations, motivational interviews, counselling, or shared decision-making. This necessitates the development and strengthening of motivational skills among healthcare professionals.

In conclusion, the efficacy of multidimensional interventions to improve adherence not only in older patients with heart failure but also across various groups of patients with chronic illnesses needs further testing for a better understanding of this issue.

Conflict of interest

The authors declare that they have no competing interests.

Funding

None.

Ethical statement

The research protocol was approved by the institution where the study took place. Respondents were assured that all data collected would be anonymous and confidential.

Informed consent

Informed consent was obtained from all participants involved in the study.

Availability of data and materials

All data are available in the manuscript

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Miniinvazívne operácie mitrálnnej chlopne cestou videoasistovanej torakotómie – štúdia jedného centra

(Minimally Invasive Mitral Valve Surgery via Video-Assisted Thoracotomy – A Single Center Study)

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SÚHRN

Miniinvazivní chirurgie mitrální chlopě (MIMVS), pomocí videoasistované torakoskopie (VATS), se etablovala jako efektivní přístup v kardiologii za posledních 30 let. Tento typ operace umožňuje menší řezy, což vede k rychlejší rekonvalescenci a sníženým pooperačním komplikacím.

V této retrospektivní studii bylo analyzováno 54 pacientů, kteří podstoupili miniinvazivní operaci mitrální chlopě mezi máj 2018 a máj 2024 na Klinice srdcovej chirurgie Východoslovenského ústavu srdcových a cievnych chorôb (VÚSCH a.s.). Výsledky ukázali, že 92 % pacientů podstúpilo plastiku mitrální chlopě s implantací anuloplastického ringu, zatímco v 8 % případů bylo nutné vykonať náhradu chlopě. Pooperačne došlo k významnému zlepšeniu funkcie chlopne a zníženiu regurgitácie, pričom nebola zaznamenaná mortalita. Pooperačné sledovanie ukázalo priemernú ejekčnú frakciu 56,2 %.

MIMVS vykazuje výhody v kratších rekonvalescenčných časoch a zníženej potrebe transfúzií, je spojený s vyššími operačnými nárokmi a rizikom komplikácií. Štandardné operačné výsledky je možné dosahovať už v prvých prípadoch aj napriek technickej náročnosti MIMVS. Zavedenie tejto procedúry negatívne neovplyvňuje výsledky samotnej operácie a naše krátkodobé výsledky naznačujú, že klinické výsledky a trvácnosť opravy mitrální chlopě nie sú narušené. Môžeme predpokladať, že v prípade skompletizovania ďalších štúdií a rozsiahlejšej štandardizácie operačných postupov dôjde k širšiemu uplatneniu tejto metódy.

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ABSTRACT

Minimally invasive mitral valve surgery (MIMVS), using video-assisted thoracoscopic surgery (VATS), has established itself as an effective approach in cardiac surgery over the past 30 years. This type of surgery allows for smaller incisions, leading to faster recovery and fewer postoperative complications.

This retrospective study analyzed 54 patients who underwent minimally invasive mitral valve surgery between May 2018 and May 2024 at the Department of Heart Surgery, East Slovak Institute for Cardiovascular Diseases. The results showed that 92% of patients underwent mitral valve repair with the implantation of an annuloplasty ring, while in 8% of cases, valve replacement was necessary. Postoperatively, there was a significant improvement in valve function and a reduction in regurgitation, with no recorded mortality. Postoperative monitoring showed an average ejection fraction of 56.2%.

MIMVS offers advantages in shorter recovery times and reduced need for transfusions, but it is associated with higher surgical demands and a risk of complications. Standard surgical outcomes can be achieved in early cases despite the technical complexity of MIMVS. The introduction of this procedure does not negatively affect the surgery's outcomes, and our short-term results suggest that clinical outcomes and the durability of mitral valve repair are not compromised. It can be assumed that with the completion of further studies and wider standardization of surgical procedures, the application of this method will become more widespread.

Keywords:

Annuloplasty ring

Minimally invasive surgery

Mitral regurgitation

Mitral valve

Mitral valve repair

Video-assisted thoracoscopic surgery

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Úvod

Miniinvazívna chirurgia mitrálnnej chlopne (MIMVS) bola zavedená v 90. rokoch minulého storočia, od tej doby sa tento typ operačného prístupu dostáva do popredia a etabluje sa do operačnej rutiny na viacerých pracoviskách.¹ Jedným zo základných prístupov využívaných pri operáciách mitrálnnej chlopne je videoasistovaná torakoskopia (VATS). VATS môže byť použitá pri rôznych typoch operácií v hrudnej, ale taktiež v srdcovej chirurgii.

MIMVS je síce spojený s predĺženými operačnými časmi, ale metaanalýzy preukazujú zníženie pooperačných komplikácií (fibrilácia predsiení, zlyhanie obličiek, transfúzia krvi, infekcia rany), skrátenie dĺžky pobytu na jednotke intenzívnej starostlivosti, skrátenie celkovej hospitalizácie a tým pádom aj so znížením celkových nákladov na pacienta.¹⁻³ Metaanalýza publikovaná v roku 2023 poukázala na fakt, že MIMVS môže byť spojená s významným znížením pooperačnej mortality v ranom a strednodobom období, čo by v prípade ďalších štúdií mohlo preukázať, že prínosy MIMVS prevažujú nad jeho nevýhodami.¹

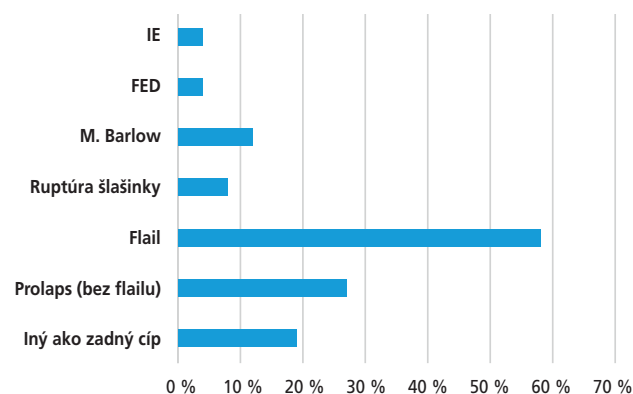
Materiál a metodika

Retrospektívna analýza sledovala 54 pacientov, ktorí podstúpili MIMVS medzi májom 2018 a májom 2024 na Klinike srdcovej chirurgie VÚSCH a.s. Indikácia pacientov bola z dôvodu izolovaného alebo kombinovaného výkonu na mitrálnnej chlopni. Výber pacientov bol na základe vhodnosti anatomických pomerov pre metódu VATS. Pacienti podstúpili kontroly predoperačne, včasne pooperačne, kontroly pri prepustení z nemocnice a následne v pravidelných intervaloch stanovených krajskou chlopňovou poradňou VÚSCH, a.s. V rámci štúdie boli hodnotené vek pacienta, body surface area (BSA), body mass index (BMI), komorbidity a nasledujúce echokardiografické (ECHO) parametre: stupeň mitrálnnej insuficiencie, nález na chlopni, ejekčná frakcia ľavej komory (LVEF) pred operáciou, účinná oblasť regurgitačného ústia (EROA), end-systolický a end-diastolický objem (ESV, EDV) a veľkosť pravej komory (RV). Pri peroperačných parametroch boli zaznamenávané parametre: typ výkonu na mitrálnnej chlopni, respektíve jej náhrada, dĺžka mimotelového obehu, trvanie kardioplegiekej zástavy, použitie anuloplastického ringu počas operácie, jeho veľkosť a ďalší konkomitantný výkon počas intervencie. Včasne pooperačne bola hodnotená LVEF, funkcia chlopne, regurgitačný stupeň a prípadne komplikácie. Počas kontrolných echokardiografických vyšetrení boli sledované LVEF, ESV, EDV, stupeň regurgitácie a mortalita.

Kvantitatívne údaje sú prezentované ako priemer $\pm$ štandardná odchýlka a kvalitatívne parametre sú prezentované v percentách výskytu v skupine.

Výsledky

Súbor pacientov tvorilo 44 mužov a 10 žien vo veku $53 \pm 1,4$ roka. V čase operácie bolo BSA pacientov $2,0 \pm 0,2$ m², BMI $26,2 \pm 3$. Pacienti mali pridružené komorbidity, pričom v 2 % sa vyskytoval diabetes mellitus (DM), 38 % sa liečilo



Obr. 1 Echokardiografický nález na mitrálnnej chlopni spôsobujúci mitrálnu regurgitáciu

na arteriálnu hypertenziu, fibrilácia alebo flutter predsiení bol zaznamenaný v 13 % a ischemická choroba srdca v 2 % pacientov. Z ECHO parametrov boli zaznamenané LVEF $60 \pm 6,6\%$, EROA $0,6 \pm 0,3$ cm², ESV $60,3 \pm 19,8$ ml, EDV $162,4 \pm 45,5$ ml, RV $90,5 \pm 36,7$ ml. Predoperačný stupeň mitrálnnej regurgitácie na základe kvantifikácie bol v danej skupine väčší ako 3. stupeň.

Mechanizmus spôsobujúci mitrálnu regurgitáciu bol zapríčinený v 27 % samotným prolapsom, v 58 % flailom cípu, v 8 % bola prítomná ruptúra šlašinky, v 12 % sa jednalo o morbus Barlow, v 4 % bola prítomná fibroelastóza (FED) a taktiež v 4 % sa jednalo o infekčnú endokarditídu (IE), 19 % pacientov malo prítomný flail cípu spolu s iným mechanizmom vzniku regurgitácie (obr. 1). Priemerná dĺžka mimotelového obehu bola 145 ± 6 minút a dĺžka kardioplegiekej zástavy bola 114 ± 21 minút, bez potreby opätovnej zástavy srdca. V 50 prípadoch bola vykonaná plastika mitrálnnej chlopne s implantáciou anuloplastického ringu. V 8 % prípadov sa pristúpilo primárne k náhrade mitrálnnej chlopne, pre peroperačný nález nevhodný k plastike, pričom vo všetkých prípadoch bola použitá mechanická protéza. Resekcia P2 segmentu bola vykonaná v 63 %, v 17 % bola potrebná implantácia neochořdy a v 15 % sa vyžadovala sutúra segmentu cípu mitrálnnej chlopne. Priemerná veľkosť použitého mitrálnneho anuloplastického ringu bola $32,4 \pm 9,7$ mm. Priemerná veľkosť mechanickej protézy bola $29,5 \pm 1,91$ mm. Konkomitantný výkon bol realizovaný v 19 % pacientov. V štyroch prípadoch bola realizovaná procedúra Cox-MAZE, piatim pacientom bol implantovaný anuloplastický ring do trikuspidálneho prstenca, v jednom prípade bol korigovaný defekt predsieňového septa. Dvomi pacientom bola pooperačne implantovaná mimotelová membránová oxygenácia (ECMO) pre prítomnosť hemodynamickej instability po odpojení z mimotelového obehu. V oboch prípadoch bolo ECMO včasne explantované, bez potreby ďalšej intervencie. Výsledky ukazujú, že 92 % pacientov podstúpilo plastiku mitrálnnej chlopne s použitím anuloplastického ringu s optimálnym pooperačným echokardiografickým nálezom, čo potvrdzuje vysokú využiteľnosť tohto operačného prístupu.

Priemerne sledovanie prežívania bolo $2,2 \pm 1,8$ roka. Echokardiografické sledovanie skupiny bolo $1,0 \pm 0,7$ roka. Pri poslednej kontrole bola zaznamenaná LVEF $56,2 \pm 5,3$ %, mitrálna regurgitácia $0,8 \pm 0,6$ stupňa, ESV $34,5 \pm$

Tabuľka 1 – Zhrnutie echokardiografického sledovania

Parameter	Predoperačne	Pooperačne	Follow-up
EF (%)	60,6 ± 6,6	54,3 ± 7,1	56,2 ± 5,3
MiR (stupeň)	3,5 ± 0,5	0,3 ± 0,4	0,8 ± 0,6
ESV (ml)	60,3 ± 36,7	–	34,5 ± 13,4
EDV (ml)	162,4 ± 45,5	–	77,5 ± 24,7

13,4 ml, EDV 77,5 ± 24,7 ml (tabuľka 1). V skupine nebola zaznamenaná mortalita, ani zlyhanie plastiky, v jednom prípade bolo prítomne zhoršenie nálezu mitrálnej regurgitácie klasifikované do 2. stupňa.

Diskusia

Od roku 1996, kedy Carpentier predstavil miniinvazívnu operáciu mitrálnej chlopne cez pravú minitorakotómiu, sa tento prístup začal osvedčovať ako bezpečný a efektívny.³ Systematický prehľad a metaanalýza autorov Cheng a spol. sledovala 271 pacientov, ktorí podstúpili MIMVS. Vstupná LVEF pacientov bola 65 ± 9,4 %, pričom priemerový vek bol 58 ± 13 rokov. Dĺžka mimotelového obehu 168 ± 56 minút a kardioplegickej zástavy 115 ± 41 minút. V danej štúdii bol v 263 prípadoch použitý anuloplastický ring s priemernou veľkosťou 31,4 ± 2,9 mm. V pooperačnom ECHO sledovaní bola pozorovaná mitrálňa insuficiencia 0,7 ± 0,7 stupňa, čo zodpovedá výsledkom našej sledovanej skupiny. Táto štúdia nezistila významné rozdiely medzi MIMVS a tradičnou operáciou cestou mediálnej sternotómie, pokiaľ porovnávame krátkodobú a dlhodobú mortalitu. MIMVS vykazovala tendenciu k zníženiu potreby transfúzie krvi, sternálnych infekcií, výskytu pooperačnej fibrilácie predsiení, dĺžky pobytu na jednotke intenzívnej starostlivosti a celkovej dĺžky hospitalizácie.⁴ V roku 2025 bola publikovaná retrospektívna štúdia autorov Aichi a kol., ktorá pozorovala 476 pacientov v priebehu 12 rokov. Výsledky tejto analýzy sa zhodovali s Cheng a kol. a nezaznamenali pri MIMVS nárast výskytu poranení aorty alebo CMP.⁵

Štúdia autorov McClure a kol. pozorovala skutočnosť, že sa u pacientov s myxomatóznym ochorením zadného cípu neobjaví opakovaná mitrálňa regurgitácia (stupeň ≥ 3+) v 76 ± 4 % po 10 rokoch. Tento výsledok bol výrazne lepší v porovnaní so skupinou s postihnutím predného alebo oboch cípov, kde bola táto pravdepodobnosť 49 ± 9 % v rovnakom sledovanom období.⁶

MIMVS sa stalo bežnou metódou pre mnohých pacientov podstupujúcich chirurgiu mitrálnej chlopne. V Spojených štátoch amerických využitie tejto metódy vzrástlo z 11,9 % v roku 2004 na 20,1 % v roku 2008, v Nemecku sa zvýšilo z 13,1 % v roku 2004 na 45,2 % v roku 2013, pričom v roku 2017 presiahlo 50 %.⁷ Pochybnosti o použití MIMVS, napriek rastúcemu trendu, pramenia hlavne zo skutočnosti, že tento prístup je technicky náročnejší a vyžaduje dlhší čas na osvojenie postupov.⁸

Medzi hlavné obavy z používania MIMVS patrí riziko spojené s krivkou učenia. Počet pacientov potrebných na úspešné zvládnutie tejto krivky a správna selekcia pa-

cientov je stále rozsiahlym predmetom diskusie. Literatúra uvádza množstvo analytických metód na hodnotenie krivky učenia pri miniinvazívnej chirurgii, pričom jednou z najčastejšie používaných metód je CUSUM. Táto metóda pomáha sledovať zmeny v čase trvania mimotelového obehu a času naloženého klemu.⁸ Výsledky sa medzi autormi líšia. Autori popisujú rôzny počet výkonov na prekonanie krivky. Podľa Wu a kol. sa jedná o 33 operácií, Holzhey a kol. stanovili bod učenia medzi 75 a 125 operáciami, čo potvrdili aj podobné výsledky Vo a kol.^{9,10,11} Analýza podľa Papadopoulos a kol. ukázala, že pre prekonanie krivky učenia bolo potrebných 55 operácií. Okrem počtu operácií je kľúčový aj správny výber pacientov pre bezpečné zavedenie programu MIMVS.¹²

Záver

MIMVS cestou VATS sa stávajú dostupnejšími a čoraz viac používanými metódami v chirurgii mitrálnej chlopne. Existuje viacero štúdií, ktoré porovnávajú miniinvazívnu chirurgiu mitrálnej chlopne s konvenčnou chirurgiou cez mediálnu sternotómiu. Napriek tomu, že miniinvazívny prístup je spojený s dlhšími operačnými časmi, je dokázané, že znižuje pooperačné komplikácie, akými je výskyt zlyhania obličiek, fibrilácia predsiení, potreba transfúzie a infekcie rán. Taktiež je preukázané, že je spojený s kratšími pobytmi pacientov na JIS a celkovým časom hospitalizácie. Z pohľadu pacienta sa jedná hlavne o minimálny kozmetický zásah (obr. 2).

Snahou nášho pracoviska je etablovať mininvazívne postupy do štandardnej operatívy a v krátkom čase iniciovať plne endoskopické operačné výkony.

Je potrebné poznamenať, že nie každý je vhodným kandidátom na MIMVS a skupina pacientov v našej sledo-



Obr. 2 – Zobrazenie pooperačného stavu pacientky

vanej skupine bola starostlivo vybraná. Správny výber pacienta v rámci predoperačného hodnotenia je kľúčovým faktorom úspechu, resp. neúspechu MIMVS a zohráva rozhodujúcu úlohu ako prediktor úspešnosti plastiky mitrálnej chlopne. Pacienti s chorobnou obezitou, hlbokou hrudnou dutinou, prípadne deformitami hrudnej steny môžu predstavovať značné technické výzvy pri využití minimálne invazívnych metód.

Z hľadiska perspektívy je stále potrebné skúmanie dlhodobých výsledkov a efektivity danej procedúry. Na potvrdenie trvalých výhod MIMVS a definovanie optimálnych indikácií a výberu pacientov pre tento postup sú nevyhnutné ďalšie dlhodobé štúdie. Napriek potrebe zručnosti a technickej náročnosti MIMVS je možné už v prvých prípadoch dosahovať štandardné operačné výsledky. Zavedenie tejto procedúry negatívne neovplyvní výsledky samotnej operácie a naše krátkodobé výsledky naznačujú, že klinické výsledky a trvácnosť opravy mitrálnej chlopne nie sú pri použití MIMVS metód narušené.

Vyhlásenie o konfliktach záujmov

Autori vyhlasujú, že nemajú žiadny konflikt záujmov.

Vyhlásenie o financovaní

Spracovanie tejto štúdie nebolo podporené žiadnym grantom ani iným financovaním.

Vyhlásenie etickej komisie

Štúdia bola vykonaná v súlade s Helsinskou deklaráciou a schválená etickou komisiou Východoslovenského ústavu srdcových a cievnych chorôb, a.s. (kód protokolu: A3012025; dátum schválenia: 7. január 2025).

Vyhlásenie o informovanom súhlase

Pacienti podpísali informovaný súhlas na vyšetrenie, hospitalizáciu a operáciu. Vzhľadom na retrospektívny charakter štúdie etická komisia nezistila potrebu získania dodatočného súhlasu na publikáciu. Informovaný súhlas je dostupný pre editora.

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Reimagining Medicine

Cardiac sequelae after COVID-19: results of a one-year follow-up study with ECG monitoring

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SOUHRN

Cíl: Vyhodnotit potřebu EKG monitorace u neselektovaných pacientů po prodělané infekci covid-19 a odhadnout riziko rozvoje arytmií a změny variability srdeční frekvence.

Metody: Mezi březnem 2020 a lednem 2021 byli pacienti, kteří se zotavili ze symptomatické infekce SARS-CoV-2 prokázané polymerázovou řetězovou reakcí (PCR) (varianty alfa a beta), zařazeni do prospektivní observační kohortové studie CoSuBr (COvid SUrvivals in BRno). Byly provedeny dvě sedmidenní monitorace EKG ve dvou časových intervalech: nejméně šest týdnů po infekci a s ročním odstupem. Vedle demografických parametrů, anamnézy a klinického vyšetření byla hodnocena i variabilita srdeční frekvence (HRV).

Výsledky: Studijní soubor tvořilo 74 jedinců, z toho 42 žen (56,8 %). Průměrný věk činil 48 let (rozmezí 21–77 let). Průměrný časový interval mezi nástupem nákazy a první návštěvou dosahoval 105 dní. V době zařazení se u 61 % pacientů projevovaly přetrvávající příznaky, přičemž více než polovina celého souboru (51,3 %) zmínila alespoň jeden příznak možného srdečního původu (dýchací potíže, bušení srdce, nevýkonnost, únava). Nedošlo k žádné změně v průměrné srdeční frekvenci mezi návštěvami ($72,7 \pm 8$ vs. $72,5 \pm 8$ min; $p = 0,756$) a nebyla zaznamenána žádná změna výskytu supraventrikulární nebo komorové ektopie. Nebyl zjištěn rozdíl v EKG parametrech mezi symptomatickými a asymptomatickými skupinami. Při roční kontrolní návštěvě po infekci covid-19 nedošlo ke změně variability srdeční frekvence hodnocené pomocí SDNN (V1 vs. V2 $156,6 \pm 40,6$ vs. $156,0 \pm 38,0$; $p = 0,855$), rMSSD (V1: $33 \pm 13,95$ vs. $30,6 \pm 12,89$; $p = 0,175$) a trianglu (V1: $28,5 \pm 7,8$ vs. $29,5 \pm 8,8$; $p = 0,488$). Hodnotili jsme přítomnost supraventrikulárních a komorových arytmií a monitorování EKG neprokázalo žádnou významnou patologii.

Závěr: Navzdory mnoha informacím o srdečním poškození způsobeném SARS-CoV-2 naše studie nenaznačuje zvýšené riziko vzniku arytmií po covidu-19 v ročním sledování. Na základě našich výsledků se po zotavení z covidu-19 nedoporučuje rutinní monitorování EKG.

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ABSTRACT

Objective: To evaluate the need for ECG monitoring of unselected patients recovered from COVID-19 and to estimate the risk of development of arrhythmias and heart rate variability change after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Methods: Between March 2020 and January 2021 patients who had recovered from PCR-proven SARS-CoV-2 symptomatic infection (alfa and beta variants) were enrolled in a prospective observational cohort study CoSuBr (COvid SUrvivals in BRno) and those with two 7-day ECG monitoring have been analysed.

Demographic parameters, patient history, clinical evaluation, and 7-day ECG monitoring were recorded within two times intervals: the first at least six weeks after infection and a follow-up visit one year later to establish any changes in heart rate variability (HRV).

Keywords:

COVID-19

ECG monitoring

Follow-up

Heart rate variability

SARS-CoV-2

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Results: The study group consisted of 74 individuals, 42 of which were females (56.8%), with 7-day ECG monitoring performed in both time intervals. The mean age was 48 years (range 21–77 years). The mean time interval between the onset of the infection and the follow-up visit was 105 days. At the time of enrolment, 61% of the patients were experiencing ongoing symptoms, while more than half of the whole group (51.3%) mentioned at least one symptom of possible cardiac origin (breathing problems, palpitations, exercise intolerance, fatigue). There was no change in the average heart rate between visits (72.7 ± 8 vs. 72.5 ± 8 /min; $p = 0.756$), and no difference in the incidence of supraventricular or ventricular ectopy. There was no difference in parameters between symptomatic/asymptomatic groups.

At the one-year follow-up visit after COVID-19 infection, there was no change in heart rate variability evaluated by SDNN (V1 vs. V2 156.6 ± 40.6 vs. 156.0 ± 38.0 ; $p = 0.855$), rMSSD (V1: 33 ± 13.95 to 30.6 ± 12.89 ; $p = 0.175$) and triangle (V1: 28.5 ± 7.8 to 29.5 ± 8.8 ; $p = 0.488$). We evaluated the presence of supraventricular and ventricular arrhythmias, and the ECG monitoring showed no significant pathology.

Conclusion: Despite a lot of information regarding cardiac impairment caused by SARS-CoV-2, our study does not suggest an increased risk in developing arrhythmias after COVID-19 in the one-year follow-up. Based on our results, routine ECG monitoring is currently not recommended after recovery from COVID-19.

COVID-19 is primarily a respiratory disease with potential extra pulmonary manifestations. Lethality is generally low, and most patients recover within one or two weeks. The COVID-19 pandemic hopefully reached its peak during the last couple of years, during which it left behind not only fatalities but also many patients with ongoing problems. The condition where the symptoms of COVID persist beyond week 4 or beyond week 12 are called “long COVID” and “post-COVID syndrome”, respectively.¹

Approximately 5–10% fail to recuperate fully. Considering the number of people infected worldwide, dealing with post-COVID patients can be challenging for health care systems. The symptoms may affect many organ systems, including the cardiovascular system,² and may develop regardless of the severity of acute infection. The care and management of these long haulers is nowadays based especially on the effort to rule out other common causes of the present symptomatology.³ As the manifestation of post-COVID syndrome is highly varied and different phenotypes have recently been established,⁴ an interdisciplinary approach is recommended and physicians across many fields of medicine are involved. This investigation is consuming in terms of time and personnel, is expensive, and the efficacy is not very high. There is thus a need for a comprehensive evidence-based plan to manage post-COVID symptoms. No specific therapy is available so far, and recommendations are mostly guided by our experiences with non-COVID diseases.⁵

Many symptoms of post-COVID syndrome may overlap with those of a cardiovascular origin. Despite data from MRI studies about myocardial damage,⁶ the clinical significance of these findings is still unknown. Large epidemiological studies have provided data about higher cardiovascular risk after hospitalisation for COVID-19,⁷ but an evidence-based recommendation for single patients, even with ongoing symptomatology, is still based mainly on recommendations from authorities.

To better understand the cardiovascular sequelae of COVID-19, we initiated a prospective observational cohort study called CoSuBr (COvid SURvivals in BRno). Results of the echocardiographic parameters and biomarkers have been recently published⁸ and in these subsequent analyses we were focused on arrhythmias and heart rate variability. The aim of our study was to help physicians and

their patients with a tool which is commonly available in their practise – 7-day ECG monitoring to estimate the risk of developing arrhythmias during a one-year follow-up after COVID-19 recovery and to detect possible changes in heart rate variability as a marker of autonomic dysfunction.

Methods

We recruited patients in an outpatient clinic for post-COVID care at least 6 weeks after their recovery from acute symptomatic COVID-19 infection (PCR-verified SARS-CoV-2 from a nasopharyngeal swab). After signing an informed consent form, a clinician interviewed all patients. The demography (age, sex), medical history, and data about the acute phase of COVID-19 infection were collected. The severity of the disease was classified as follows: mild without dyspnea or abnormal chest imaging; moderate for evidence of a lower respiratory tract infection without a decrease of oxygen saturation $<94\%$; severe with a need for oxygen; critical with respiratory failure and/or shock, need for oxygen/artificial ventilation. The need for intensive care, type, and duration of the symptomatology, and treatment were also evaluated. Special interest was paid to ongoing ailments. Two 7-day ECG monitoring was recorded: first at least 6 weeks after acute infection (V1), and the second one a year later (V2). All patients underwent also body plethysmography at the beginning of the trial and those with moderate/severe respiratory impairment have been excluded.

The trial protocol was approved by the institutional review board at University Hospital Brno (08-100620/EK). The data were managed using REDCap electronic data capture tools, and a data analysis was carried out using SAS software. The mean (and standard deviation) was used to present average values for normal data distribution, and the median (and interquartile range) was used to present data of non-normal distribution. Prevalence is reported as the number of and percentage of patients reporting the symptom within the group. A paired t-test or its non-parametric alternative (Wilcoxon test) was used to compare variables for one subject between the visits.

Results

The whole study group consisted of 106 individuals, while an evaluation with an ECG Holter monitor was performed in 96 of them on V1, and 74 on V2. The analyses performed for the study group consisted of 74 individuals, 42 of which were females (56.8%), with 7-day ECG monitoring performed in both time intervals. The mean age was 48 years (range 21–77 years). The mean time interval between the onset of the infection and the follow-up visit was 105 days. The most prevalent comorbidities were arterial hypertension ($n = 15$, 20.3%) and dyslipidemia ($n = 12$, 16.2%); others included obesity, e.g. BMI over 30 ($n = 8$, 10.8%), hepatic steatosis ($n = 3$, 4.1%), asthma ($n = 4$, 5.4%) and renal insufficiency ($n = 5$, 6.8 %); see **Table 1**. Almost a quarter of the patients (23.0%) required hospitalisation during the acute phase of the disease, with only two of them requiring artificial ventilation; the rest recovered at home with a mild form of the disease. At the time of enrolment, 61% of the patients were experiencing ongoing symptoms, while more than half of the whole group (51.3%) mentioned at least one symptom of possible cardiac origin (breathing problems, palpitations, exercise intolerance, fatigue).

We assessed the presence of supraventricular premature beats (SPBs) and ventricular ectopy (premature

ventricular contractions), and the ECG monitoring after the one-year period showed no significant pathology or trend in the incidence of both these events. These data are summarised in **Table 1**.

During the one-year follow-up after COVID-19 infection, there was no change in heart rate variability evaluated by SDNN (V1 vs. V2 156.6 ± 40.6 vs. 156.0 ± 38.0 ; $p = 0.855$), rMSSD (V1: 33 ± 13.95 to 30.6 ± 12.89 ; $p = 0.175$) and triangle (V1: 28.5 ± 7.8 to 29.5 ± 8.8 ; $p = 0.488$). Dividing heart rate oscillations into low-frequency (LF), and high-frequency (HF) bands, we found significant statistical changes between V1 and V2 for LF (718 ± 433.7 to 646 ± 361 ; $p = 0.024$) and HF (341.5 ± 335 to 268.0 ± 266 ; $p = 0.032$).

There was no difference in presence of supraventricular premature beats (SPBs), ventricular ectopy (premature ventricular contractions), and heart rate variability between the group with ongoing symptomatology of possible cardiovascular origin and those without these symptoms.

During the one-year follow-up, one patient was diagnosed with asymptomatic paroxysmal atrial fibrillation, and one with second degree atrioventricular block. No patient died during the follow-up period.

The change in heart rate variability, as well as the incidence of ventricular and supraventricular ectopy during the follow-up visit, are summarised in **Table 2**.

Table 1 – Incidence of supraventricular and ventricular ectopy in visit 1 and 12 months later (V2)

	V1 mean (SD)	V2 mean (SD)	<i>p</i>
Heart rate	72.7 (8.5)	72.5 (8.6)	0.756
Min. HR	44.9 (6.2)	45 (5.2)	0.982
Max. HR	154.5 (21.6)	151.7 (21.2)	0.186
Afib, flutter	0 (0)	0.8 (7.2)	1
SVT non-sustained	9.8 (29.8)	15 (50.6)	0.800
SPBs	1142 (4225)	1278.9 (4262)	0.790
SPB couplets	24.9 (98.5)	23.8 (87.5)	0.043
PVCs isolated	482 (2214.5)	941 (5451.5)	0.965
PVCs couplets	2.9 (16.7)	1.6 (5.3)	0.674
PVCs bigeminy	2.3 (11.6)	16 (116.5)	0.984
VT non-sustained	0.2 (0.58)	0.4 (0.9)	0.127

SBPs – supraventricular premature beats, premature ventricular contractions; SVT – supraventricular tachycardia; VT – ventricular tachycardia.

Table 2 – Parameters of heart rate variability in visit 1 and 12 months later (V2)

	V1 mean (SD)	V2 mean (SD)	<i>p</i>
HF bands	341.5 (334.9)	268 (266.3)	0.032
LF bands	718.8 (433.7)	646.8 (361)	0.024
rMSSD	33 (13.9)	30.6 (12.8)	0.175
pNN50	10.8 (9.28)	9.3 (8.7)	0.255
SDNN	156.6 (40.6)	156 (38.2)	0.855
SDDN index	59.5 (18)	55.8 (15.7)	0.036
Triangle	28.5(7.8)	29.5 (8.8)	0.488

HF – high frequency; LF – low frequency.

Discussion

Our 7-day study with an ECG Holter monitor is a part of a larger follow-up project (CoSuBr) on the subjects after SARS-CoV-2 infection. Echocardiographic parameters and biomarkers from the whole study group ($n = 106$) have been published recently.⁸ These subanalyses of ECG Holter were done only for the subset of participants ($n = 74$), where both recordings were available.

A majority of our patients had a mild course of the acute disease, which is the same proportion of COVID-19 disease's severity globally. Our population represents a wide spectrum of ages. More than half of the study group (61%) fulfilled the criteria of post-COVID syndrome at the time of enrolment, which is given by the source of our subjects – mainly an outpatient clinic for post-COVID care.

Except for hypertension (20%), none of our patients suffered from cardiovascular disease before the enrolment. The rate of repeated infection was rare – only four patients had recidivism of COVID during the one-year follow-up period. In addition, an analysis of vaccinated and unvaccinated is impossible, because recruitment to the study had nearly been completed by the time the vaccine became available.

Despite the high rate of symptomatic patients in our study group, the incidence of clinical significance arrhythmias was rare, and their distribution was in the oldest tenth of our study group. One patient was diagnosed with *de novo* paroxysmal atrial fibrillation (female, 73 years old, dilated left atrium), another with atrioventricular block with an indication for implantation of a pacemaker (male, 71 years old; cardiac MRI did not find any signs of myocardial inflammation). We do not suspect these endpoints to be the direct result of SARS-CoV-2 infection. Also the absence of difference in ECG parameters in symptomatic and asymptomatic subjects doesn't support the cardiovascular apparatus as organ system responsible for ongoing problems in post-COVID patients. No patients died during the follow-up period.

The impairment of the cardiovascular system during the acute phase of COVID-19 infection has been well described.⁹ The impact of hypoxia and cytokine storm during severe inflammatory responses in predisposed individuals can cause a broad spectrum of cardiovascular pathologies, including arrhythmias. In addition, myocardial damage caused by SARS-CoV-2 is suspected for reasons including its spike affinity to the ACE2 receptor binding domain, which plays an essential role in the renin-angiotensin system.¹⁰

A significant proportion of patients suffered ongoing problems during the weeks and months after acute COVID infection. Common complaints have included persistent fatigue, shortness of breath, brain fog, and also palpitations. Davies et al.¹¹ in an online survey of a post-COVID population report tachycardia in 61.4% of patients and suspect possible postural orthostatic tachycardia syndrome in almost a third of them. There are also several possible mechanisms for decreased arrhythmic burden after COVID infection: direct cytotoxic injury, antibody or cytokine induced damage, changes in microcirculation, inflammatory cardiac channelopathies and many

others.^{12,13} During all waves of the pandemic, hospitalisation was high especially in elderly individuals and/or in those with comorbidities. Large epidemiological studies and data from registries brought strong evidence of cardiovascular risk for the post-COVID population between 30 days and one year after acute illness (hazard ratio for dysrhythmias was 1.69),¹³ and similar results for any cardiovascular endpoints were described also by Wang et al. (HR 1.552 [1.526–1.578]).⁷ The risk was only slightly higher in the non-hospitalised and mainly driven by the severe and critical forms of the disease. An explanation of these findings may be hidden in the frailty of the subjects hospitalised for acute coronavirus infection and the need for admission may only be a marker of lower general health and pre-existing cardiovascular risk. This is in concurrence with the results of our study, when in the early post-acute phase of recovery and one year after there was no change in the incidence of ventricular or supraventricular ectopy. This does not support the theory of SARS-CoV-2-induced arrhythmias. Even if our sample is not large, the sequential 7-day ECG monitoring in predefined time frame of one year is robust enough to be able to find possible changes. Considering that in our study population, there were more than 60% of patients with ongoing problems and that previously published analyses of the whole CoSuBr study group did not find dynamics of echocardiographic parameters and cardio markers in the one-year follow-up after COVID-19,⁸ we assumed that SARS-CoV-2's influence on the heart in the post-COVID period is weak (if at all). We also conclude that the symptoms related to post-COVID syndrome are not of cardiac origin.

Observational and epidemiological studies observed a higher rate of atrial fibrillation,⁷ while another study from Italy reported an increase of ventricular tachycardia in heart disease patients with implanted devices and the authors suggest an association with lower physical activity during the pandemic.¹⁴ Significantly higher rates of isolated ventricular premature beats (VPB) and supraventricular premature beats (SVPB) were found in 53.3% and 52.5% of 90 post-COVID athletes, respectively, but no malignant arrhythmias were identified.¹⁵ These data are in concordance with our results and also do not support the theory of a direct relationship between infection and higher risk of arrhythmias during recovery.

Our study group of mostly outpatients with ongoing symptomatology is quite similar to the population enrolled in a Polish long-covid cardiovascular study, which found 6.9% patients with myocardial dysfunction based on echo or MRI.¹⁶ This was not dependent on the severity of the disease course. In their observational study they also found more ($p=0.008$) heart rhythm disturbances (atrial fibrillation, supraventricular extrasystole, ventricular extrasystole) in patients with vs without myocardial dysfunction after COVID. In contrast to classic post-COVID pattern, patients affected were mostly men of average age 51 ± 13 and also the absence of previous cardiovascular disease was based only on patient's history. No serious arrhythmias and/or conduction disorders were pointed out. They conclude that ECG changes can indicate the possibility of cardiovascular dysfunction. Relationship between changes described and SARS-CoV-2 infection remains uncertain.

In post-COVID syndrome patients, mainly in young women, inappropriate sinus tachycardia was described.¹⁷ Moreover, a decrease in physical activity after acute infection, especially in those with ongoing symptomatology, can lead to deconditioning and secondarily to increased heart rate. In our study there was no statistical significant difference in HR between visits. There was only one subject (20-year-old female) fulfilling the condition for inappropriate sinus tachycardia who was successfully treated by Ivabradin. This condition can be related to autonomic dysfunction, which is one of the possible mechanisms of the development of post-COVID symptomatology.^{18,19}

Heart rate variability (HRV) from at least a 24-hour measurement is a tool for stratifying cardiovascular risk, when the SDDN values are able to predict morbidity and mortality.²⁰ In the one-year follow up after COVID-19 infection, our study did not detect any change in heart rate variability as evaluated by SDNN, rMSSD, and triangle (Table 2). Dividing heart rate oscillations into low-frequency (LF) and high-frequency (HF) bands, we found significant statistical changes between V1 and V2 for LF and HF. These parameters are mostly affected by breathing rate,²¹ which can be a result of the lungs healing and/or regaining conditioning. These parameters also represent possible autonomic dysregulation (HF/LF ratio) and sympathetic/parasympathetic system activity, which was also described after COVID infection.²² One of them is postural orthostatic tachycardia syndrome (POTS), which has been described mainly in young woman after a mild course of the acute disease and appears to be the most common autonomic phenotype among these patients.²³ Our data for heart rate variability analyses were not obtained under controlled conditions, but come from our subjects under normal living conditions. Based on this, we are not able to express a final statement on HRV.

There are surely limitations of our study. First of all the sample size is too small to be able to make definite conclusion about the risk of arrhythmias in post-COVID patients. Another problem is also the change of immune response of virus naïve population, on which our study has been performed and the nowadays people, who surly underwent several waves of coronavirus infection and the most vulnerable are usually (or should be) vaccinated. There is also a change of virus itself, when all of our patients were enrolled in time when original SARS-CoV-2 or beta variant dominated in the Czech Republic and before current variants or omicron and even delta have been on stage.

Conclusion

Despite a lot of information regarding cardiac impairment of SARS-CoV-2, our study does not suggest an increased risk in developing arrhythmias after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a one-year follow-up, even in a population with a high proportion of ongoing symptomatology. There was no difference in parameters between symptomatic/asymptomatic groups. We have not found any change in heart rate variability during the one-year follow-up, but some findings from our study may suggest autonomic dysfunction after CO-

VID-19. Based on our results, routine ECG monitoring is currently not recommended during COVID-19 recovery.

Conflict of interest

None declared.

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Ethical statement

The studies involving human participants were reviewed and approved by Ethic Comitee FN Brno, 08-100620/EK.

Informed consent

The patients/participants provided their written informed consent to participate in this study.

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Surgical Management and Postoperative Outcomes of Ventricular Septal Rupture Following Acute Myocardial Infarction: A Case Series

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Oprava ruptury záplatou

Ruptura komorového septa

SOUHRN

Úvod: Ruptura komorového septa (ventricular septal rupture, VSR) představuje vzácnou, ale život ohrožující komplikaci akutního infarktu myokardu (AIM), s níž se lze setkat přibližně v 0,2 % případů po AIM. Chirurgická léčba jako definitivní řešení je spojena s vysokým rizikem úmrtí, zvláště pokud se provádí v naléhavých případech.

Cíl: V této studii představujeme případy pěti pacientů s VSR po AIM a hodnotíme chirurgickou léčbu a pooperační výsledky ve všeobecné nemocnici Dr. Soetomo General Hospital (Indonésie).

Metody: Provedli jsme retrospektivní analýzu případů pěti pacientů (mužů) ve věku 44 až 63 let, u nichž byla v letech 2023 a 2024 stanovena diagnóza VSR po AIM. Jejich demografické údaje, charakteristiky VSR, chirurgický výkon i pooperační výsledky byly systematicky zkontrolovány. Emergentní chirurgický výkon měl prioritu u hemodynamicky nestabilních pacientů, u nichž byl následně doplněn intenzivní pooperační péčí.

Výsledky: Rozsah VSR se pohyboval v rozmezí od 0,55 cm do 3,0 cm, přičemž většina z nich se vyskytla v oblasti srdečního hrotu. Přežili čtyři z pěti pacientů; u jednoho došlo k rozvoji fatálních komplikací včetně kardiogenního šoku, nesetřvalé komorové tachykardie, nozokomiální (nemocniční) pneumonie a akutního poškození ledvin 10. pooperační den. Mezi pooperační komplikace patřily akutní poškození ledvin (u čtyř pacientů), kardiogenní šok a pleurální výpotek. Délka pobytu v nemocnici se pohybovala v rozmezí 8 až 16 dní, přičemž u jednoho pacienta bylo nutno použít intraaortální balonkovou kontrapulsaci.

Závěr: Časná chirurgická intervence je pro léčbu VSR po AIM naprosto zásadní, stejně jako je pro lepší výsledky léčby nezbytné pečlivé načasování výkonu a výběr pacienta. Intenzivní pooperační péče hraje zásadní úlohu při mírnění komplikací a rychlejším zotavení této vysoce rizikové populace.

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ABSTRACT

Introduction: Ventricular septal rupture (VSR) is a rare but life-threatening complication of acute myocardial infarction (AMI), occurring in approximately 0.2% of post-AMI cases. Surgical repair is the definitive treatment, it carries a high mortality risk, particularly when performed emergently.

Aim: To present a case series of five patients with VSR following AMI and evaluate their surgical management and postoperative outcomes at Dr. Soetomo General Hospital

Methods: A retrospective analysis was conducted on five male patients, aged 44 to 63 years, diagnosed with VSR post-AMI between 2023 and 2024. Patient demographics, VSR characteristics, surgical interventions, and postoperative outcomes were systematically reviewed. The management strategy prioritized emergent surgical repair in hemodynamically unstable patients, supplemented by intensive postoperative care.

Results: VSR sizes ranged from 0.55 cm to 3.0 cm, predominantly located in the apical region. Four of the five patients survived, while one patient experienced fatal complications, including cardiogenic shock, non-sustained ventricular tachycardia, hospital-acquired pneumonia, and acute kidney injury on postoperative day 10. Postoperative complications included acute kidney injury (in four patients), cardiogenic shock, and pleural effusion. Hospital stays varied from 8 to 16 days, with one patient requiring intra-aortic balloon pump support.

Conclusion: Early surgical intervention is critical in managing post-AMI VSR, with precise timing and careful patient selection essential for improving outcomes. Intensive postoperative management is pivotal in mitigating complications and enhancing recovery in this high-risk population.

Keywords:

Acute myocardial infarction

Cardiac surgery

Coronary artery bypass grafting

Patch repair

Ventricular septal rupture

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Introduction

In 1847, Latham first identified ventricular septal rupture (VSR), which occurs in the interventricular septum that separates the right and left ventricles. This septum is composed of two primary sections: the muscular part and the membranous part. The muscular part makes up the bulk of the septum, located beneath the membranous part, and is thick, arising from the bulboventricular flange. Conversely, the membranous part is smaller and thinner, positioned above the muscular part, and is derived from neural crest cells. Ventricular septal rupture (VSR) is an infrequent but life-threatening complication of acute myocardial infarction (AMI), with an incidence of approximately 0.2% post-AMI. It typically presents within the first week following infarction, leading to acute left-to-right shunting, heart failure, and cardiogenic shock.¹ Despite advances in revascularization and medical therapy, surgical repair remains the definitive treatment, though it is associated with high mortality rates, especially when performed emergently.²

The management of VSR is challenging due to the hemodynamic instability of patients and the complexity of surgical repair. This case series reports five patients who underwent surgical intervention for VSR at Dr. Soetomo General Academic Hospital Surabaya between 2023 and 2024, detailing their presentations, surgical techniques, and outcomes.

Case description

This retrospective case series was conducted at Dr. Soetomo General Academic Hospital Surabaya between January 2023 and September 2024. Data were collected from medical records, including demographics, clinical presen-

tation, imaging findings, surgical approach, and postoperative outcomes. The inclusion criteria were diagnosis of VSR confirmed by echocardiography, the fact that the patients underwent surgical repair within the study period, aged 18 years or older. The exclusion criteria were VSR managed non-surgically, incomplete medical records. Surgical techniques used in these cases were surgeries under cardiopulmonary bypass, with defect closure performed using either pericardial or synthetic patches.

In this case series of five patients who underwent surgical repair for ventricular septal rupture (VSR), all patients were male, with ages ranging from 44 to 63 years (mean age of approximately 57.6 years). All patients profile and demographics are provided in **Table 1**. The majorities of the patients presented with typical symptoms of VSR following acute myocardial infarction (AMI), including chest pain, dyspnoea, and hypotension. In terms of AMI type, most of the cases were associated with apical infarctions, with one patient having an antero-septal infarction and another having a rupture at the border between the interventricular septum (IVS) and the right ventricular (RV) free wall. VSR was confirmed by transthoracic echocardiography in all cases, revealing defects varied significantly, from 0.55 cm to 3.0 cm in size. The Intraoperative findings are shown in **Figure 1**.

The postoperative outcomes of the five patients undergoing ventricular septal rupture (VSR) repair varied, with most experiencing significant complications, reflecting the high-risk nature of this surgical procedure. Four patients required preoperative vasopressor or intra-aortic balloon pump (IABP) support due to hemodynamic instability. Surgery was performed between 12 and 29 days after diagnosis, depending on the severity of the patients' conditions. Postoperative outcomes varied, with four out of five patients surviving, resulting in an 80% survival rate. However, one patient (patient 2) passed away on post-

Table 1 – Patient profile and demographics

No.	Age	Gender	Presentation before surgery	AMI type	VSR size (cm)	Timing of surgery after diagnosis (days)	Surgical technique	Complication	Outcome
1	44	Male	Chest pain, dyspnoea, hypotension (on support vasopressor)	Apical	3.0	29	CABG + patch repair	Low cardiac output, acute kidney injury	Discharged POD-8
2	63	Male	Chest pain, dyspnoea, hypotension (on support max. dose vasopressor)	Apical	0.55 and 1.0	20	CABG + patch repair + IABP	Cardiogenic shock, non-sustained VT, HAP, acute kidney injury	Passed away on POD-10
3	60	Male	Chest pain, dyspnoea	Apical, antero septal	1.2	27	CABG + patch repair	Right pleural effusion	Discharged POD-16
4	62	Male	Chest pain, hypotension (on support IABP and vasopressor)	Apical	2.5	12	CABG + patch repair	Acute kidney injury	Discharged POD-10
5	59	Male	Chest pain, dyspnoea, hypotension (on support IABP and vasopressor)	Border between IVS and RV free wall	2.5	16	Patch repair	Cardiogenic shock, acute kidney injury	Discharged POD-10

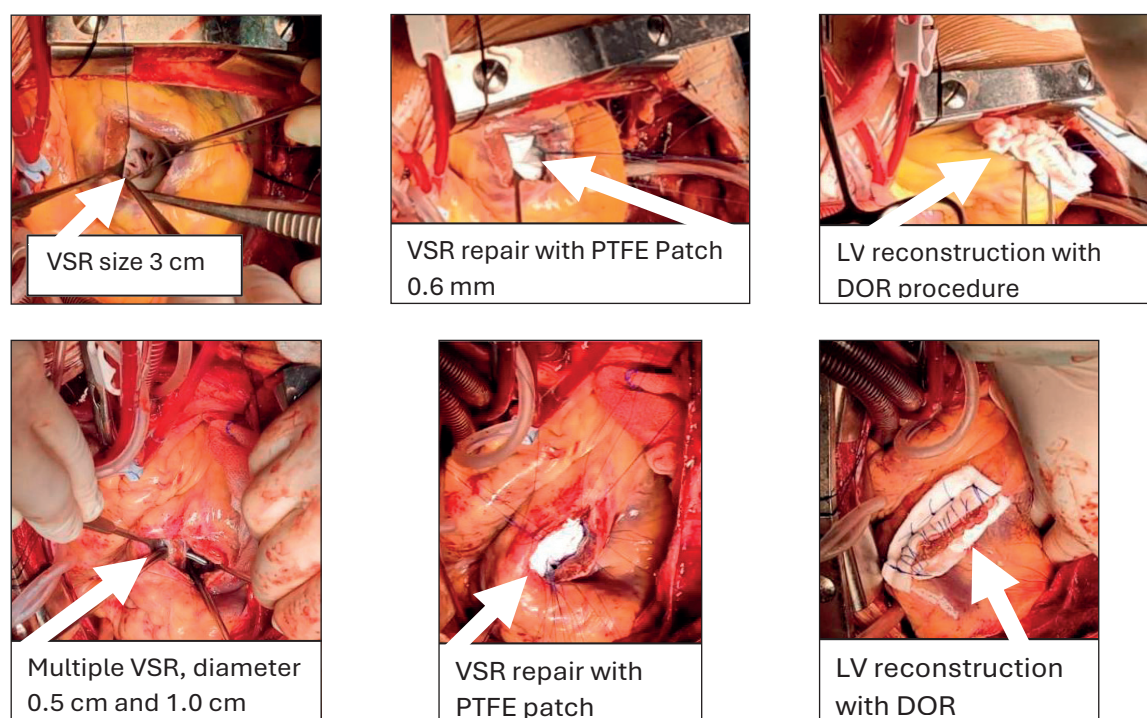


Fig. 1 – Intraoperative images of ventricular septal rupture (VSR) repair and left ventricular (LV) reconstruction.

operative day 10 due to complications including cardiogenic shock, non-sustained ventricular tachycardia (VT), hospital-acquired pneumonia (HAP), and acute kidney injury. The majority of the patients experienced serious postoperative complications. These included: 1) low cardiac output syndrome and acute kidney injury in patient 1; 2) cardiogenic shock, VT, hospital-acquired pneumonia, and acute kidney injury in Patient 2 (who did not survive); 3) right pleural effusion in patient 3; 4) acute kidney injury in patients 4 and 5. Hospital stays ranged from 8 to 16 days, with the longest being in a patient who experienced pleural effusion. In summary, while the majority of patients survived, the postoperative course was complicated by significant morbidities, including renal failure, respiratory complications, and hemodynamic instability. These findings highlight the high risk associated with VSR repair, underscoring the importance of comprehensive perioperative management and close monitoring of potential complications.

Discussion

This case series highlights the significant challenges and complexities involved in the surgical management of ventricular septal rupture (VSR) following acute myocardial infarction (AMI). The condition remains a serious complication of AMI, despite advancements in medical therapy and revascularization strategies. The five cases presented here demonstrate the wide spectrum of clinical presentations and the variable outcomes associated with VSR repair.³ All patients in this series were male, with a mean age of 57.6 years, which is consistent with the typical demographic profile of VSR patients as documented in

other studies.⁴ The majority of the cases involved apical infarctions, with one patient having an antero-septal infarction and another having a rupture near the interventricular septum and right ventricular free wall. These findings align with the known distribution of VSR locations following AMI, where apical and antero-septal regions are more prone to rupture due to high myocardial wall stress in these areas during infarction.⁵

In terms of preoperative presentation, all patients exhibited common symptoms of VSR, including chest pain, dyspnoea, and hypotension, which are indicative of heart failure and hemodynamic instability. Four out of five patients required preoperative support with inotropic agents or vasopressors due to severe hemodynamic compromise, with two of these patients also needing intra-aortic balloon pump (IABP) support. This demonstrates the critical instability that many VSR patients face before surgery. The timing of surgery after diagnosis varied between 12 and 29 days, reflecting the need for individualized decisions based on the patient's clinical stability and optimization before surgery. The variability in timing also highlights the dilemma in managing VSR, where earlier intervention is necessary for unstable patients but delaying surgery may allow for myocardial stabilization and reduce the risk of complications.⁶

The outcomes from this case series reinforce the high-risk nature of VSR repair, with four out of five patients surviving, resulting in an 80% survival rate. This survival rate is slightly higher than historical averages, which report mortality rates ranging from 20% to 60%, depending on patient stability and the timing of surgery.⁷ However, significant postoperative complications were common, with acute kidney injury occurring in four of the five patients. Other complications included low cardiac output

syndrome, cardiogenic shock, and pleural effusion. The patient who did not survive (patient 2) experienced cardiogenic shock, non-sustained ventricular tachycardia (VT), hospital-acquired pneumonia (HAP), and acute kidney injury, illustrating the vulnerability of patients even after surgical correction of the VSR.

The length of hospital stay ranged from 8 to 16 days, with longer stays associated with more severe complications such as pleural effusion and cardiogenic shock. This variation in recovery times further highlights the complexity of managing postoperative care in VSR patients³. Intensive monitoring and management of potential complications, such as renal failure and hemodynamic instability, are essential for improving patient outcomes. The timely use of mechanical circulatory support, such as IABP, in some patients proved critical in stabilizing these high-risk patients perioperatively.

Surgical techniques were consistent across all cases, with the use of cardiopulmonary bypass and patch repair being the standard approach. In three patients, concomitant coronary artery bypass grafting (CABG) was performed, a reflection of the significant coronary artery disease often associated with these patients. Combined CABG and VSR repair are not uncommon, particularly when significant coronary occlusion has contributed to the infarction and rupture. The timing of surgery remains a key point of debate. While delayed surgery is often preferred to allow for myocardial stabilization, emergent surgery may be the only option in critically unstable patients, as seen in patient 2, who ultimately succumbed to complications despite timely intervention.

This case series has several limitations that should be acknowledged. First, the small sample size, comprising only five patients, restricts the generalizability of the findings; a larger cohort would provide more robust data on the outcomes and complications of VSR surgery, better reflecting the variability in patient presentations and responses to treatment. Additionally, as a single-centre study conducted at Dr. Soetomo General Academic Hospital, the results may be influenced by the specific protocols, surgical techniques, and postoperative care practices at that institution, highlighting the need for multicentre studies to validate these findings in different settings. Furthermore, the retrospective design relies on the accuracy and completeness of medical records, leaving room for potential biases due to incomplete documentation or missing data. The focus on short-term postoperative outcomes also limits insights into long-term survival and quality of life post-discharge, making long-term follow-up essential for assessing the durability of VSR repairs. Lastly, the variability in the size and location of the VSRs, along with differing preoperative hemodynamic stability and comorbidities, complicates the ability to draw definitive conclusions regarding the factors that most significantly influence outcomes; a more homogeneous patient population might provide clearer insights.

Conclusion

In conclusion, the management of VSR remains a formidable challenge, even with modern surgical techniques and postoperative care. This case series demonstrates that while the majority of patients can survive VSR repair, the procedure is associated with significant morbidity, particularly renal and respiratory complications. The results underscore the need for individualized surgical strategies, early intervention when necessary, and comprehensive postoperative care to optimize patient outcomes. Future research should focus on identifying the optimal timing for surgical repair and exploring new treatment modalities to further reduce the high risk of mortality and complications associated with VSR.

Conflict of interest

Nothing to declare from all authors.

Funding

Nothing to declare from all authors.

Ethical statement

This case series was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Dr. Soetomo General Hospital Surabaya, Indonesia.

Informed consent

Informed consent was obtained from all patients included in this case series. The study was conducted in accordance with ethical standards and institutional guidelines.

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Short-term effects of exercise training program on patients with compensated chronic heart failure

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6MWT

SOUHRN

Kontext: Se srdečním selháním (heart failure, HF), což je komplexní syndrom s významnými klinickými důsledky i důsledky pro veřejné zdraví, se lze setkat přibližně u 1 % až 2 % dospělých osob. Smyslem programu pohybového tréninku při HF je zvýšit tělesnou zdatnost pacientů a zlepšit kvalitu jejich života při současném snižování pravděpodobnosti hospitalizací a úmrtí. Přes opakované zdůrazňování potřeby cvičení v doporučených postupech pro kardiorehabilitaci byla zjevná nedostatečná účast pacientů s HF v těchto programech. **Cíle:** Zhodnotit, jaký dopad má krátký, strukturovaný program pohybového tréninku na jedince s kompenzovaným chronickým srdečním selháním ve smyslu zlepšení hodnot klinických, laboratorních a echokardiografických parametrů.

Metody: Randomizované kontrolované studie se zúčastnilo 107 ambulantních pacientů s chronickým srdečním selháním (HFrEF a HFmrEF) v klinicky stabilizovaném stavu. V období od května 2022 do června 2023 byli účastníci studie zařazováni buď do skupiny s cvičením, nebo do kontrolní skupiny.

Intervence: Obvyklá péče plus aerobní pohybový trénink po dobu 12 týdnů.

Shromažďovaly se hodnoty 6MWT, KCCQ-12, krevní vzorky pro rutinní laboratorní vyšetření a hodnoty NT-proBNP v séru; při vstupu do studie a po 12 týdnech bylo provedeno klasické echokardiografické vyšetření a vyšetření metodou dvourozměrného „speckle tracking“ (2D-speckle tracking); rovněž se zaznamenávaly nežádoucí příhody včetně úmrtí z kardiovaskulárních příčin, převozu na oddělení urgentního příjmu (ER) a hospitalizace po 12 týdnech.

Výsledky: Pacienti byli náhodně zařazováni do skupiny s cvičením ($n = 60$) nebo do kontrolní skupiny ($n = 47$). V obou skupinách převažovali muži, 58 % účastníků ve skupině s cvičením a 68 % účastníků v kontrolní skupině mělo ischemickou etiologii.

Při celkové adherenci k programu pohybového tréninku 83,7 % absolvovalo 58 účastníků (96,7 %) kontinuální pohybový trénink, zatímco ostatní účastníci absolvovali vysoce intenzivní intervalový trénink.

Náš výzkum prokázal, že u skupiny s cvičením se statisticky významně zvýšila funkční kapacita v podobě prodloužené vzdálenosti v testu 6MWT (420 vs 260 m; $p \leq 0,001$) a VO_{2max} (16,8 vs 14,7 ml/kg/min; $p \leq 0,001$); navíc bylo v dotazníku KCCQ-12 zaznamenáno zlepšení kvality života o 8 bodů v srovnání s kontrolní skupinou ($p \leq 0,001$).

U skupiny s cvičením bylo ve srovnání s kontrolní skupinou pozorováno i statisticky významné zlepšení u globální longitudinální deformace ($-12,5$ vs. $-9,7$ %; $p = 0,005$) a ejekční frakce (37,8 vs. 33,1 %; $p = 0,04$).

Během sledování byl nalezen statisticky nevýznamný rozdíl v hodnotách NT-proBNP mezi oběma skupinami. Ve skupině s cvičením bylo hospitalizováno méně pacientů než v kontrolní skupině; tento rozdíl byl statisticky významný ($p = 0,045$). Incidence ostatních příhod byla v obou skupinách srovnatelná.

U skupiny s cvičením bylo v hodnotách 6MWT, VO_{2max} ($p \leq 0,001$), NT-proBNP ($p = 0,05$), snížené srdeční frekvence ($p = 0,005$), snížené ejekční frakce LK na konci diastoly ($p = 0,007$), sníženého objemu na konci systoly ($p \leq 0,001$) a zlepšené ejekční frakce ($p \leq 0,001$) zaznamenáno statisticky významné zlepšení při srovnání vstupních hodnot a hodnot na konci sledování.

Závěry: Pravidelně cvičící účastníci s chronickým srdečním selháním uvedli zlepšení ejekční frakce, zvýšení kvality života a funkční kapacity a nižší incidenci nežádoucích příhod včetně počtu hospitalizací.

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ABSTRACT

Background: About 1% to 2% of adults suffer from heart failure (HF), a complex syndrome with significant clinical and public health issues. Exercise training for heart failure seeks to enhance patients' physical fitness and quality of life while simultaneously diminishing the likelihood of hospitalizations and mortality. Poor heart failure patient participation was apparent despite strong guidelines for cardiac rehabilitation.

Objectives: For evaluating how a brief, structured exercise training program impacts those suffering from compensated chronic heart failure in terms of improving clinical, laboratory, and echocardiographic parameters.

Methods: 107 medically stable outpatients with chronic heart failure (HFREF and HFmrEF) participated in a randomized control trial. Participants were allocated to either the exercise or control groups between May 2022 and June 2023.

Intervention: usual care plus aerobic exercise training for 12 weeks.

6MWT, KCCQ-12, blood samples for routine labs and serum NT-proBNP were collected and conventional echocardiography and 2D-speckle tracking studies were done at baseline and after 12 weeks, the adverse events after 12 weeks were recorded including cardiovascular death, ER visits and hospitalization.

Results: Exercise group (n = 60) and control group (n = 47) were allocated at random to the patients.

Both groups were dominated by males, and 58% of the exercise group and 68% of the control group had ischemic etiology. With the overall adherence to the exercise training program being 83.7%, the 58 exercise group patients (96.7%) underwent continuous exercise training while the rest underwent high intensity interval training.

Our research revealed that the exercise group significantly improved their functional capacity by increasing their 6MWT distance (420 vs 260 m, $p \leq 0.001$) and VO_{2max} (16.8 vs 14.7 ml/kg/min, $p \leq 0.001$), additionally their quality of life by 8 points on the KCCQ-12 when compared to the control group ($p \leq 0.001$).

The exercise group's global longitudinal strain (-12.5 vs. -9.7%, $p = 0.005$) and ejection fraction (37.8 vs. 33.1%, $p = 0.04$) both significantly improved when in comparison to the control group.

At the follow-up, there was insignificant difference in the NT-proBNP between the two groups.

The exercise group experienced fewer hospitalized patients than the control group, which was statistically significant ($p = 0.045$). Other adverse events were comparable in both groups.

6MWT, VO_{2max} ($p \leq 0.001$), NT-proBNP levels ($p = 0.05$), decreased heart rate ($p = 0.005$), decreased LV end-diastolic ($p = 0.007$), end-systolic volumes ($p \leq 0.001$), and improved ejection fraction ($p \leq 0.001$) were all significantly improved when comparing baseline and follow-up data of the exercise group.

Conclusions: Regular exercisers with chronic heart failure report improving ejection fraction, quality of life, functional capacity, and fewer adverse events, encompassing hospitalization as well.

Keywords:

Exercise training

Heart failure

6MWT

Background

Heart failure (HF) is a complex clinical syndrome with several signs and comorbidities,¹ continues to be a significant health problem that impacts 1% to 2% of humans.² Due to a population that is increasing in age, the prevalence of heart failure continues to increase,³ decreasing the quality of life⁴ and raising the financial strain on the public healthcare system and patients.⁵

Over the past three decades, cardiac rehabilitation has transformed from a sole emphasis on exercise training to a comprehensive, multidisciplinary approach. It now encompasses patient evaluation, education, risk factor management comprising dietary guidance and lifestyle changes – smoking cessation support, psychological care, and strategies to address adherence challenges.^{6,7}

Improving a patient's capacity for physical activity and overall health-related well-being, as well as enhancing the effects of medications and devices in lowering the risk of death and hospital stay, are the main goals of exercise training for heart failure.⁶⁻⁸

Cardiac rehabilitation aims to help patients reach goals for controlling coexisting conditions, such as psychological disorders, musculoskeletal limitations, and sleep apnea; adhere to guidelines for medical therapies; and achieve cardiovascular health and guidelines for controlling blood pressure, lipids, weight, blood glucose, and tobacco exposure.⁹

In the last ten years, evidence from numerous meta-analyses has highlighted the advantages of exercise training for heart failure, comprising a relative reduction in hospitalizations for both heart failure, all cause cardiovascular events and better health-related quality of life outcomes.^{10,11}

Findings from research employing safe exercise regimens support the idea that heart failure patients can benefit from activity-based rehabilitation. The studies encompassed in the systematic review and meta-analyses reported no significant adverse effects linked to exercise training.¹⁰⁻¹²

Despite strong recommendations in the ESC¹ 2021 and AHA¹³ 2022 heart failure guidelines for cardiac rehabilitation. There was a clear lack of involvement from heart failure patients, which has been linked to several important contributing factors involving patients, healthcare providers, and systemic problems.⁶

This study's objective is assessing how a brief, structured exercise training program can enhance clinical, laboratory, and echocardiographic parameters in patients with compensated chronic heart failure.

Methods**Study design and patients' selection**

This was a randomized controlled interventional study which included 107 patients presented with chronic sta-

ble heart failure (NYHA I–III) to Kasr Al Ainy specialized heart failure clinic in the period from May 2022 to June 2023

Inclusion criteria

Patients with compensated heart failure who had a reduced or mildly reduced ejection fraction (EF <50%) were recruited for the study.

Exclusion criteria

Exclusion criteria comprised recent acute coronary syndrome patients, untreated life-threatening cardiac arrhythmias, atrial fibrillation, significant primary valvular abnormalities, patients with prosthetic valves, high degree atrioventricular block, pregnancy, acute myocarditis and/or pericarditis, severe hypertrophic obstructive cardiomyopathy with the resting or provoked LVOT gradient >50 mmHg, intracardiac thrombi, history of significant myocardial ischemia or arrhythmia during low-intensity exercise, acute systemic illness or fever, cerebrovascular or musculoskeletal disease preventing exercise testing or training, severe chronic obstructive pulmonary disease, poor echocardiographic window 'low patients' adherence in the exercise group (defined as non-adherent <20% and partially adherent patients [20–80%]) and consent refusal.

Ethical committee approval

On August 4, 2022, the Cairo University Faculty of Medicine's local ethics committee approved the study protocol, which was assigned the code MD-214-2022.

Patients' consent

All patients signed an informed consent after explaining the study protocol and they approved on publication of study results.

Randomization

Heart failure patients were randomized through asking them to choose a number; either 1 or 2, where 1 was assigned to the exercise group and 2 was assigned to the control group. All patients were on optimal treatment for heart failure including diuretics, maximally tolerated doses of RAAS blockers (angiotensin receptor/neprilysin inhibitor [ARNI], angiotensin receptor blockers [ARBs], angiotensin-converting enzyme [ACE] inhibitors, mineralocorticoid receptor antagonist [MRA], sodium-glucose cotransporter-2 [SGLT2] and beta-blockers [BB]) in accordance with the latest recommendations of the European Society of Cardiology guidelines for HF treatment.¹

Baseline assessment

■ Clinical assessment and ECG

Detailed history was taken including heart failure aetiology and cardiovascular risk factors. Thorough physical examination was performed including assessment of heart failure signs, blood pressure, heart rate and weight measurement.

■ Electrocardiogram (ECG)

A twelve lead ECG was performed to detect any form of arrhythmias and to assess ECG waves morphology and durations.

■ Echocardiography

The American Society of Echocardiography's (ASE) guidelines for adult cardiac chamber quantification were followed in all measurements.^{14,15}

The following were detected utilizing two-dimensional, M mode, and Doppler techniques: left ventricular (LV) internal dimensions and ejection fraction using the biplane Simpson's method; left atrial diameter; tricuspid annular plane systolic excursion (TAPSE); tissue Doppler-derived right ventricular systolic excursion velocity S' ; estimated pulmonary artery systolic pressure (EPASP); and left ventricular diastolic function (mitral inflow E and A-wave velocities, and e' using TDI at the lateral and medial mitral annuli. The average E/e ratio was computed automatically.

■ Echocardiography with speckle tracking

Acquiring images: To ensure that the endocardial border could be seen clearly and without foreshortening, three typical apical images were carefully taken. The frame rate was set above 60 frames per second by appropriately adjusting the gain, depth, and sector width.

Analysis of images: Clips of four cardiac cycles of the apical four chamber view, apical two chamber view, and apical three chamber view were recorded and examined either offline or during the study using the Cardiac Motion Quantification (CMQ) tool on the Q lab10 program (Philips' ultrasonography). First, the end-systole was defined using the aortic valve closure (AVC) in the apical three-chamber view. Three locations at the end diastolic frame were identified then to determine the region of interest (ROI): two mitral annular points low and within the myocardium at the level of mitral valve insertion, and one apical point at the endocardial border of the apex.

The program automatically tracked the internal (endocardial) and external (epicardial) borders during the heart cycle. The operator manually modified the tracking to ensure high-quality tracking. The longitudinal deformation characteristics were automatically converted into graphical and numerical displays for each segment from each view. The same procedure was applied to the apical 4-chamber and apical 2-chamber views using the same sequence. The average strain from the three apical images was automatically used to compute the LV global longitudinal strain (GLS).

■ Venous blood sampling

NT-proBNP plasma level was tested on presentation using standard venepuncture techniques. Prior to centrifugation, the collected material was left to coagulate for 30 minutes. Blood serum was then isolated and stored at -70°C until analysis. Serum levels of NT-proBNP were measured using the enzyme-linked immunoassay (ELISA) technique.

■ Six-minute walk test

Participants received instructions to walk as far as they could in six minutes on a 30-meter course, receiving standardized encouragement and rest periods as needed. The maximum heart rate attained and the total distance walked in six minutes while at rest were recorded.

■ Quality of life questionnaires

Utilizing the Kansas City Cardiomyopathy Questionnaire, quality of life was assessed.¹⁶

■ Exercise training program

Exercise group were subjected to pre-planned exercise program, which consisted of supervised sessions in hospital (the exercise training was held at the Cardiology department of the tertiary care center) and home-based sessions, where patients performed exercise at home.

Endurance aerobic exercise training in the form of treadmill exercise (continuous or interval training) was used for supervised session 2 to 3 times a week for a minimum of 12 sessions with full compliance to transform to a home based one and a total of 36 sessions for a fully supervised program. While for home-based sessions; patients were advised to do certain exercises as marching on the spot, sit to stand and shadow boxing⁽¹⁾. Patients were given a booklet with illustrated figures of exercises after explanation of the exercises in the clinic during the supervised sessions and they were given a logbook for writing the number and duration of sessions.

Intervals of training in order to enable the patient to engage in extended training sessions, continuous training is often carried out at moderate exercise intensities under steady-state aerobic energy yield circumstances. Starting low and moving slowly is recommended for patients who are more deconditioned (i.e. at low intensity for 5–10 min twice a week). At low or no workload, the patient is instructed to alternate short (10–30 s) bursts of moderate–high intensity (50–100% peak exercise capacity) activity with a prolonged rest (80–60 s) phase. If well tolerated, the time of each training session is raised initially, and then the number of sessions per day.

Each exercise training was preceded by a warmup period and was followed by a cool down period each lasted for 5-minutes.

By calculating the heart rate ratio method and taking a percentage of the maximum oxygen consumption (VO_{2max}), which was measured during the 6MWT, the intensity of exercise training was established $\{12.1(HR_{max} \div HR_{resting})\}$.¹⁸

Patients were transitioned from a medically supervised program to a home based one, after at least four weeks of supervised sessions.

Patients were followed by intermittent supervised sessions at least once per week and by regular phone calls once weekly to enhance compliance and to inform them about the next supervised session timing.

■ Follow-up at the end of the study

After 3 months of enrollment, both groups were called back for follow-up clinical data, 6MWT, NT pro BNP, echocardiography and KCCQ-12.

Clinical events

Clinical events included hospitalization (defined as clinical decompensation of previously stabilized HF judged to indicate intravenous HF therapies), cardiovascular death, and emergency room visits (defined as a constellation of signs, symptoms, diagnostic testing, and HF-directed therapy).

Primary outcomes

Change in six-minute walk test, NT pro-BNP levels, LV global longitudinal strain and clinical follow-up including blood pressure and heart rate after successful rehabilitation period.

Secondary outcomes

- Change in the quality of life (using KCCQ-12) after successful rehabilitation.
- Hospitalization and mortality within the study period.
- Compliance to scheduled visits and to anti-failure drugs.
- Need for muscle relaxants during the study period.

Statistical analysis

Statistical analysis was executed utilizing SPSS 26 edition. Quantitative variables were expressed as mean and standard deviation. Comparing means among groups was estimated utilizing independent samples Student t-test whereas comparison between means at baseline and after rehabilitation was done utilizing paired samples Student t-test. Qualitative variables were presented as frequency and percentages. Chi square/Fischer Exact test was used for comparing qualitative variables in the 2 study groups. Analysis was carried out to estimate the predictability of GLS, EF, KCCQ-12 and 6-minute walking distance for improvement. A p -value <0.05 was deemed significant.

Results

The 107 heart failure patients in the study were split into two groups: the exercise training group ($n = 60$) and the control group ($n = 47$) (Fig. 1).

Baseline clinical and echocardiographic data

The baseline demographic data showed male predominance in both groups with older age in the control group. The heart failure duration was longer in the control group, ischemic cardiomyopathy was comparable in both groups, and PCI was the most common procedure in both groups (Table 1).

Patients allocated to the exercise group walked a statistically greater baseline distance than those in the control group. Even so, as listed in Table 1, there were insignificant differences across the two groups in the KCCQ-12 questionnaire, resting or maximum heart rate attained during the test, or VO_{2max} .

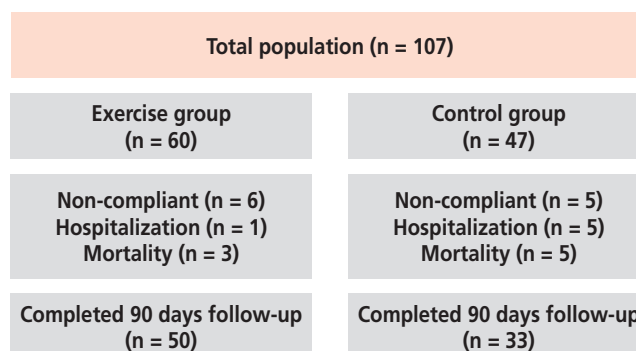


Fig. 1 – Flow diagram showing inclusion of patients

Table 1 – Baseline clinical and laboratory assessment

	Exercise group N = 60	Control group N = 47	p-value
	No. (%)	No. (%)	
Age, years (mean $\pm$ SD)	50.8 $\pm$ 10.5	57.0 $\pm$ 11.0	0.003
Sex, male	52 (86.5)	38 (81)	0.414
Diabetes	20 (33.3)	22 (47)	0.157
Hypertension	16 (26.5)	19 (40.5)	0.132
Smoking	29(48)	25 (53)	0.618
Dyslipidaemia	1 (1.7)	4 (8.5)	0.096
Coronary artery disease	34 (56.5)	32 (68)	0.228
DCM	25 (41.7)	15 (32)	0.301
ICM	35 (58.3)	32 (68)	0.30
LBbB morphology	9 (15)	7 (15)	0.605
PCI	29 (48.3)	29 (61.7)	0.168
CABG	2 (3.3)	0 (0)	0.206
	Mean $\pm$ SD	Mean $\pm$ SD	
Systolic BP	112 $\pm$ 20	113.5 $\pm$ 18.5	0.70
Diastolic BP	71 $\pm$ 12.5	70.4 $\pm$ 11.4	0.79
Heart rate	80.5 $\pm$ 15.5	82.7 $\pm$ 13.2	0.426
Weight (kg)	79.7 $\pm$ 15.2	78.3 $\pm$ 13	0.62
6MWT			
Distance (m)	304 $\pm$ 75.0	265 $\pm$ 40.0	0.001
Resting heart rate	82.1 $\pm$ 15.9	82.3 $\pm$ 13.5	0.957
Max. heart rate	100.8 $\pm$ 18	100 $\pm$ 16	0.840
SO ₂ (%)	97.2 $\pm$ 1.5	96.8 $\pm$ 1.2	0.126
Rests (N, %)	31(51.7)	33 (70)	0.134
VO _{2max} (ml/kg/min)	15 $\pm$ 1.6	14.7 $\pm$ 1.5	0.380
KCCQ-12 score	55 $\pm$ 10.5	52.5 $\pm$ 8.0	0.166
NT Pro-BNP (pg/ml)	5574.9 $\pm$ 5468.6	3880.7 $\pm$ 4485.5	0.091

CABG – coronary artery bypass graft; DCM – dilated cardiomyopathy; ICM – ischemic cardiomyopathy; KCCQ-12 – Kansas City Cardiomyopathy Questionnaire; NT-proBNP – N-terminal pro-B-type natriuretic peptide; PCI – percutaneous coronary intervention, SO₂ – oxygen saturation, VO_{2max} – maximal oxygen consumption; 6MWT – six-minute walk test.

Both groups showed comparable baseline echocardiographic results except for the GLS which was better in patients assigned to the exercise group (Table 2).

Exercise training

Among the exercise group 58 patients (96.7%) underwent continuous exercise training while the rest underwent high intensity interval training.

Regarding the frequency of the exercise 66.7% of the exercise group with lower functional capacity trained two times per week while the rest trained three times per week as shown in Table 3.

The starting exercise duration was 7 minutes with a workload of 10.5 watts with a maximum exercise duration reaching 16.6 minutes with a maximum workload of 51.5 watts.

The adherence to the exercise training program was 83.7%.

Follow-up clinical and echocardiographic data

Clinical data, comprising blood pressure, heart rate, and weight, did not significantly vary between the two groups at the follow-up. Nevertheless, the exercise group's 6MWT was significantly longer than the control groups, with fewer rests during the test and a higher VO_{2max}, as indicated in Table 4.

Regarding the symptoms we used the KCCQ-12 as that contains four subdomains: Physical limitation, Symptom frequency, Quality of life, and Social limitations which include fatigue, shortness of breath and edema as a marker for symptom improvement and it shows a significant improvement in these symptoms in the exercise group compared to the control one.

Also, we can see that quality-of-life parameters 'feelings of being disabled and self-assessment of general well-being' were positively affected by the exercise training.

Moreover, the follow-up NT-proBNP results indicated insignificant differences.

Table 2 – Baseline echocardiographic data

	Exercise group	Control group	p-value
	Mean $\pm$ SD	Mean $\pm$ SD	
LVEDD (mm)	56.5 $\pm$ 8.0	56 $\pm$ 7.0	0.678
LVESD (mm)	47.6 $\pm$ 9.0	46 $\pm$ 7.4	0.293
EDV (ml)	174.6 $\pm$ 52.3	170.6 $\pm$ 44.8	0.677
ESV (ml)	117.2 $\pm$ 48.5	115.4 $\pm$ 39.3	0.829
Ejection fraction (%)	34.2 $\pm$ 9.0	32.5 $\pm$ 8.6	0.331
E/A ratio	1.6 $\pm$ 1.0	1.5 $\pm$ 1.0	0.706
E/e' medial	15.1 $\pm$ 6.5	14.5 $\pm$ 6.7	0.591
E/e' lateral	10.0 $\pm$ 4.0	10.2 $\pm$ 4.5	0.836
E/e'	12.55 $\pm$ 5.2	12.35 $\pm$ 5.6	0.71
TAPSE (mm)	18.4 $\pm$ 4.4	16.8 $\pm$ 4.2	0.068
S-wave velocity of tricuspid annulus (cm/s)	11.1 $\pm$ 2.6	10.1 $\pm$ 2.8	0.078
EPASP (mmHg)	29 $\pm$ 15	32 $\pm$ 16	0.332
Moderate mitral regurgitation (No. %)	12 (20)	15 (31.9)	0.226
Severe mitral regurgitation (No. %)	8 (13.3)	5 (10.6)	
GLS (%)	-11.2 $\pm$ 3.8	-9.4 $\pm$ 4.0	0.017

EDV – end-diastolic volume; EPASP – estimated pulmonary artery systolic pressure; ESV – end-systolic volume; GLS – global longitudinal strain; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end systolic diameter; TAPSE – tricuspid annular plane systolic excursion.

Table 3 – Details of exercise training program

Exercise training	Exercise group N = 60
	No. (%)
Type	
Continuous training	58 (96.7)
High intensity interval training	2 (3.3)
Frequency	
Twice/week	40 (66.7)
Three times/week	20 (33.3)
Duration	
Starting duration (mins)	7.0 $\pm$ 2.4
Maximum duration (mins)	16.5 $\pm$ 4.3
Workload	
Starting workload (watts)	10.5 $\pm$ 1.1
Maximum workload (watts)	51.5 $\pm$ 33.9
Adherence (%)	83.7 $\pm$ 12.2

At the follow-up, the exercise group's global longitudinal strain and ejection fraction were greater than those of the control group (Table 5).

Clinical events

The exercise group had a decreased rate of hospitalization compared to control group (n = 1, 1.7% vs n = 5, 10.6%, $p = 0.045$). Also, the exercise group had a nume-

rically decreased rate of mortality and ER visits as compared to control group as shown in Table 6.

The exercise group had lower rate of hospitalization (n = 1, 1.7% vs n = 5, 10.6%, $p = 0.045$).

The only hospitalized patient in the exercise group was a fifty-seven-year-old male with ICM with acute decompensated heart failure after 8 weeks of exercise training. This patient was non-compliant to his medications for a week prior to hospitalization, and he stopped his exercise training after being discharged.

Whereas the hospitalized participants in the control group all were admitted with acute decompensation; one of them the precipitating factor was cellulitis and was admitted at the Cardiology ward after three follow-up visits over six weeks. In another patient the precipitating factor was chest infection and was enrolled to the CCU after 4 follow-up visits over 2 months.

Of the three patients that remained, two got admitted to the hospital with acute decompensated HF mainly with manifestations of right-sided heart failure at the Cardiology ward after 4 and 6 weeks of follow-up respectively, while the last patient was admitted with biventricular failure after 2 follow-up visits over 1 month.

Moreover, the exercise group had lesser rate of mortality and ER visits as opposed to the control group but none of them were significant.

Regarding the mortality in the exercise group the first patient was a fifty-three-year-old male patient with DCM who was admitted to the CCU with cardiogenic shock that was irreversible despite inotropic support and vasopressors and arrested after 2 days from admission. He was on his 9th week of the exercise training program, and he was compliant on it and was on loop diuretics, ACE-I, BB and MRAs and

Table 4 – Follow-up clinical, 6MWT, KCCQ-12 and laboratory data

	Exercise group	Control group	<i>p</i> -value
	Mean ± SD	Mean ± SD	
Systolic BP (mmHg)	116.4 ± 18.4	116.8 ± 22.8	0.928
Diastolic BP (mmHg)	71.9 ± 12	72.8 ± 12	0.751
Heart rate	73.5 ± 12.9	79.2 ± 14.3	0.061
Weight (Kg)	77.6 ± 15	79.1 ± 12.6	0.650
6MWT			
Distance (m)	420.4 ± 102	260 ± 55.8	≤0.001
Resting heart rate	73.4 ± 12.8	79.2 ± 14.3	0.06
Max heart rate	101.2 ± 18.2	96.1 ± 17	0.211
Rests	5 (8.3)	15 (32)	≤0.001
VO _{2max} (ml/kg/min)	16.8 ± 2.4	14.7 ± 1.3	≤0.001
KCCQ-12 score	61.7 ± 10.1	53.1 ± 8.3	≤0.001
NT-proBNP (pg/ml)	4330 ± 4418.7	4156 ± 6348.4	0.883

KCCQ-12– Kansas City Cardiomyopathy Questionnaire; NT-proBNP – N-terminal pro-B-type natriuretic peptide; VO_{2max} – maximal oxygen consumption; 6MWT – six-minute walk test.

Table 5 – Follow-up echocardiography

	Exercise group	Control group	<i>p</i> -value
	Mean ± SD	Mean ± SD	
LVEDD (mm)	54.1 ± 7.4	55.1 ± 7.2	0.596
LVESD (mm)	43.4 ± 8.8	44.6 ± 7.7	0.540
EDV (ml)	162 ± 58	164.6 ± 44.9	0.847
ESV (ml)	102.4 ± 50	111.1 ± 37.5	0.417
Ejection fraction (%)	37.8 ± 10	33.1 ± 9.0	0.040
E/A	1.4 ± 0.9	1.26 ± 0.62	0.417
E/E' medial	12.9 ± 6.5	14.4 ± 6.1	0.335
E/E' lateral	10.6 ± 15.5	9.8 ± 4.5	0.784
E/e'	11.75 ± 11.0	12.1 ± 5.3	0.559
TAPSE (mm)	19.5 ± 4.6	17.5 ± 4.3	0.057
S' velocity (cm/s)	11.7 ± 2.8	10.4 ± 2.6	0.057
EPASP (mmHg)	27 ± 15	34.5 ± 18.6	0.060
Moderate mitral regurgitation (N, %)	5	10	0.048
Severe mitral regurgitation (N, %)	7	3	
GLS (%)	−12.5 ± 4	−9.7 ± 4.2	0.005

EDV – end-diastolic volume; EPASP – estimated pulmonary artery systolic pressure; ESV – end-systolic volume; GLS – global longitudinal strain; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; TAPSE – tricuspid annular plane systolic excursion.

of LBBB morphology and had depression. The other patient was forty-five years old and entered the hospital with cardiogenic shock, and he had history of previous admission with cardiogenic shock 6 months prior to mortality. He was on his 4th week of the exercise training program.

Whereas the third patient was forty-five-year-old male patient presented with ICM, and it was because of sudden cardiac death after 3 weeks of the exercise training at home.

In the control group, two patients were admitted and died in other hospitals, the first one was a 60-year-old male who was admitted with acute decompensated heart failure precipitated by cellulitis and worsening of renal function (his baseline creatinine was 1.7 mg/dl) and was on loop and thiazide diuretics. He was not taking his beta-blockers due to borderline blood pressure. The second patient was a seventy-year-old female patient who entered the hospital with acute decompensated heart

Table 6 – Clinical events during the follow up period

	Exercise group N = 60	Control group N = 47	P value
	No. (%)	No. (%)	
Hospitalization	1 (1.7)	5 (10.6)	0.045
Emergency department visits	10 (16.7)	13 (27.7)	0.170
Mortality	3 (5)	5 (10.6)	0.271

Table 7 – Paired comparison in exercise and control group

	Exercise group Baseline	Exercise group Follow-up	p-value	Control group Baseline	Control group Follow-up	p-value
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
Systolic BP (mmHg)	114 ± 20.5	116.4 ± 18.4	0.312	113 ± 18.3	116.8 ± 22.7	0.235
Diastolic BP (mmHg)	71.7 ± 12.5	72 ± 11.9	0.871	70.6 ± 11.4	72.8 ± 12.0	0.263
Heart rate	79.5 ± 15.8	73.5 ± 12.6	0.005	81.2 ± 14.2	79.2 ± 14.2	0.334
Weight (Kg)	79.7±15.2	77.6 ± 15	0.035	79.0 ± 13.0	79.1 ± 12.6	0.883
6MWT						
Distance (m)	312 ± 75	420 ± 102	≤0.001	267.5 ± 40.4	260 ± 55.8	0.202
Resting heart rate	81.6 ± 16.6	73.5 ± 12.8	≤0.001	81.2 ± 14.2	79.2 ± 14.2	0.334
Max. heart rate	100.3 ± 19	101.3 ± 18.2	0.672	100 ± 15.8	96.2 ± 17.0	0.075
Rests	31 (51.7)	5.0 (8.3)				
VO _{2max} (ml/kg/min)	15.0 ± 1.6	16.8 ± 2.4	≤0.001	14.9 ± 1.6	14.7±1.3	0.239
KCCQ-12 score	55.4 ± 10.5	61.7 ± 10.1	≤0.001	54.2 ± 7.2	53.1 ± 8.3	0.039
NT pro-BNP (pg/ml)	6140.7 ± 6858.5	4330 ± 4418.7	0.054	3887.9 ± 3712.7	4156.0 ± 6348.4	0.835
LVEDD (mm)	55.96 ± 7.7	55.1 ± 7.2	0.007	55.3 ± 7.7	55.1 ± 7.4	0.757
LVESD (mm)	45.3 ± 8.1	44.6 ± 7.7	≤0.001	46.9 ± 8.7	43.4 ± 8.7	0.207
EDV (ml)	164.9 ± 42.8	162.1 ± 58	0.026	164.9 ± 42.8	164.6 ± 44.8	0.949
ESV (ml)	114.1 ± 49.4	102 ± 50.6	0.003	107.6 ± 33.5	111.1 ± 37.5	0.432
EF (%)	35.2 ± 9.1	37.8 ± 10	≤0.001	34.2 ± 8.3	33.1 ± 8.9	0.180
Left atrial diameter (mm)	40.6 ± 7.8	41.5 ± 5.1	0.264	43.4 ± 5.2	41.9 ± 8.8	0.286
E/A	1.5 ± 1.0	1.4 ± 0.9	0.351	1.3 ± 0.8	1.2 ± 0.6	0.534
E/E' medial	14.4±6.7	12.9±6.5	0.053	14.8 ± 7.4	14.4 ± 6.1	0.593
E/E' lateral	9.3±3.9	10.6±15.5	0.551	10.1 ± 4.6	9.8 ± 4.5	0.648
E/e'	11.85±5.3	11.75±11.0	0.302	12.45 ± 6.0	12.1 ± 5.30.6205	0.620
TAPSE (mm)	18.7±4.2	19.5±4.6	0.103	17.3 ± 4.1	17.4 ± 4.3	0.758
S' velocity (cm/s)	11.5±2.6	11.7±2.8	0.620	10.5 ± 2.7	10.4 ± 2.7	0.833
GLS (%)	-11.9±3.6	-12.5±3.9	0.052	-9.8 ± 3.8	-9.7 ± 4.1	0.892

EDV – end-diastolic volume; EPASP – estimated pulmonary artery systolic pressure; ESV – end-systolic volume; GLS – global longitudinal strain; KCCQ-12 – Kansas City Cardiomyopathy Questionnaire; LVEDD – left ventricular end-diastolic diameter; LVESD – left ventricular end-systolic diameter; NT-proBNP – N-terminal pro-B-type natriuretic peptide; TAPSE – tricuspid annular plane systolic excursion; VO_{2max} – maximal oxygen consumption; 6MWT – six-minute walk test.

failure while she was on full guideline directed medical therapy. She had a history of mastectomy 20 years ago with completed chemotherapy sessions.

Two other patients had sudden cardiac death at their homes after one month of follow-up while another one had sudden cardiac death at home after two months of follow-up.

The ER visits were all due to volume overload symptoms.

Paired comparison in exercise and control group

When comparing baseline to follow-up data of the exercise group there was significant enhancement in 6MWT, VO_{2max}, NT-proBNP levels, lower heart rate, reduction in

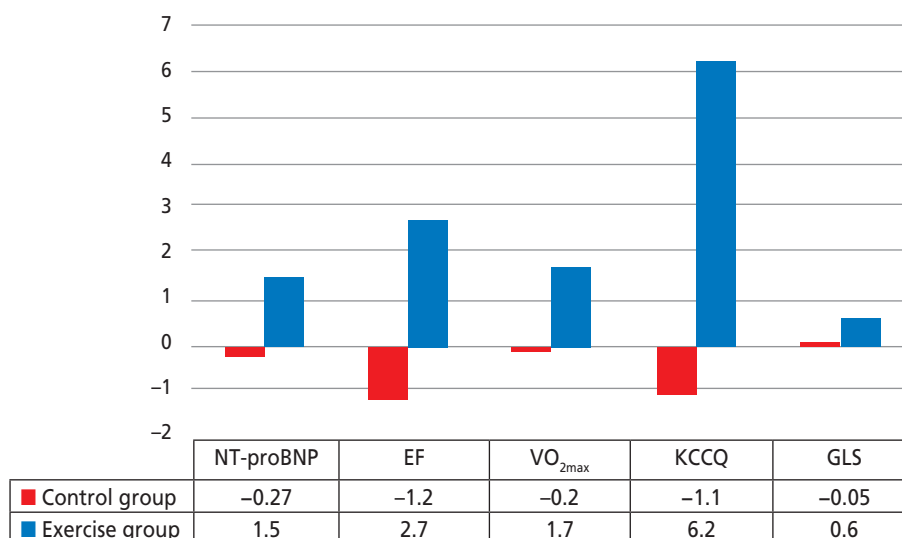


Fig. 2 – Differences between baseline and follow-up data in both groups.

LV end-diastolic and end-systolic volumes, and improvement of ejection fraction as shown in Table 7.

The exercise group indicated an enhancement in the distance walked during 6MWT (the distance was raised by a mean of 108 meters after 3 months), VO_{2max}, KCCQ-12 questionnaire score, ejection fraction and GLS.

Whereas the control group after three months of follow-up did not indicate any significant difference in the clinical and 6MWT data.

The patients showed lower score in KCCQ-12 at the follow-up which was statistically significant.

At follow-up, there was insignificant change in the NT pro-BNP level.

According to Table 7, the echocardiographic data revealed no significant variations in the global longitudinal strain, LV, or RV function.

Differences between baseline and follow-up data in both groups

The exercise group revealed an improvement in the distance walked during 6MWT (+108 meters), VO_{2 max}, KCCQ-12 questionnaire score ejection fraction and GLS that were all significant without a significant increase in the levels of NT pro BNP (Fig. 2).

Whereas the control group indicated a decline in the distance walked during 6MWT, VO_{2 max}, KCCQ-12 questionnaire score ejection fraction, GLS and NT-proBNP levels.

Discussion

About 1% to 2% of adults suffer from HF, a complicated syndrome that consists of several signs and comorbidities in addition to the cardinal symptoms.¹ HF is still a major public health issue.² As people age, the frequency of HF tends to rise,³ which lowers patients' quality of life⁴ and increases the financial burden on both individuals and the public health system.⁵

Even though evidence-based medication and device therapies have been successful in lowering mortality, length of stay and heart failure symptoms whereas also enhancing quality of life, many patients still suffer from dyspnea and fatigue, decreased exercise tolerance, a lower quality of life, repeated length of stay, and early mortality.^{6,7}

This randomized control study was designed for estimating the short-term consequences of exercise training in those suffering from compensated chronic HF during the period from May 2022 to June 2023.

The study encompassed 107 participants who were categorized into 2 groups:

- *Control group* which encompassed participants who received the standard care of a heart failure
- *Exercise training group* which encompassed patients who received the standard heart failure care in addition to a scheduled exercise program. Patients in both groups were followed up after 3 months for changes in symptoms, laboratory, and echocardiographic data.

In accordance with our study, the exercise group significantly improved their functional ability by increasing their 6MWT distance, VO_{2max}, and quality of life by 8 points on the KCCQ-12 in comparison with the control group.

Additionally, in comparison with the control group, the exercise group experienced a significant improvement in the ejection fraction and fewer hospitalizations.

6MWT, VO_{2max}, NT-proBNP levels, heart rate, LV volumes, and ejection fraction all significantly improved when comparing baseline and follow-up data for the exercise group.

Impact of exercise training on functional capacity

In our study the distance covered during the follow-up 6MWT by the exercise group was significantly longer than that of the control group that was in concordance with HF-ACTION trial¹⁹ that proved a great enhancement

in the 6-minute walk test distance ($P < 0.001$). Similarly, **ELVD-CHF** study,²⁰ **Jónsdóttir S et al.**²¹ and **Norman JF et al.**²² studies showed improvement in 6MWT with exercise.

Yet, **EXERT** study²³ showed no differences between the exercise and the control groups at either 3 m ($p = 0.36$) or 12 m ($p = 0.81$) follow-up.

The exercise group's greater 6MWT distance in comparison to the control group shows that the patients' exercise capacity has improved **Spertus et al.**²⁴ and **Ingle et al.**²⁵ who revealed that a rise of 55 and 54 meters, respectively, were linked to a significant enhancement in clinical status and quality of life of individuals with HF.

Moreover, 6MWD is also known to be a well-established independent predictor of clinical outcomes in HF, with increases in such magnitude associated with favourable reductions in nonfatal cardiovascular events, heart failure hospitalisations, and cardiovascular death.^{26,27}

In our study the exercise group showed an improvement in the VO_{2max} compared to the control group, the VO_{2max} was measured using heart rate equation method through the minimum and maximum heart rate during the 6MWT.

Most of the studies measure the VO_{2max} using cardiopulmonary exercise testing (CPET) but unfortunately it was not available at our institute.

Voutilainen A et al.²⁸ reported that 6MWT as a complement to spirometry to determine the 6MWT reliability in assessing maximum aerobic capacity comparing it with the VO_{2max} measured by the cardiopulmonary exercise test.

Our study was in concordance with **HF ACTION**, **CROSS-HF**²⁹ meta-analysis, **Edwards JJ et al.**³⁰ and **Gristina T et al.**³¹ which showed statistically significant increase in peak VO_{2max} in the exercise group compared to control group.

This showed the effect of improved exercise capacity with exercise training in patients with heart failure; improvement in functional capacity after exercise training seems related for the most part to peripheral adaptation.^{32,33}

Impact of exercise training on quality of life

Our study's follow-up quality of life assessment revealed that the exercise group outperformed the control group by 8 points on the KCCQ-12.

We decided to use KCCQ-12 that contains four subdomains: Physical limitation, Symptom frequency, Quality of life, and Social limitations.

Also, we can see that quality-of-life parameters 'feelings of being disabled and self-assessment of general well-being' were positively affected by the exercise training.

Our study was in concordance with **Belardinelli et al.**³⁴ who stated that only trained patients saw a significant enhancement in their quality-of-life questionnaire score after two months.

Also, **Dattilo G et al.**³⁵ demonstrated that anti-failure drugs as sacubitril/valsartan therapy improves significantly quality of life, physical effort resistance, BNP and NT-proBNP and NYHA functional class in patients with HFrEF.

Impact of exercise training on biomarkers

Our study's follow-up of NT-proBNP revealed insignificant differences between the two groups.

In concordance with **Ahmad T et al.**,³⁶ who assessed NT-proBNP at baseline and after three months later in a cohort of 928 subjects from the **HF-ACTION** trial¹⁹ and found that at three months, the NT-proBNP levels of the exercise training and usual care groups did not change statistically significantly ($p = 0.59$).

Moreover, **Nilsson BB et al.**,³⁷ **Arad et al.**³⁸ and **Prescott et al.**³⁹ indicated no significant change in the NT-proBNP levels in both groups.

On the other hand, **Pearson MJ et al.**⁴⁰ meta-analysis explained a statistically significant enhancement in NT-proBNP ($p = 0.006$).

Our explanation that the biomarker measurements were made after 3 months of structured exercise training, and there is a possibility that changes in levels might have been noted after a longer exercise period.

The use of biomarkers in clinical trials are made for many reasons as an establishment of inclusion criteria, explaining therapeutic efficacy and as a target for therapy and predict adverse outcomes.

Different biomarkers may provide further insight into the downstream molecular mechanisms associated with improvements from exercise training. It could be possible that different biomarker profiles respond differently to different intervention characteristics, such as intensity, perhaps allowing further tailoring of the exercise to the individual. Furthermore, biomarkers, with their prognostic utility, may provide useful postintervention information, indicating improvements when other favourable outcomes may be absent.

The follow-up NT-proBNP in our investigation revealed insignificant difference across both groups.

Impact of exercise training on echocardiographic parameters

Comparing the control group, the exercise group's global longitudinal strain and ejection fraction improved, according to our study's follow-up echocardiographic data. This is the first study that we are aware of those measures and evaluates changes in GLS in patients with heart failure who received exercise training.

Our study was in concordance with **ELVD-CHF** study,²⁰ **Mehani et al.**,⁴¹ and **Hambrecht et al.**⁴² which showed improvement of ejection fraction in the exercise group compared to the control group. Additionally, endurance training increased LVEF from 30 ± 8 to $35 \pm 9\%$ after 6 months of training, which is consistent with the **LEICA** trial,⁴³ which utilized both invasive and non-invasive assessments of LV systolic function and demonstrated that endurance training improved LVEF after 6 months of training from 30 ± 8 to $35 \pm 9\%$.

Edward JJ et al.³⁰ demonstrated the effect of exercise training in both HFrEF and HFpEF and showed that there is a significant improvement of exercise capacity and quality of life in both HFpEF and HFrEF patients. In HFpEF patients, ET significantly improved an important index of diastolic function, with significant improvements in LVEF and NT-proBNP/BNP seen in HFrEF patients only.

In contrast **EXERT** study²³ and **Dubach et al.**⁴⁴ showed no variation in the ejection fraction between the exercise and control groups.

We can explain the improvement of the ejection fraction in the exercise group due to decrease in LV diameters

which causes a reduction in the left ventricular volumes and hence improvement of ejection fraction

Also exercise training leads to a partial correction of peripheral endothelial dysfunction in patients with HF.^{45,46}

Given that vascular tone of peripheral arteries is component of afterload. So, it can be assumed that the reduction in cardiac size and improvement in LV performance is at least partially the result of an exercise training-induced decline in afterload.

Moreover, exercise training is known to enhance phosphorylation of the survival kinase AKT at serine 477, which is associated with an augmentation in cardiac contractility.^{47,48}

Also, **Correale M et al.**⁴⁹ demonstrated the anti-remodelling effects of anti-failure medications such as beta-blockers and angiotensin receptor neprilysin inhibitor which inhibit cardiac remodelling and improve echocardiographic parameters

Aşkın L et al.⁵⁰ showed the benefits of sacubitril/valsartan on patients with low ejection fraction regarding cardiac remodelling and improvement of cardiac function.

Impact of exercise training on clinical events

In our study the exercise group had a significantly lower hospitalization rate, and a non-significant lower rate of mortality and ER visits in comparison to the control group.

This was in concordance with **ExTraMATCH**,⁵¹ meta-analysis that revealed a significant drop in length of stay for the exercise group without a significant difference in mortality

In the HF-ACTION²⁰ trial, reductions in the primary endpoint of all-cause hospitalization or mortality were not statistically significant. Nonetheless, supplementary analyses that accounted for prognostic factors revealed a significant treatment impact for the primary endpoint and for reducing cardiovascular mortality and hospitalizations ($p = 0.03$).

Edwards JJ et al.,³⁰ **CROSS-HF**,⁵² and **EXERT** ⁽²³⁾ study which showed no significant difference in incidence of all-cause mortality, all-cause hospitalisation or all composite endpoints between the exercise and control groups.

Limitations

This is a single-centre study, with exercise training done only using a treadmill with no other equipment such as cycle ergometer or arm ergometer. VO_{2max} was measured utilizing the heart rate equation method not the cardiopulmonary exercise testing. They only utilized echocardiography for assessing the LV systolic function. Even so, as the gold standard magnetic resonance imaging can estimate the volumes and the ejection fraction more accurately, yet because of the extra cost and inconvenience to some patients, the test was not performed.

Conclusion

Regular exercise training in systolic heart failure patients is proven to be safe and was shown to be associated with improved in the 6MWT distance and the VO_{2max} .

Furthermore, exercise training is linked to improved GLS, ejection fraction, and quality of life in those who suffer from heart failure. Hospitalization rates were lower for patients who participated in the exercise program than for the control group, but other adverse events like mortality and emergency room visits were similar for both groups.

Conflict of interest

None.

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Ethics approval

On August 4, 2022, the Cairo University Faculty of Medicine's local ethics committee approved the study protocol, assigning it the code MD-214-2022.

Informed consent

Every participant in the study gave their informed consent.

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KV – kardiovaskulární; IM – infarkt myokardu; CMP – cévní mozková příhoda

Zkrácená informace o léčivém přípravku REPATHA

Název léčivého přípravku: Repatha 140 mg injekční roztok v předplněném peru. **Kvalitativní a kvantitativní složení:** Jedno předplněné pero obsahuje evolokumabum 140 mg v 1 ml roztoku. **Léková forma:** Injekční roztok (injekce) v předplněném peru (SureClick). **Terapeutické indikace:** Primární hypercholesterolemie (heterozygotní familiární a nefamiliární) nebo smíšená dyslipidemie u dospělých a heterozygotní familiární hypercholesterolemie u pediatrických pacientů ve věku 10 let a starších jako přídavek k dietě, a to: 1. v kombinaci se statinem nebo statinem a s dalšími hypolipidemiky u pacientů, u kterých není dosaženo cílových hladin LDL-C maximální tolerovanou dávkou statinu, nebo 2. v monoterapii nebo v kombinaci s dalšími hypolipidemiky u pacientů, kteří netolerují statin nebo u kterých je statin kontraindikován. **Homozygotní familiární hypercholesterolemie v kombinaci s dalšími hypolipidemiky u dospělých a pediatrických pacientů ve věku 10 let a starších:** Prokázané aterosklerotické kardiovaskulární onemocnění u dospělých ke snížení kardiovaskulárního rizika, a to 1. v kombinaci s maximální tolerovanou dávkou statinu s dalšími hypolipidemiky nebo bez nich, nebo 2. v monoterapii nebo v kombinaci s dalšími hypolipidemiky u pacientů, kteří netolerují statin nebo u kterých je statin kontraindikován. **Dávkování a způsob podání:** Podává se subkutánně do břicha, stehna nebo do horní oblasti paže. **Primární hypercholesterolemie a smíšená dyslipidemie (včetně heterozygotní familiární hypercholesterolemie) dospělí a pediatrické pacienti (ve věku 10 let a starší):** Prokázané aterosklerotické kardiovaskulární onemocnění u dospělých: Doporučená dávka je 140 mg 1x za dva týdny nebo 420 mg 1x měsíčně. Obě dávky jsou klinicky ekvivalentní. **Homozygotní familiární hypercholesterolemie u dospělých a pediatrických pacientů ve věku 10 let a starších:** Úvodní doporučená dávka je 420 mg 1x měsíčně. Pokud nebylo po 12 týdnech dosaženo klinicky významné odpovědi na léčbu, frekvenci dávek je možné zvýšit na 420 mg 1x za 2 týdny. Pacienti na aferze mohou zahájit léčbu dávkou 420 mg 1x za 2 týdny, aby toto schéma odpovídalo cyklu aferzy. **Kontraindikace:** Hypersenzitivita na léčivou látku nebo na kteroukoli pomocnou látku. **Zvláštní upozornění a opatření pro použití:** Sledovatelnost: Má se přehledně zaznamenat název podaného léčivého přípravku a číslo šarže. **Porucha funkce jater:** Pacienti s těžkou poruchou funkce jater (Child-Pugh C) nebyli studováni a evolokumab se má používat s opatrností. **Suchý přírodní kaučuk:** Kryt skleněné předplněné injekční stříkačky je vyroben ze suchého přírodního kaučuku (derivát latexu), který může vyvolávat závažné alergické reakce. **Interakce s jinými léčivými přípravky a jiné formy interakce:** Nebyly provedeny žádné studie interakcí. V klinických studiích byla hodnocena farmakokinetická interakce mezi statiny a evolokumabem. Při použití kombinace statinu a evolokumabu není nutná úprava dávky statinu. **Fertilita, těhotenství a kojení:** Údaje o podávání těhotným ženám jsou omezené nebo nejsou k dispozici. V těhotenství lze použít pouze tehdy, když klinický stav ženy vyžaduje léčbu evolokumabem. Není známo, zda se evolokumab vylučuje do lidského mateřského mléka. Riziko pro kojení novorozence/kojenice nelze vyloučit. Na základě posouzení prospěšnosti kojení pro dítě a prospěšnosti léčby pro matku je nutno rozhodnout, zda přerušit kojení nebo ukončit/přerušit podávání přípravku Repatha. Nejsou k dispozici žádné údaje o vlivu evolokumabu na fertilitu u člověka. **Nežádoucí účinky:** Nejčastěji hlášené nežádoucí účinky při podávání doporučených dávek jsou nasopharyngitida (7,4 %), infekce horních cest dýchacích (4,6 %), bolest zad (4,4 %), artralgie (3,9 %), chřipka (3,2 %) a reakce v místě vpichu injekce (2,2 %). **Zvláštní opatření pro uchování:** Uchovávejte v chladničce (2 °C – 8 °C). Chraňte před mrazem. Uchovávejte v původním obalu, aby byl přípravek chráněn před světlem. **Držitel rozhodnutí o registraci:** Amgen Europe B.V., Minervum 7061, 4817 ZK Breda, Nizozemsko. **Registrační číslo:** EU/1/15/1016/003. **Datum revize textu:** 30. března 2023.

Před předepsáním přípravku se, prosím, seznámte s úplným zněním Souhrnu údajů o přípravku. Výdej léčivého přípravku je vázán na lékařský předpis. Přípravek je hrazen z prostředků veřejného zdravotního pojištění v indikaci primární hypercholesterolemie nebo smíšené dyslipidemie u pacientů adherujících k dietním opatřením i ke stávající hypolipidemické léčbě v kombinaci s vysokou intenzivní hypolipidemickou terapií.

URČENO PRO ODBORNOU VĚŘEJNOST

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Association of insertion/deletion (I/D) polymorphism of angiotensin-converting enzyme gene (ACE) with ST segment elevation myocardial infarction and factors risk in Western Algeria: case-control study

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SOUHRN

Kontext: Kardiovaskulární onemocnění jsou celosvětově hlavní příčinou mortality. Akutní koronární syndrom (AKS) je multifaktoriální onemocnění, které je výsledkem interakce mezi environmentálními a genetickými faktory. Polymorfismus I/D genu pro ACE byl již zmíněn v souvislosti s rizikem rozvoje AKS. Cílem naší studie případů a kontrol byl zhodnotit zkoumat možnou souvislost mezi polymorfismem inserce/delece (I/D) genu pro angiotenzin konvertující enzym (ACE) a infarktem myokardu s elevací úseku ST (STEMI) ve vzorku pacientů ze západního Alžírsko.

Metody: Provedli jsme studii případů a kontrol zahrnující 169 jedinců, zdravých osob a 99 pacientů po STEMI. ACE I/D polymorfismus byl zjišťován metodou polymerázové řetězové reakce se specifickými primery.

Výsledky: Prevalence genotypů DD, ID a II v naší skupině pacientů byla 48,48 %, 43,43 % a 8,08 % ve srovnání s 2,85 %, resp. 35,75 % a 61,42 % v kontrolní skupině. Tyto výsledky prokázaly, že frekvence genotypu DD a alely D je statisticky významně vyšší v případech s AKS než u kontrol ($\chi^2 = 67,63$; $p = 0,0001$) ($p < 0,05$; OR = 9,03; 95% CI 5,41–15,01). Rovněž jsme nezjistili žádnou statisticky významnou souvislost mezi ACE I/D polymorfismem a tradičními rizikovými faktory spojenými se STEMI, jako jsou věk, pohlaví, diabetes, hypertenze a kouření.

Závěr: Závěrem lze konstatovat, že uvedené výsledky naznačují statisticky významnou souvislost mezi I/D polymorfismem genu pro ACE a rizikem rozvoje AKS ve zkoumaném vzorku.

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ABSTRACT

Background: Cardiovascular diseases are the leading cause of mortality worldwide. Acute coronary syndrome (ACS) is a multifactorial disease resulting from the interaction of environmental and genetic factors. The I/D polymorphism of the ACE gene has been associated with the risk of developing acute coronary syndrome (ACS). Our case-control study aimed to access the potential association of insertion/deletion (I/D) ACE (angiotensin converting enzyme) gene polymorphism and ST segment elevation myocardial infarction (STEMI) among a sample of Algerian patients from Western Algeria.

Methods: We conducted a case-control study comprising 169 individuals including 70 healthy subjects and 99 STEMI patients. ACE I/D polymorphism was detected by polymerase chain reaction with specific primers.

Results: The prevalence of DD, ID, and II genotypes in our patients group were 48.48%, 43.43%, and 8.08% respectively vs 2.85%, 35.75% and 61.42% in the control group. These results showed that the frequency of the DD genotype and the D allele was significantly higher in cases with ACS compared to controls ($\chi^2 = 67.63$; $P = 0.0001$) ($P < 0.05$, OR = 9.03, 95% CI: 5.41-15.01). We also noticed that there was no significant association between ACE I/D polymorphisms and STEMI-relevant traditional risk factors like age, gender, diabetes mellitus, hypertension, smoking.

Conclusion: In conclusion, these results suggest a statistically significant association between the I/D polymorphism of the ACE gene and the risk of developing ACS in the studied sample.

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Introduction

Acute myocardial infarction (AMI) remains a major cause of morbidity and mortality worldwide and in Algeria specifically.^{1,2} The ST segment elevation myocardial infarction (STEMI) is one of the most severe types of acute AMI. It primarily occurs due to the rupture of atherosclerotic plaques. The pathogenesis of MI involves a complex interplay between genetic and environmental factors with an estimated heritability ranging from 50 to 60%.¹ Among the genetic factors, the angiotensin-converting enzyme (ACE) gene has attracted considerable attention due to its role in the renin-angiotensin-aldosterone system (RAAS) and its involvement in cardiovascular diseases.

The renin-angiotensin-aldosterone system (RAAS) is a crucial regulator of blood pressure and exerts a significant influence on the development and progression of coronary artery disease (CAD). Serving as one of the primary regulatory systems in cardiovascular physiology, the RAAS plays a pivotal role in various aspects, including cardiovascular remodeling, maintenance of vascular tone, and sodium homeostasis.³

Different studies have suggested that polymorphisms occurring in the components of RAAS play a crucial role in the development and progression of coronary artery disease (CAD) in certain individuals.⁴ Among these components, the angiotensin-converting enzyme (ACE) has garnered significant attention, leading to frequent investigations into the potential association between ACE insertion/deletion (I/D) polymorphisms and cardiovascular disease like hypertension⁵ and CAD.^{6,7}

The ACE gene, located on chromosome 17q23, encodes the angiotensin-converting enzyme responsible for the conversion of angiotensin I to angiotensin II. This enzyme is also involved in the inactivation of bradykinin, a vasodilator peptide. The ACE gene contains a common insertion/deletion (I/D) polymorphism in intron 16, characterized by the presence or absence of a 287 base pair Alu repeat sequence. The D allele is associated with higher ACE activity and increased levels of angiotensin II, which promotes vasoconstriction, inflammation, oxidative stress, and vascular remodeling.⁸ Angiotensin II is also known to be an essential regulator of proliferation, migration, and hypertrophy of vascular smooth muscle cells, increasing thus its association with CAD and MI risk of occurrence.⁹

The association between the ACE I/D polymorphism and the risk of MI has been extensively investigated in various populations. Indeed, it was reported in many studies that the DD genotype is associated with various cardiovascular diseases, including myocardial infarction.^{10,11} However, results from other association studies between ACE I/D polymorphism and MI revealed conflicting results^{11,12,13} and did not consider the relationship between the ACE I/D polymorphism and MI.

Thus, we aim in this study to investigate the association between the ACE I/D polymorphism and the risk of MI in Algerian patients from the city of Oran.

Methods

Population study

We have enrolled a case-control study from 2021 until 2022 where we have included 169 Algerian subjects. All the implicated subjects have already given their written consent to participate in this study which was conducted according to the declaration of Helsinki Principles and approved by the local ethics committee.

The study covered all the files of patients hospitalized for ACS with ST segment elevation myocardial infarction (STEMI) at the Cardiology Service of the University Hospital Center of the Oran city. We included all patients of both sexes and of all ages in the study. We excluded all incomplete records or patients who presented with traumatic or non-ischemic chest pain from this study. Data is collected using pre-established forms. All patients had undergone an electrocardiogram (ECG), a cardiac ultrasound and a biological assessment (blood count, creatinine, glycemia, troponin, cholesterol, triglyceride, prothrombin level, activated partial thromboplastin time). The control group was selected from healthy blood donors.

Diagnosis of STEMI

The diagnosis of ACS was done according to the American College of Cardiology/ American Heart Association (ACC/AHA) definitions.^{14–16} We classified ACS patients according to the electrocardiographic results as having ST-segment elevations in the case of the presence of clinical symptoms of myocardial infarction lasting ≥ 30 min with ECG changes of either ST elevation of at least 0.1 mv in two contiguous precordial leads or two limb leads, or the presence of a new left bundle branch block (LBBB). Moreover, troponin I levels and the myocardial band (MB) fraction of total creatinine phosphokinase (CPK) were measured in order to confirm myocardial cell death. We excluded from this study all incomplete records or patients who presented with traumatic or non-ischemic chest pain.

Risk factors assessment

We used a standardized questionnaire to record data as socio-demographic characteristics. Risk factors of each patient were identified. The identification of dyslipidemia was based on whether patient is taking lipid lowering drugs or biochemically indicated by total cholesterol > 240 mg/dL, triglycerides > 150 mg/dL, low density lipoproteins (LDL) > 130 mg/dL and high-density lipoproteins (HDL) < 50 mg/dL, < 40 mg/dL for females and males respectively. Diabetes mellitus was defined as either the patient is under medication or presenting clinical symptoms and having plasma glucose concentration ≥ 200 mg/dL (11.1 mmol/L) or fasting blood sugar ≥ 126 mg/dL (7.0 mmol/L). Hypertension was also defined as having systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or being on antihypertensive treatment. Moreover, other risk factors like smoking and hormonal status for women were assessed.

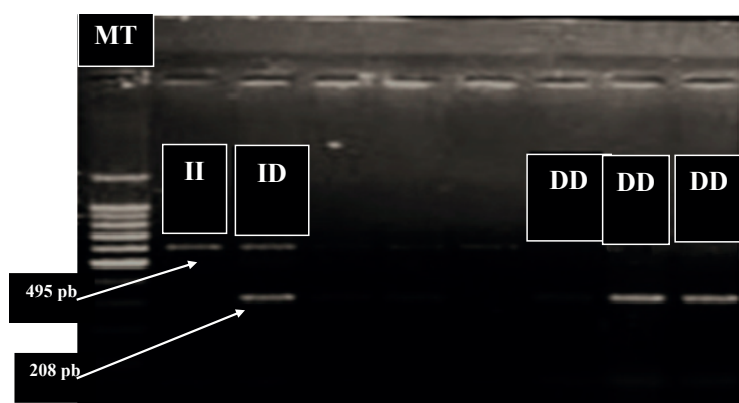


Fig. 1 – Representative gel picture of ACE I/D polymorphism in 2% agarose gel.

Genotyping methods

Genomic DNA was extracted using five milliliters of blood samples using Salting-out method as previously described by Miller et al.¹⁷ and quantified following spectrophotometric analysis. We used polymerase chain reaction (PCR) to genotype DNA samples for the I/D ACE polymorphism, as previously described Chou et al.¹⁸ using primers flanking the polymorphic region of intron 16 with the following primer sequences: 5' TGGAGACCACTCCCATCCTTCT-3' and 5'-CAGGTCTTCATATTTCCGATGTGG-3'. Reactions were carried out in 25- μ L volumes containing 50 ng of genomic DNA, 0,4 μ M of each primer, 200 mM dNTP, 1X Taq polymerase buffer and 1U Taq DNA polymerase (Wiragen, Algeria). The cycling conditions for I/D were set as follows: an initial denaturation at 94 °C for 4 minutes, 35 cycles at 94 °C for 30 seconds, 58 °C for 30 seconds, and 72 °C for 60 seconds, and a final extension at 72 °C for 10 minutes. Electrophoresis of the amplified products in 2% agarose gel allowed detection of a 495-base pair (bp) fragment (insertion) and a 208-bp fragment (deletion) (Fig. 1).

Statistical analysis

Data analysis was done with the help of an (SPSS Inc., Chicago, Illinois, USA) version 26.0. Clinical characteristics of all the subjects are expressed as means $\pm$ SD. Descriptive statistics were used to analyze all studied variables such as the socio-demographic characteristics, anthropometric measurements, biological parameters. A two-tailed Student's *t*-test was used to compare continuous variables

between the two groups. Allele frequencies were calculated from genotype frequencies and they were compared between the two groups using chi-squared (χ^2) statistics. Odds ratio (OR) were calculated to estimate the association between genotypes and MI risk with a confidence interval (CI) of 95%. Hardy-Weinberg's equilibrium was checked by a χ^2 test. *P*-value <0.05 was considered statistically significant.

Results

Allelic and genotypic distribution of I/D ACE gene polymorphism in cases and controls

Table 1 presents the distribution of alleles and genotypes of the ACE I/D polymorphism among cases and controls. Among cases, the frequencies of the ACE genotypes II, ID, and DD were 8.08%, 43.4%, and 48.4%, respectively. In contrast, the control group exhibited genotype frequencies of 61.42% for II, 35.71% for ID, and 2.85% for DD.

A statistically significant difference was observed in the genotype distribution between cases and controls ($\chi^2 = 67.63$, *p* = 0.0001).

Additionally, the frequency of the D allele was significantly higher among cases (70%) compared to controls (29%) (*p* < 0.05, OR = 9.03, 95% CI: 5.41–15.01). These findings suggest a strong association between the D allele and acute coronary syndrome.

Association between ACE genotypes and traditional risk factors

Age distribution

No significant association was identified between age categories and ACE genotypes (*p* = 0.847). The DD genotype was more prevalent in the oldest age group (>68 years, 58.33%), but the overall distribution of genotypes across age groups was balanced, indicating no clear relationship between ACE polymorphism and age in this cohort (Table 2).

Gender distribution

Gender differences did not significantly correlate with ACE genotypes (*p* = 0.546). Males were more represented in the ID (48.38%) and DD (41.93%) genotypes, whereas females were slightly more prevalent in the DD genotype

Table 1 – Allelic and genotypic distribution of I/D ACE polymorphism among cases and controls

Variables	Patients N (%) N = 99	Controls N (%) N = 70	χ^2	<i>p</i> -value	OR 95% CI
II	8 (8.08%)	43 (61.42%)	67.63	0.0001*	
ID	43 (43.43%)	25 (35.75%)			
DD	48 (48.48%)	02 (2.85%)			
I allele	59 (29.79%)	111 (79.28%)	80,34	0.0001*	9.08 (5.41–15.01)
D allele	139 (70.20%)	29 (20.71%)			

Table 2 – Traditional risk factors according to ACE genotypes distribution among STEMI cases

	STEMI cases (N = 99)			
	II n (%)	ID n (%)	DD n (%)	p-value
Age (years)				
<45	1 (4.54%)	10 (45.45%)	11 (50%)	0.847
46–56	1 (3.22%)	15 (48.38%)	15 (48.38%)	
57–67	4 (11.76%)	14 (41.17%)	16 (47.05%)	
>68	1 (8.33%)	4 (33.33%)	7 (58.33%)	
Gender				0.546
Male	3 (9.67%)	15 (48.38%)	13 (41.93%)	
Female	4 (5.88%)	28 (41.17%)	36 (52.94%)	
Hypertension				0.213
Yes	3 (4.54%)	27 (40.9%)	36 (54.54%)	
No	4 (12.12%)	16 (48.48%)	13 (39.39%)	
Diabetes				0.102
Yes	0 (0%)	18 (50%)	18 (50%)	
No	7 (11,11%)	25 (39.68%)	31 (49.2%)	
Dyslipidemia				0.03*
Yes	2 (4.44%)	26 (57.77%)	17 (37.77%)	
No	5 (9.25%)	17 (31.48%)	32 (59.25%)	
Smoking				0.317
Yes	3 (13.04%)	11 (47.82%)	9 (39.13%)	
No	4 (5.26%)	32 (42.1%)	40 (52.63%)	

(52.94%). These results suggest that gender does not significantly influence the distribution of ACE genotypes among STEMI patients.

Hypertension

Hypertension prevalence was highest in the DD genotype group (54.54%), followed by ID (40.90%) and II (4.54%). Despite this trend, no significant association was observed between hypertension and ACE genotypes ($p = 0.213$). This aligns with prior studies indicating a potential, but non-conclusive, link between the DD genotype and hypertension.

Diabetes mellitus

No significant association was detected between diabetes and ACE genotypes ($p = 0.102$). Notably, no diabetes cases were observed in the II genotype group (0%), whereas diabetes was evenly distributed among ID and DD genotypes (50% each). These findings may suggest population-specific variability regarding the impact of ACE polymorphism on diabetes risk.

Dyslipidemia

A statistically significant association was identified between dyslipidemia and ACE genotypes ($p = 0.03$). The ID genotype exhibited the highest prevalence of dyslipidemia (57.77%), followed by DD (37.77%) and II (4.44%). Conversely, non-dyslipidemic individuals were more likely to belong to the DD group (59.25%). These results suggest a potential role of the ID genotype in lipid metabolism disturbances and its contribution to STEMI development.

Smoking

No significant association was found between smoking status and ACE genotypes ($p = 0.317$). However, smokers were more prevalent in the II genotype group (13.04%) compared to the ID (47.82%) and DD (39.13%) genotypes. Non-smokers predominated across all genotypes, particularly in the DD group (52.63%). This suggests that ACE polymorphism does not significantly influence smoking behavior in this cohort.

Discussion

Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality worldwide, accounting for 31% of total global mortality.¹⁸ Coronary heart disease is a polygenic and multifactorial disease characterized by the formation of atherosclerotic plaque in the coronary vessels.³

Many studies reported the contribution of genetic variations in the pathogenesis of cardiac disorders including hypertension⁵ and myocardial infarction.⁶ Angiotensin I-converting enzyme (ACE) gene insertion/deletion (I/D) polymorphism, characterized by an insertion/deletion of a 287 bp nucleotide sequence at intron 16, has been extensively studied and several studies reported its eventual association with MI by modifying ACE activity and contributing to enhanced plaque vulnerability, ulceration and thrombosis.^{20–22} However, the contribution of ACE gene polymorphism as a risk factor of CAD remains controversial with conflicting results.^{22,23}

In our study, we found that the percentage of DD genotype was higher in cases compared to controls (OR

= 9, 03, 95% CI: 5.41–15.01) which was confirmed in different studies of African and Western populations.^{6,24–27} However, other Asian studies reported the lowest percentage of the DD genotype compared to the II and ID genotypes.^{28–31}

Similarly, Dai et al.³² reported in a case-control study that the ACE DD genotype is an independent risk factor for STEMI. This result was also confirmed in many studies of different populations.^{33,34} Furthermore, we noticed no significant association between conventional risk factors of CAD like advanced age, diabetes mellitus, hypertension, smoking, and *ACE* genotypes. Indeed, Moorthy et al.³⁵ did not find any association between these risk factors and *ACE* genotypes in an Indian cohort of 934 STEMI patients. Nevertheless, other studies reported a significant association between *ACE* genotypes and hypertension,^{5,36–38} diabetes mellitus and its complications.^{39–42} However, we have found a significant association between dyslipidemia and *ACE* genotypes in STEMI patients. This result has been already confirmed in many studies.³⁹

It should be noted that the increased risk of ACS in DD subjects could be the consequence of chronic coronary vasoconstriction or a predisposition to spasm linked to the action of *ACE* on the vasoactive peptides that it metabolizes. In the presence of coronary vasoconstriction, a myocardial infarction could occur in an atherosclerotic lesion of smaller size than in the absence of vasoconstriction.

These conflicting results underscore the intricate nature of association studies in complex diseases like acute coronary syndrome (ACS). Several factors have been proposed to explain these inconsistencies, such as differing selection criteria for control and disease groups, uncontrollable environmental influences within populations, variations in genetic and ethnic backgrounds, and age disparities among the subjects. Additionally, emerging evidence suggests that epigenetic mechanisms, particularly DNA methylation, may play a key role in the etiology of coronary artery disease (CAD). Alterations in DNA methylation patterns can affect gene expression, potentially contributing to the development of CAD by modulating pathways linked to inflammation, lipid metabolism, and vascular function.⁴³

Conclusion

The *ACE* DD genotype was observed to correlate with the severity of CAD compared to the II or ID genotypes in Algerian patients. This research marks the first study in Algeria exploring the association between a genetic polymorphism and coronary artery lesion severity, thus adding valuable insights to the role of *ACE* I/D polymorphism in AMI pathophysiology within Algerian populations. Consequently, considering *ACE* I/D status could enhance the comprehensive assessment and aggressive management of AMI patients.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical statement

The study was conducted in accordance with Helsinki declaration.

Informed consent

The patients signed the informed consent.

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Nefarmakologická léčba komorových tachykardií v komplexním kardiovaskulárním centru

(Non-Pharmacological Management of Ventricular Tachycardias in a Complex Cardiovascular Center)

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SOUHRN

Komorové arytmie se do značné míry podílejí na morbiditě a mortalitě pacientů se strukturálním onemocněním srdce. Implantace kardioverteru-defibrilátoru u těchto nemocných prokazatelně snižuje mortalitu, avšak nevede k prevenci dalších epizod arytmií. Donedávna představovalo základ léčby komorových arytmií podávání antiarytmik, která však mají omezenou účinnost a nezanedbatelné riziko nežádoucích účinků. Proto se do popředí dostávají další, nefarmakologické možnosti léčby komorových arytmií, a to především katetrizační ablace. Zlatým standardem je použití radiofrekvenční energie, jejíž účinnost lze modifikovat použitím různých druhů katétrů, proplachovacích roztoků či techniky ablace. Alternativou je použití kryoablace nebo energie pulsního pole, které se již plně etablovalo v léčbě fibrilace síní a představuje příslib také u pacientů s komorovými arytmiemi. Další možností je alkoholová ablace, která spočívá v aplikaci vysoce koncentrovaného etanolu do tepny nebo žíly drénující oblast předpokládaného arytmogenního substrátu. Neinvazivní alternativou, především při selhání předchozích možností, je stereotaktická radioterapie. Cílem přehledového článku je shrnout nefarmakologické možnosti léčby komorových tachykardií.

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ABSTRACT

Ventricular arrhythmias significantly influence morbidity and mortality in patients with structural heart disease. Implantable cardioverter-defibrillators positively affect survival but do not prevent ventricular arrhythmias. Until recently, the cornerstone of management of ventricular arrhythmias was administration of antiarrhythmic drugs, which have limited efficacy and non-negligible side effects. Nowadays, newer non-pharmacological treatment modalities have emerged, namely catheter ablation. Radiofrequency energy is considered the gold standard and its effect can be further augmented by using different types of catheters, alternative perfusion agents, or modified ablation techniques. Alternatively, cryoablation or pulse field ablation make a promise for the future as pulse field ablation has already become an established treatment strategy for managing atrial fibrillation. Additionally, alcohol ablation by administering concentrated ethanol into coronary arteries or veins subtending blood flow to the arrhythmogenic substrate may be used in a selected population. Newer non-invasive treatment method is stereotactic arrhythmia radiotherapy, especially for patients after catheter ablation failure. The aim of this review is to summarize up-to-date non-pharmacological treatment options for ventricular tachycardias.

Keywords:

Alcohol ablation

Catheter ablation

Cryoablation

Pulsed field ablation

Stereotactic arrhythmia radiotherapy

Ventricular tachycardia

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Úvod

Komorové tachykardie (KT) jsou definovány přítomností alespoň tří konsektivních stahů s frekvencí $> 100/\text{min}$, které pocházejí ze svaloviny komor nebo převodního systému pod úrovní Hisova svazku.¹ Můžeme je klasifikovat podle mnoha kritérií, avšak z prognostického hlediska je důležité rozlišovat idiopatické a KT při strukturálním onemocnění srdce. Samostatnou skupinu pak tvoří primární arytmiické syndromy, které jsou nejčastěji podmíněny genetickou mutací v některém z genů kódujících iontové kanály na membráně kardiomyocytů. Zatímco idiopatické KT jsou považovány za benigní, arytmie v přítomnosti strukturálního onemocnění srdce jsou častou příčinou morbidit a mortality. Náhlá srdeční smrt může být první klinickou manifestací srdečního onemocnění.² Zvláště závažným stavem je tzv. arytmiická bouře, která je definována jako tři a více epizod setrvalé hemodynamicky významné KT v průběhu 24 hodin, které odděluje alespoň pět minut a pro jejich ukončení je nutná intervence.³ V terapii KT hrají důležitou úlohu antiarytmika, nicméně s výjimkou betablokátorů žádné z nich neprokázalo mortalitní benefit, a navíc je jejich užívání spojeno se závažnými nežádoucími účinky.^{1,4} Další nedílnou a všeobecně uznávanou součástí léčby KT, která prokazatelně snižuje mortalitu, je implantace kardioverteru-defibrilátoru (ICD) v rámci primární a sekundární prevence náhlé srdeční smrti.^{5,6} Tyto přístroje dokáží potenciální KT sice přerušit, implantovaný ICD ale nebrání recidivám arytmií, což může vést k opakovaným výbojům ICD s nutností další léčby.⁷ Tato přehledová práce přibližuje současné možnosti terapie KT se zaměřením na intervenční léčbu.

Katetrizační ablace

Katetrizační ablace je v současnosti považována za nejefektivnější nefarmakologickou léčbu rekurentních KT.⁸ Její dlouhodobá úspěšnost se v závislosti na základním strukturálním onemocnění srdce pohybuje v rozmezí od 30 % do 70 %.^{9–12}

Tabulka 1 – Doporučení pro katetrizační ablací komorové tachykardie ve třídě I (upraveno podle guidelines European Society of Cardiology, 2022)¹

A, symptomatické idiopatické komorové tachykardie nebo komorové extrasystoly z výtokového traktu pravé komory nebo levostranných fasciкул
B, symptomatická raménková reentry komorová tachykardie
C, chronická ischemická choroba srdeční a rekurentní setrvalé monomorfnní komorové tachykardie nebo adekvátní výboje ICD při zavedené terapii amiodaronem
D, incesantní komorová tachykardie nebo elektrická bouře z důvodu setrvalé monomorfnní komorové tachykardie refrakterní na antiarytmickou terapii
E, setrvalé monomorfnní komorové tachykardie nebo rekurentní symptomatické adekvátní výboje ICD po korekci Fallotovy tetralogie

ICD – implantabilní kardioverter-defibrilátor.

Dle současných doporučení Evropské kardiologické společnosti je katetrizační ablace doporučena ve třídě I u vybrané skupiny pacientů (**tabulka 1**).¹

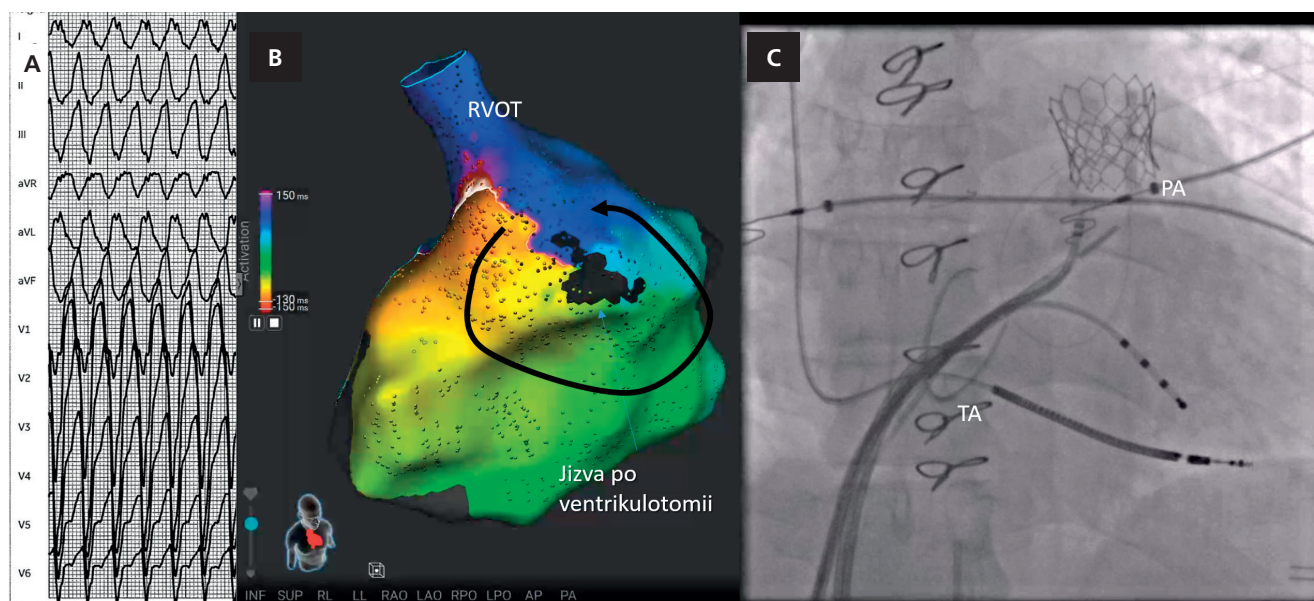
Změnu v doporučeních by mohla přinést recentně publikovaná studie VANISH2, která prokázala, že u pacientů s ischemickou kardiomyopatií (KMP) a dokumentovanou setrvalou KT je katetrizační ablace v porovnání s antiarytmickou terapií účinnější pro snížení cílového ukazatele složeného z celkové mortality, adekvátních výbojů ICD, elektrické bouře a KT pod detekčním limitem ICD.¹³

Strategie ablace u strukturálního postižení srdce a její úspěšnost závisí na řadě faktorů, z nichž jedním z nejdůležitějších je přesná definice arytmogenního substrátu.⁸ U pacientů se strukturálním postižením srdce je hlavním mechanismem vzniku KT reentry. Předpokladem reentry je zpomalené šíření vzruchu v oblasti jizevnaté tkáně. Charakteristickým příkladem je subendokardiální jizva po infarktu myokardu, která je protkána pruhy přežívších kardiomyocytů obklopených fibrózní tkání. U neischemických kardiomyopatií je arytmogenní substrát často tvořen difúzní fibrózou. Jiným příkladem jsou jizvy a protetický materiál po operacích srdce pro vrozené vady (tzv. postincizionální arytmie). Místa zpomaleného vedení vzruchu představují kritickou část potřebnou k udržení reentry a jsou cílem katetrizační ablace.

Optimální cíl katetrizační ablace KT lze stanovit různými způsoby. Donedávna bylo hlavní metodou mapování šíření vzruchu při běžící arytmií (tzv. mapování aktivační sekvence) (**obr. 1**). Přesnost aktivačního mapování zlepšilo výrazně zavedení tzv. elektroanatomických mapovacích systémů, které dovoluují vytvoření trojrozměrné virtuální mapy příslušné komory s projekcí šíření elektrického vzruchu.¹⁴ Kritický isthmus pomalého vedení vzruchu se obvykle projeví jako middiastolické nebo presystolické diskrétní potenciály. K ověření účasti těchto míst v okruhu reentry se používají stimulační manévry jako entrainment. Principem je salva stimulace z mapovacího katétru rychleji, než je frekvence KT. Pokud je dané místo v zóně pomalého vedení, dojde k urychlení kroužení vzruchu bez změny morfologie komplexu QRS, přičemž první cyklus po skončení stimulace má stejnou délku cyklu jako běžící arytmie (tzv. skrytý entrainment). Tento způsob mapování je však možné použít u méně než 30 % pacientů, protože aktivační mapování vyžaduje běžící arytmií, která většinou není hemodynamicky tolerována.¹⁵

Použití elektroanatomických mapovacích systémů dovolilo tzv. substrátové mapování při sinusovém rytmu nebo při stimulaci komory.¹⁶ Jeho cílem je identifikace arytmogenního substrátu a jeho rozsahu kombinací zobrazení lokálních voltáží (které jsou v oblasti jizvy nízké) a tzv. pacemappingu (stimulace z ablačního katétru k posouzení rychlosti a směru šíření vzruchu). Při pacemappingu se posuzuje interval mezi stimulem a počátkem komplexu QRS a morfologie QRS. Mapování lze obohatit i tzv. funkčním mapováním za použití extrasystol z opačné komory o krátkém vazebném intervalu a sledování pomalého šíření vzruchu. Dalším doplňkem je zobrazení substrátu pomocí intrakardiální echokardiografie nebo preprocedurální výpočetní tomografií (CT) či magnetickou rezonancí (MR) srdce.

Mezi nejčastěji používané ablační strategie založené na substrátovém mapování, které vedou k modifikaci

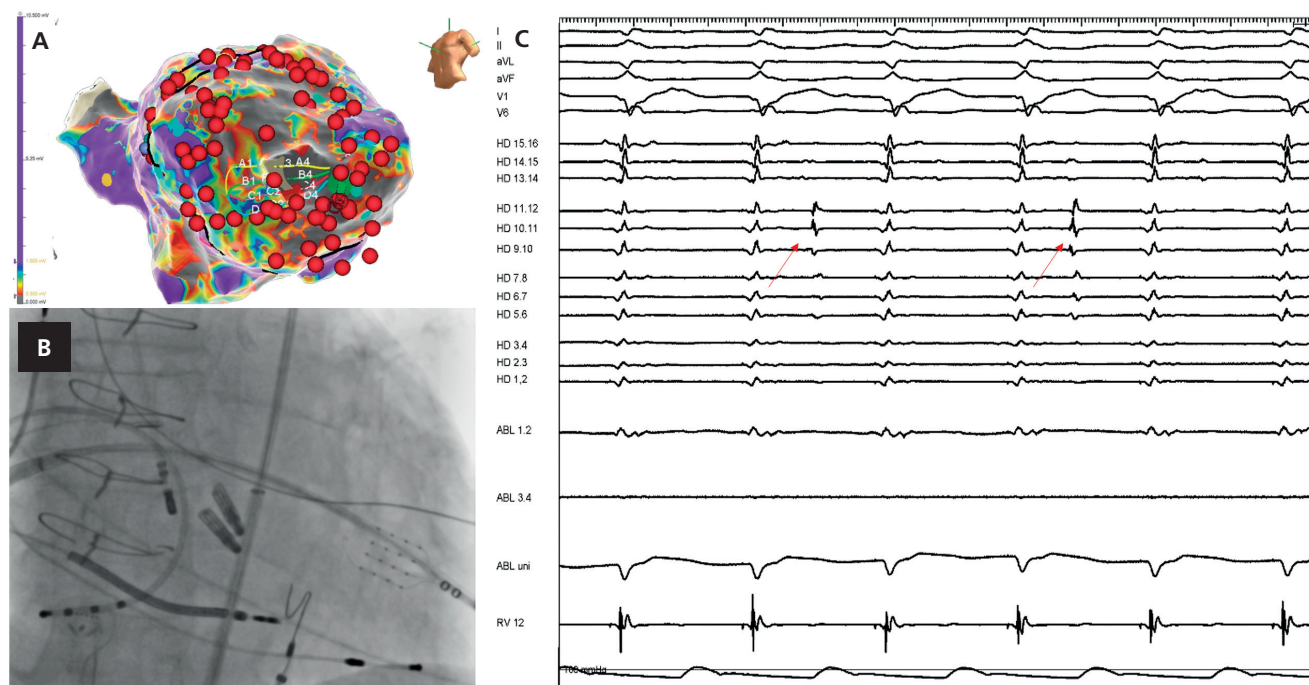


Obr. 1 – Aktivační mapování. (A) 12svodové EKG při běžící tachykardii u pacienta s vrozenou vadou srdeční po opakované chirurgické korekci. (B) Aktivační mapa pravé komory při běžící tachykardii. Lokální aktivace je barevně kódována (červená barva – nejčasnější aktivace, fialová barva – pozdní aktivace). Mapa ukazuje reentry okolo centrální jizvy na boční stěně ve výtokovém traktu pravé komory. Ablace byla provedena od jizvy směrem k plicnicové chlopi, což vedlo k přerušení reentry okruhu. (C) Skiagram s ablačním katétrem v pozici, kde došlo k terminaci arytmie.

arytmogenního substrátu (obr. 2), patří lineární ablace, homogenizace jizvy, izolace jádra jizvy, rozrušování kanálů pomalého vedení (tzv. dechanneling), eliminace pozdních potenciálů a lokálních abnormálních komorových elektrogramů.¹⁷

I při použití substrátového mapování a ablace může v průběhu výkonu dojít ke spontánnímu vzniku mnoho-

četných epizod KT s nutností opakovaných kardioverzí. To může mít za následek rozvoj hemodynamické nestability nebo dekompenzace srdečního selhání po výkonu. K řešení takového stavu nebo jeho prevenci lze použít krátkodobé mechanické srdeční podpory (MSP).¹⁸ Na jejich využití existují rozdílné názory a dosud neexistují přesvědčivá data, která by podporovala jejich širší využi-



Obr. 2 – Substrátové mapování u pacienta s poinfarktovým aneurysmatem přední stěny a implantovaným Mitraclipem. (A) Voltážová mapa zobrazující rozsáhlou jizvu hrotu a přední stěny. Ablační místa jsou označena červenými body. (B) Skiagram zobrazující ablační katétr zavedený retrogradním přístupem do levé komory; multipolární mapovací katétr (HD grid, Abbott) je zaveden transeptálním přístupem. (C) Lokální elektrogramy z multipolárního katétru umístěného uvnitř aneurysmatu. Červenou šipkou jsou označeny reziduální pozdní potenciály. Další aplikace radiofrekvenční energie do okrajové zóny aneurysmatu vedly k jejich vymizení.

tí při katetrizační ablací KT u strukturálního onemocnění srdce.¹⁹

Dlouhodobě bylo zlatým standardem dosažení neindukovatelnosti arytmií na konci výkonu.²⁰ Změnu v paradigma přinesla studie VISTA, která prokázala, že extenzivní substrátová ablace a eliminace abnormálních elektrogramů vede v porovnání s limitovanou ablací klinické KT k výraznému snížení rekurencí arytmií při srovnatelném riziku periprocedurálních komplikací.²¹ To prokazuje i metaanalýza zahrnující celkem 787 pacientů v 13 studiích.²²

Strategie katetrizační ablace je také ovlivněna lokalizací a charakterem arytmogenního substrátu. Zatímco u pacientů s ischemickou KMP je jizva lokalizována především subendokardiálně a je dobře přístupná endokardiální ablací, v případě neischemické KMP je její distribuce variabilnější a jizevnatá tkáň může být více difúzní. U této skupiny pacientů je arytmogenní substrát často lokalizován perivalvulárně, intramurálně nebo epikardiálně. Lze rozlišit dva základní typy distribuce: anteroseptální (AS) a inferolaterální (IL). V případě AS distribuce je jizva typicky lokalizována septálně intramurálně s extenzí do periaortální oblasti s dobrou dostupností k endokardiální ablací. Na druhou stranu IL distribuce je charakterizována substrátem v oblasti bazální části volné stěny levé komory s převažujícím epikardiálním postižením, což často vyžaduje použití epikardiálního přístupu.^{23,24} Rozdíl v charakteristice a lokalizaci jizvy může být vysvětlením pro lepší klinické výsledky katetrizační ablace KT u pacientů s ischemickou KMP v porovnání s neischemickou KMP.^{25,26} Epikardiální a perivalvulární lokalizace arytmogenního substrátu je také typická pro arytmogenní KMP, kdy kombinovaný endokardiální a epikardiální přístup vede k excelentním dlouhodobým výsledkům.²⁷

V případě endokardiální ablace a potřeby dosažení levé komory je možné zavádět katétr transvenózně za využití transeptální punkce anebo retrográdně, nejčastěji punkcí femorální tepny. Epikardiální perkutánní přístup ze subxiphoida popsali poprvé Sosa a kol.²⁸ Limitací tohoto přístupu je přítomnost aortokoronárních bypassů nebo srůstů po předchozích kardiokirurgických výkonech nebo zánětech v perikardu. U vybraných pacientů je k dosažení lepší expozice možné využít chirurgický subxifoidální přístup.²⁹

Radiofrekvenční ablace

Použití radiofrekvenční (RF) energie při katetrizační ablací KT bylo popsáno již v roce 1992, kdy autoři provedli úspěšně katetrizační ablací u 16 pacientů bez strukturálního onemocnění srdce.³⁰ V roce následujícím byla publikována práce, která ukázala, že katetrizační ablace KT je možná i u pacientů s ICHS.³¹

Základním mechanismem účinku RF energie je zahřívání tkáně v místě kontaktu katétru s myokardem s následným šířením tepla do okolí.³² Dosažení teploty $> 50^{\circ}\text{C}$ vede ke vzniku termální nekrózy a permanentní léze.³³ Okolní tkáň, která nedosáhne kritické teploty, může být poškozena reverzibilně s následnou úpravou funkce.³⁴ V průběhu ablace je potřeba vyhnout se přehřátí tkáně, neboť se při teplotách $> 100^{\circ}\text{C}$ zvyšuje riziko erupce vodních par (tzv. steam pop). To může mít za následek i lo-

kální roztržení myokardu a jeho perforaci.³⁵ Riziko erupce vodních par je často spojeno se zvýšením echogenity tkáně (tzv. tissue whitening), kterou je možno detekovat při použití intrakardiální echokardiografie. Předpokládá se, že tento jev je způsobený tvorbou mikrobublinek plynu uvnitř tkáně.³⁵ Při RF ablací dochází také k zahřívání elektrody katétru, kdy překročení teploty $> 70^{\circ}\text{C}$ vede ke koagulaci krevních proteinů, které adherují na povrch katétru, čímž zmenšují kontaktní plochu s tkání se vzestupem impedance a koagula mohou být zdrojem systémových embolizací.³⁶

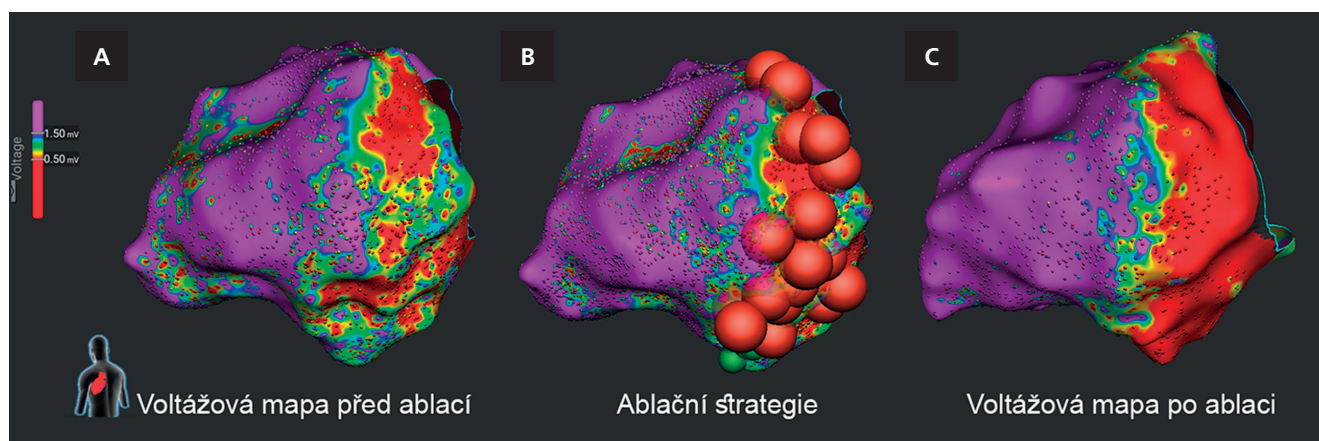
Hlavní limitací, která snižuje dlouhodobou úspěšnost RF ablace, je neschopnost dosažení dostatečně hluboké myokardiální léze. Riziko vzniku koagul a erupce vodních par do značné míry limituje navyšování dávky RF proudu. Navíc je velikost myokardiální léze modifikována také charakterem tkáně a její perfúzí, kdy přítomnost fibrózní tkáně a tuku v místě jizvy snižuje velikost dosažené léze.^{37,38}

Používání proplachovaných katétrů pomocí chladného fyziologického roztoku umožňuje dosažení hlubších lézí a snížení tvorby koagul.³⁹ Použití alternativních proplachových roztoků, které mění lokální impedanci v okolí katétru, může vést k dalšímu prohloubení léze, zároveň však dochází ke zvýšení rizika myokardiální ruptury nebo cévní mozkové příhody.^{40,41} Standardně používané RF ablační katétrů dosahují hloubky léze kolem 7 mm.⁴²

Ke zvýšení efektivity ablace lze použít i alternativní techniky. Bipolární a simultánní unipolární ablace za využití dvou katétrů možno použít především k ablacím v oblasti interventrikulárního septa.⁴³ Bipolární ablace je realizována za použití konvenčního generátoru RF proudu, kdy jeden ablační katétr je zapojen do standardního portu, zatímco druhý do konektoru pro disperzní povrchovou elektrodu.^{44,45} Tímhle způsobem dochází v průběhu ablace k přechodu proudu mezi oběma elektrodami katétrů, což umožňuje dosáhnout léze o hloubce až 17 mm.^{46,47} V případě simultánní unipolární ablace se používají dva samostatné generátory RF proudu a dva separátní katétrů, které se umísťují z obou stran septa v místě předpokládaného substrátu.^{48,49} Jinou možností je použití katétru se zasuvací jehlou (tzv. needle-tip catheter), který byl vytvořen k ablací substrátu uloženého hluboko v myokardu.^{50–52} Použití této metody prokázalo uspokojivé akutní a střednědobé výsledky.⁵³ K širšímu zavedení zmíněných alternativních metod do klinické praxe jsou nutné další studie, a to především k ověření jejich bezpečnosti.

Kryotermální ablace

Použití kryotermální energie je v současnosti již etablovanou metodou při katetrizační ablací fibrilace síní.⁵⁴ Mechanismus účinku kryoablace je komplexní a vede ke vzniku ischemické nekrózy buněk.^{55,56} V první fázi, při dosažení teploty $< -15^{\circ}\text{C}$, dochází ke vzniku ledových krystalů v extracelulárním prostoru, přičemž při dalším poklesu teploty $< -40^{\circ}\text{C}$ se krystaly ledu formují i intracelulárně.⁵⁵ To má za následek mechanické rozrušení buněk. Dominujícím procesem vedoucím k poškození buněk jsou však biochemické změny.^{56,57} Druhá fáze kryoablace pro-



Obr. 3 – Ukázka ablační strategie u pacienta po infarktu myokardu. (A) Voltážová mapa levé komory před ablací (voltáž je barevně kódována – červená nízká voltáž; fialová – vysoká voltáž) ukazuje jizvu po infarktu posterolaterálně bazálně. (B) Voltážová mapa s vyznačením ablační strategie, červenými body jsou označena místa aplikace radiofrekvenční energie. Ablace pokrývá celou oblast jizvy. (C) Voltážová remapa po ablací prokazuje kompletní homogenizaci arytmogenního substrátu.

bíhá po ukončení mrazení při pasivním vzestupu teploty tkáně na tělesnou teplotu. Jejím podkladem je osmotické poškození a vznik smykového napětí (tzv. shear stress), které vedou k dalšímu rozrušení architektiky tkáně.^{57,58} Navíc obnova mikrocirkulace je asociována s vaskulární obliterací, poškozením endotelu a vznikem mikrotrombů.^{55,56,59} Finální fáze je charakterizována procesem fibrózy, která v průběhu týdnů formuje zralou lézi. Ta je tvořena centrální, dobře ohraničenou oblastí denzní fibrózy obklopenou užším lemem tkáně s variabilně vyjádřenou buněčnou smrtí.⁶⁰

Hlavní výhodou kryotermální energie je v porovnání s RF vyšší přilnavost k tkáni, což vede k lepšímu kontaktu a stabilitě katétru. Použití kryotermální energie při endokardiální ablací nachází využití hlavně u pacientů, u kterých selhala RF ablace KT z důvodu nestability katétru. Úspěšné použití téhle metodologie bylo popsáno při katetrizační ablací KT vycházející z papilárních svalů levé komory nebo septomarginální trabekuly pravé komory.^{61–63} Studie Cryocure-VT byla pilotní multicentrická studie hodnotící využití a bezpečnost nové technologie kryoablace s využitím ultranízké teploty dosahující $-196\text{ }^{\circ}\text{C}$.⁶⁴ Do studie bylo zařazeno 13 pacientů s KT při strukturálním onemocnění srdce za použití systému Adagio Medical (Laguna Hills, California) v CLAS™ ULTC System. Akutní úspěšnost dosáhla 90,9 %. Ze závažných nežádoucích účinků byl u jednoho pacienta v souvislosti s výkonem pozorován vznik asymptomatického pseudoaneuryzmatu LK a u dalšího pacienta malý perikardiální výpotek.

Další možností je využití epikardiálního přístupu. Chirurgická epikardiální kryoablace prokázala přínos u pacientů s neischemickou KMP a KT se substrátem uloženým epikardiálně a intramurálně.⁶⁵ První ablační katétrů využívaly k ablací plynné skupenství oxidu dusného, který umožňoval vznik lézí do hloubky pouze 6 mm.^{66,67} Liuba a kol. recentně publikovali preklinickou práci, kdy na prasečím modelu prokázali možnost použití nového kryoablačního systému (HeartPad XLT, Corfigo Inc, Montclair, NJ), který využívá studené hélium s teplotou až $-250\text{ }^{\circ}\text{C}$ a dva katétrů různé velikosti (HeartPad Mini a HeartPad Micro). Výkon může být proveden perkutánním anebo

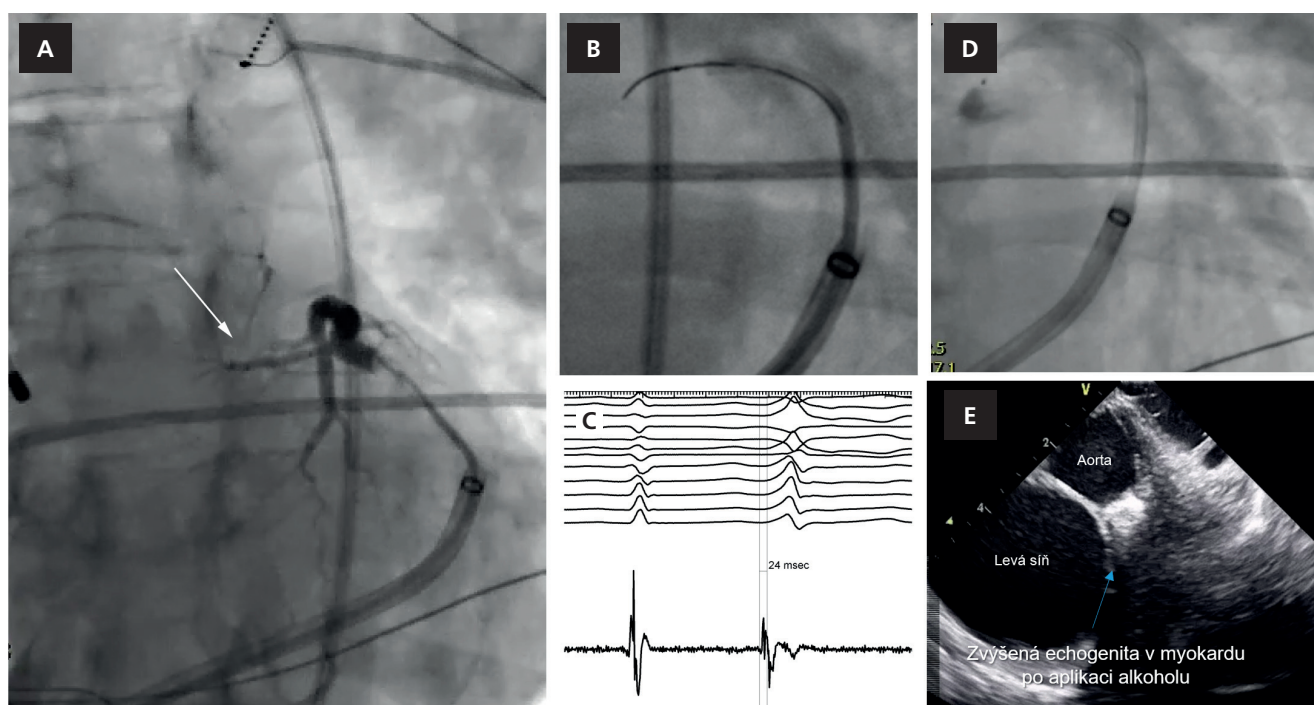
chirurgickým přístupem s dosažením průměrné velikosti ablační léze až 16 mm, přičemž hloubka léze může být modulována délkou aplikace s největším efektem dosaženým při aplikaci v trvání 120 sekund.⁶⁸

Ablace pulsním polem

Ablace pulsním polem představuje novou, netermální modalitu v katetrizační léčbě srdečních arytmií. Mechanismus účinku spočívá v aplikaci ultrakrátkých pulsů stejnosměrného elektrického proudu o vysokém napětí, který vede ke vzniku mikropórů v buněčné membráně s následným zvýšením její permeability. Nízká intenzita pulsního pole vede k přechodné tvorbě pórů, zatímco silnější pulsní pole navozuje ireverzibilní elektroporaci s následnou aktivací programované smrti buňky – apoptózy. Výsledkem je zánik buněk bez vzniku koagulační nekrózy a následné fibrózy. Efekt elektroporace je závislý na elektrických vlastnostech jednotlivých typů buněk a parametry elektrického proudu mohou být optimalizovány k dosažení efektu na kardiomyocyty se zachováním integrity okolních struktur.^{69–75} Efektivita a bezpečnost katetrizační ablace fibrilace síní pomocí energie pulsního pole byla ověřena v registru MANIFEST-PF.⁷⁶ Nutno však zmínit, že aplikace pulsního pole v těsné blízkosti probíhající koronární tepny vede ke vzniku subklinických vazospasmů s dobrou reakcí na podání nitrátů.⁷⁷

Efekt pulsního pole na komorový myokard u zvířecího modelu byl úspěšně popsán v řadě studií.^{78–81} Další práce porovnávající charakter léze po aplikaci RF energie a pulsního pole u prasečího modelu ve zdravé a infarktové tkáni prokázala dosažení hlubší léze v případě aplikace v místě poinfarktové jizvy.⁸² Tato optimistická data představují základ dalšího použití pulsního pole v klinické praxi u lidí.

Data o použití pulsního pole u lidí při katetrizační ablací KT jsou omezena na případové studie nebo zkušenosti jednotlivých center. V roce 2024 jsme publikovali dvě práce zabývající se využitím pulsního pole u pacientů s KT. V první studii se jednalo o prvotní zkušenosti



Obr. 4 – Alkoholová ablace komorové ektopie vycházející ze summitu levé komory. (A) Venogram distální části koronárního sinu. Šipkou je označena septální větev vedoucí do summitu levé komory. (B) Vodič zavedený do septální žilní větve. (C) Dobrá časnost lokálního elektrogramu při klinické ektopii. (D) Depo kontrastu v myokardu po ablaci alkoholu. (E) Zvýšená echogenita po aplikaci alkoholu v oblasti sumitu levé komory zobrazená na intrakardiální echokardiografii.

dvou center s použitím systému CENTAURI (CardioFocus), a to jak u pacientů s četnou komorovou ektopií, tak u KT při strukturálním onemocnění srdce. Celkem byl výkon proveden u 44 pacientů s akutní úspěšností 84 % v případě komorových extrasystol, u pacientů s KT bylo dosaženo akutní neinducibility v 81 %. Ve skupině s KT byla při průměrné době sledování 116 ± 75 dní úspěšnost výrazně nižší, a to 52 %.⁸³ Další práce zahrnuje pacienty se strukturálním srdečním onemocněním a KT, kteří podstoupili ablaci za použití nového mapovacího a ablačního katétru (Sphere-9, Medtronic, Minneapolis, MN) a dedikovaného elektroanatomického mapovacího systému a ablačního generátoru (Affera, Medtronic, Minneapolis, MN) s možností doručení jak RF energie, tak pulsního pole (obr. 3). V této sérii bylo zařazeno 18 pacientů s rekurentní KT. U 89 % pacientů bylo dosaženo neinducibility na konci výkonu s tříměsíční úspěšností 78 %. U čtyř pacientů byla ablace provedena epikardiálním přístupem, přičemž nutno zmínit, že u tří z nich byl angiograficky verifikován spasmus koronární tepny s následnou úplnou rezolucí po intrakoronárním podání nitrátu.⁸⁴ Tato data představují příslib pro širší využití pulsního pole k ablaci KT, avšak k ověření účinnosti a bezpečnosti jsou potřebné další studie.

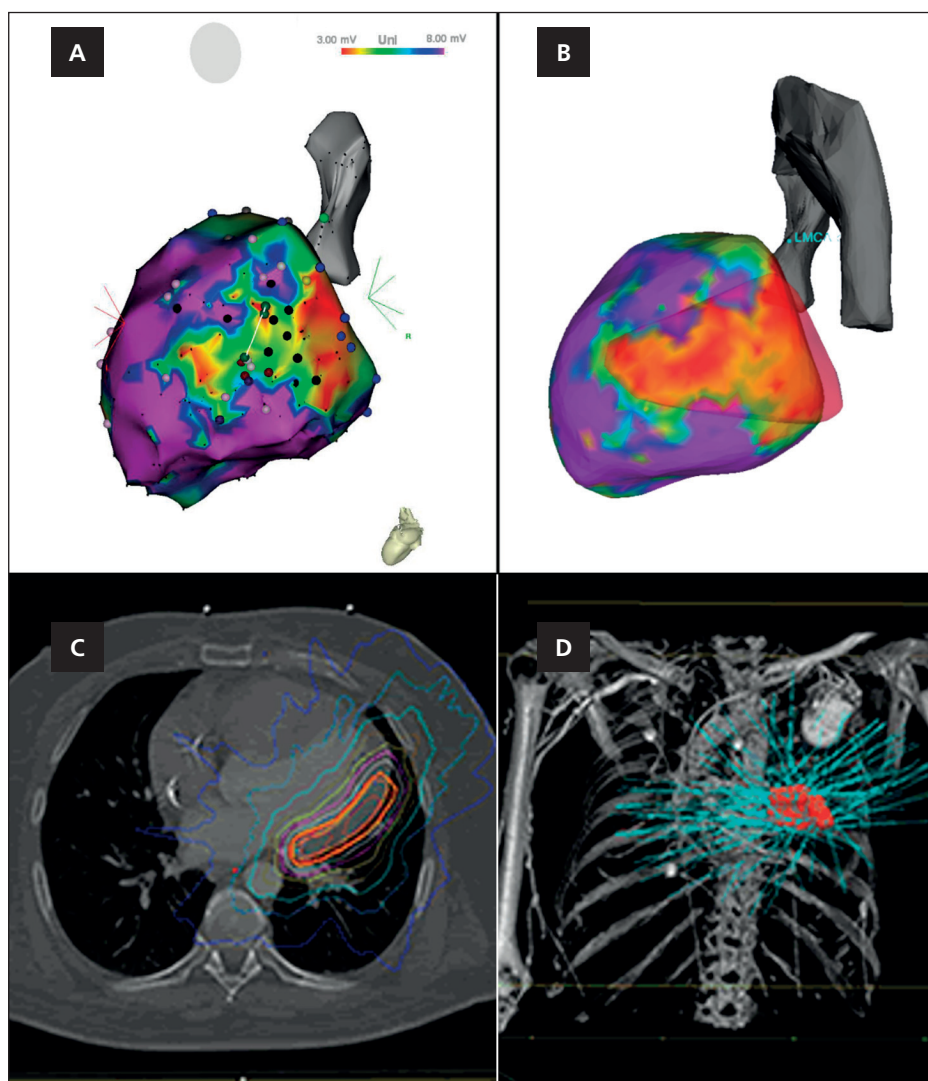
Alkoholová ablace

Další alternativou v terapii refrakterních KT je alkoholová ablace, která spočívá v podání vysoce koncentrovaného etanolu do arterie nebo vény, která zásobuje/drenuje oblast arytmogenního substrátu. Vysoké kon-

centrace etanolu vedou k solubilizaci buněčné membrány a okamžité buněčné smrti.⁸⁵ Úspěšnost výkonu může být ovlivněna přítomností kolaterálního zásobení dané oblasti, což vede ke snížení účinnosti ablace. Jednou z komplikací výkonu je zvýšené riziko vzniku reentry KT v důsledku nekompletní léze způsobené podáním etanolu.⁸⁶ Mezi další popsané komplikace patří především kompletní atrioventrikulární blokáda (AVB) při ablaci bazálního septálního substrátu, okluze necílové koronární tepny, perforace tepny nebo koronární vazospasmus.⁸⁷

První transarteriální podání etanolu bylo popsáno v roce 1987, kdy na psím modelu došlo po podání etanolu k arteriální trombóze a myokardiální nekróze s úspěšnou eliminací KT.⁸⁸ Následně Brugada a kol. prokázali možnost alkoholové ablace KT u tří pacientů s ischemickou KMP.^{89,90} V následujících letech byla publikována řada prací prokazujících úspěšné použití této techniky, včetně transvenózní koronární aplikace etanolu.^{91–93} Výsledky byly reprodukovány také v mezinárodní multicentrické studii.⁹⁴ Metaanalýza zahrnující deset studií a celkem 174 pacientů prokázala akutní úspěšnost etanolové ablace v 72,4 %, přičemž hlavní limitací výkonu byla absence vhodné cílové cévy drenující oblast arytmogenního substrátu nebo technická nemožnost její kanylace. Transvenózní aplikace etanolu se jeví jako bezpečnější a účinnější v porovnání s transarteriálním podáním.⁹⁵

V současnosti představuje alkoholová ablace alternativu u pacientů s refrakterními KT, které jsou špatně dostupné konvenční katetrizační ablací, a to především v oblasti sumitu levé komory srdeční (obr. 4).



Obr. 5 – Ukázka stereotaktické radioterapie. (A) Voltážová epikardiální mapa u pacienta s neischemickou kardiomyopatií a jizvou na bočné stěně levé komory. Kvůli výrazné hypertrofii myokardu konvenční radiofrekvenční ablace nevedla k účinnému odstranění všech forem komorových tachykardií. (B) Interpolace cílového místa pro radioterapii s elektroanatomickou mapou. (C, D) Plánovací CT vyšetření s označením cílových míst pro radioterapii.

Stereotaktická radioterapie

Stereotaktická radioterapie arytmií (STAR) je novou alternativní neinvazivní metodou v léčbě KT, a to především při selhání předchozí antiarytmické terapie a katetrizační ablace.

Léčba spočívá v aplikaci ionizujících fotonů, které jsou generovány lineárním urychlovačem nebo roboticky asistovaným lineárním urychlovačem (CyberKnife) na vybranou část srdeční tkáně. Na rozdíl od konvenční radioterapie se při STAR využívá trojdimenzionální zobrazení a ozáření tkáně z více úhlů. Přesný mechanismus účinku radioterapie na myokard není zcela objasněn. Prvotní hypotézou byla modulace vedení vzruchu v myokardu způsobená radiací indukovanou fibrózou.⁹⁶ STAR v dávce 25 Gy anebo více vedla v animálních modelech k fibróze a transmurálnímu poškození myokardu měsíce od její aplikace.⁹⁷ V některých klinických sériích bylo však pozorováno, že ke snížení zátěže KT může docházet u pacientů

již v průběhu několika dní až týdnů, a tedy radioterapií indukovaná fibróza zcela nevysvětluje časný efekt léčby.^{98–100} Zhang a kol. ukázali na zvířecím modelu, že STAR vede k zvýšené expresi NaV1.5 (podjednotka napěťově řízeného sodíkového kanálu, který se uplatňuje ve fázi depolarizace) a connexinu 43 (hlavní podjednotka skupinového spojení, tzv. gap junction).¹⁰¹ Do jaké míry se tato modulace vedení elektrického vzruchu klinicky uplatňuje, není zatím jasné.

Předpokladem použití STAR je přesná identifikace substrátu způsobujícího KT. K tomu lze použít elektroanatomické mapování, echokardiografii, pozitronovou emisní tomografii-výpočetní tomografii (PET-CT) či magnetickou rezonanci (MR). V České republice je užívána fúze elektroanatomického mapování s CT obrazem (obr. 5).¹⁰² Na základě preklinických studií a zkušeností z onkologie byla ve většině studií použita dávka 25 Gy aplikovaná jednorázově bez nutnosti celkové anestezie či sedace.

První kazuistiky o použití STAR byly publikovány před ne více než deseti lety.^{103,104} Poté následovalo několik dalších sérií kazuistik či klinických studií s omezeným počtem pacientů.^{100,105–111} Zatímco krátkodobá úspěšnost terapie byla ve většině studií vysoká, při dlouhodobějším sledování byly rekurence KT vysoké. Většina studií prokázala bezpečnost v krátkodobém a střednědobém sledování. K nejčastěji popsaným nežádoucím účinkům asociovaným s léčbou patřila nauzea, pleuritida, perikarditida, perikardiální výpotek a progresse chlopenní vady.

První větší prospektivní prací byla studie ENCORE VT, provedená na 19 pacientech s refrakterní KT.¹¹² Významné redukce epizod KT nebo komorové ektopie bylo dosaženo u 94 % pacientů po dobu sledování 13 měsíců. Nutno ale zmínit, že rekurence KT v období šesti týdnů až šesti měsíců po STAR byla až 69 %. Recentně byla publikována práce prezentující výsledky STAR v České republice.¹⁰² Zahrnuje celkem 36 pacientů s refrakterní KT a minimálně jednu předchozí katetrizační ablací. Mortalita skupiny dosahovala v 12 měsících od výkonu 47 % a prakticky u všech přežívajících pacientů byla po dobu sledování (průměrně 13,7 měsíce) zaznamenána adekvátní intervence ICD. Hlavním přínosem práce je analýza dlouhodobých nežádoucích účinků léčby, která byla hodnocena u 32 pacientů s průměrnou dobou sledování 33,5 měsíce. Nejčastěji se jednalo o progresi známé mitrální regurgitace, a to u osmi pacientů (25 %), z nichž tři museli podstoupit intervenci na chlopni. Další nežádoucí příhodou byla plicní fibróza v malém okrsku tkáně v blízkosti cílového místa ozařování u čtyř pacientů (12 %). K nejzávažnějším komplikacím patřila ezofagitida u dvou pacientů, z nich jeden zemřel devět měsíců po STAR na nerezekabilní ezofagoperikardiální píštěl. Vzhledem k uvedenému lze v současnosti považovat STAR za terapeutickou metodu pouze pro vybrané skupiny vysoce rizikových pacientů s rekurentní KT po předchozí katetrizační ablací.

Závěr

Léčba KT u pacientů se strukturálním onemocněním srdce vyžaduje komplexní přístup, jehož důležitou součástí je nefarmakologická terapie. Katetrizační ablace má potenciál snížit četnost arytmií nebo je úplně odstranit. V současnosti lze k dosažení tohoto cíle použít různé typy energie a ablační techniky, které v rukou zkušeného elektrofyziologa zvyšují úspěšnost výkonu při nízké míře komplikací. Alternativní metodou je použití stereotaktické radioterapie, její účinnost a především bezpečnost je nutno ověřit v dalších prospektivních studiích. Nemocné, u kterých i přes výše uvedenou léčbu dochází k recidivám KT, je možné po zohlednění dalších přidružených onemocnění a faktorů vyšetřovat jako potenciální kandidáty k transplantaci srdce.

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Izolovaná disekcia arteria carotis interna

(Isolated dissection of the internal carotid artery)

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SÚHRN

Izolovaná disekcia arteria carotis interna je závažné ochorenie pre riziko rozvoja ischemickej cievnej mozgovej príhody, a to najmä u mladých pacientov. Jej manažment je komplexný, pozostáva z farmakologickej a nefarmakologickej – endovaskulárnej liečby. Každá z liečebných možností musí byť prísne indikovaná po splnení striktných indikácií. Cieľom tohto článku je priniesť čitateľovi komplexný pohľad na toto ochorenie od etiopatogenézy po liečbu a prognózu. Najdôležitejším cieľom je poskytnúť najaktuálnejšie poznatky o spôsobe liečby a indikáciách jednotlivých liečebných postupov.

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ABSTRACT

Isolated dissection of the internal carotid artery is a serious medical condition due to the risk of ischemic stroke developing, especially in young patients. Its management is complex, consisting of pharmacological and non-pharmacological, endovascular treatment. Each of the treatment options must be strictly indicated after meeting the strict indications. The aim of this article is to provide the reader with a comprehensive view of this disease from etiopathogenesis to treatment and prognosis. The most important goal is to provide the most up-to-date knowledge about the method of treatment and the indications of each treatment option.

Úvod

Izolovaná disekcia arteria carotis interna (ACI) je príčinou približne 2 % zo všetkých cievnych mozgových príhod (CMP), pričom tento počet je závislý od veku a výrazne stúpa u mladých pacientov. U jedincov mladších ako 45 rokov je to až 20 %.¹ Disekcia tepny je vo všeobecnosti výsledkom roztrhnutia vnútornej výstelky tepny (tunica intima), po ktorej nasleduje jej oddelenie od strednej vrstvy tepny (tunica media) v dôsledku pulzujúceho prietoku krvi medzi nimi. Separácia vrstiev steny tepny sa zvyčajne odohráva v smere prietoku krvi, čo môže viesť k vzniku intraluminálneho trombu, stenózy, oklúzie alebo disekujúcej aneurizmy. Takýmto

mechanizmom môže karotická disekcia spôsobiť sekundárnu ischémiu mozgu. ACI prebieha parciálne extra- a parciálne intrakraniálne, preto analogicky izolovanú disekciu ACI môžeme rozdeliť na extra- a intrakraniálnu. Extrakraniálna karotická disekcia (EKD) bola extenzívne študovaná, jej ročná incidencia sa pohybuje medzi 1,72² až 2,6–3 prípadov na 100 000 obyvateľov.^{3,4} Incidencia intrakraniálnej karotickej disekcie (IKD) nie je známa, ale predpokladá sa, že je nižšia ako incidencia extrakraniálnej. Pomer medzi extra-/intrakraniálnou lokalizáciou disekcie je závislý od regiónu. V Európe predstavuje IKD asi 11 %, v Latinskej Amerike asi 27 %⁶ a vo východnej Ázii asi 67–78 %^{7,8} z celkového počtu prípadov izolovanej disekcie ACI.

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Etiológia

Presná etiológia karotickej disekcie nie je známa, nakoľko ide o multifaktorálne ochorenie. Rizikové faktory vzniku IKD nie sú dostatočne známe a charakterizované. V etiopatogenéze EKD boli identifikované tieto potenciálne rizikové faktory:

Mechanické faktory

■ Anatómia – Eaglov syndróm

V etiopatogenéze disekcie karotickej tepny môže zohrávať úlohu dĺžka processus styloideus ossis temporalis, ktorého fyziologická dĺžka je asi 20–25 mm. V roku 1948 otorynolaryngológ W. W. Eagle publikoval článok popisujúci symptómy súvisiace s predĺžením processus styloideus ossis temporalis, neskôr súhrne označené ako Eaglov syndróm.

Ide o raritné ochorenie spôsobené útlakom nervových alebo vaskulárnych štruktúr uni/bilaterálnym predĺžením processus styloideus ossis temporalis a/alebo kalcifikáciou ligamentum stylohyoideum. Ak sú utláčané hlavové nervy (n. facialis, vagus, glossopharyngeus a hypoglossus), hovoríme o „neurologickej forme“ a symptómy zahŕňajú jednostrannú bolesť hrdla, krku, tváre a ucha, ako aj tinitus a dysfágiu.^{9,10} V prípade tlaku na ACI v jej extrakraniálnom úseku ide o vaskulárnu formu, respektíve stylokarotický syndróm a medzi symptómy patrí bolesťivosť pozdĺž priebehu tepny, poruchy zraku a ischemická CMP. Disekcia ACI patrí medzi ďalšie komplikácie stylokarotického syndrómu.¹¹ Predĺženie processus styloideus na viac ako 30 mm zvyšuje riziko vzniku karotickej disekcie,¹² avšak zvyčajne sú prítomné aj ďalšie rizikové faktory, ako je ochorenie mäkkých tkanív, trauma, chirurgické poškodenie (napr. tonzilektómia), endokrinné príčiny.¹⁰

■ Manipulácia s krčnou chrbticou – rehabilitačné techniky

Je možné predpokladať, že manipulácie s krčnou chrbticou v rámci rehabilitácie budú narastať vzhľadom na aktuálny spôsob života v populácii charakterizovaný dlhodobým sedením a vykonávaním stereotypných činností (napr. práca s PC, smart telefóny atď.). Niektoré práce poukázali na riziko vzniku disekcie ACI po takýchto procedúrach.¹³ Išlo zvyčajne o „case“ reporty. Avšak veľká štúdia charakteru meta-analýzy nedokázala potvrdiť súvislosť medzi manipuláciou s krčnou chrbticou a rizikom vzniku disekcie ACI.¹⁴

■ Zranenia

Do tejto skupiny môžeme zaradiť autonehody, zranenia v športe, pády, napadnutie, obesenie.^{15–20}

■ Zdravotné výkony – iatrogénna disekcia

■ Iné

Genetické faktory

Existujú solídne argumenty podporujúce hypotézu, že genetické faktory hrajú zásadnú úlohu v etiológii a patogenéze disekcie ACI, a to zriedkavo ako súčasť poruchy jedného génu alebo častejšie ako súčasť multifaktoriálnej predispozície.

Prevláda hypotéza, že genetické pozadie spôsobuje konštitučnú slabosť cievnej steny a faktory, ako je akútna infekcia alebo malá trauma, môžu spustiť disekciu tepny.^{15,21}

■ Monogénne ochorenia a disekcia ACI

U pacientov s disekciou ACI boli realizované biopsie kože za účelom genetickej analýzy mutácií kandidátskych génov vybraných na základe predpokladanej súvislosti medzi disekciou karotickej tepny a bežnými abnormalitami spojivového tkaniva pri známych hereditárnych poruchách spojivového tkaniva ako vaskulárny Ehlersov–Danlov syndróm (EDS), Marfanov syndróm (MFS), pseudoxanthoma elasticum, osteogenesis imperfecta a Loeysov–Dietzov syndróm, ako aj ďalšie gény zapojené do syntézy komponentov extracelulárnej matrix. Výsledok bol zväčša negatívny. Prevalencia hereditárnych ochorení spoja u pacientov s disekciou ACI je celkovo veľmi nízka (0,5–2,0 % pre EDS IV; 0,6–0,9 % pre MFS).^{22,23} Podobne, až na niekoľko výnimiek, je výskyt disekcie karotickej tepny zriedkavý medzi pacientmi s dokázanou diagnózou hereditárneho ochorenia spoja.^{22,23}

Na druhej strane, iné štúdie preukázali patologické génové mutácie u pacientov s familiárnym výskytom karotickej disekcie, preto možno povedať, že monogénne genetické ochorenia zohrávajú dôležitú úlohu najmä v etiopatogenéze disekcie ACI s familiárnym výskytom.^{24–26}

■ Disekcia karotickej tepny ako multifaktoriálne ochorenie s genetickou zložkou

U väčšiny pacientov sa nepotvrdila jednoznačná súvislosť medzi monogénnymi ochoreniami a nefamiliárnou disekciou ACI, preto sa o danom ochorení uvažuje ako o multifaktoriálnom s genetickým spolupodielom. Na základe výsledkov štúdie GWAS (genome-wide association study) bol identifikovaný výskyt alely A genetického variantu (rs9349379) génu *PHACTR1* (phosphatase and actin regulator 1 gene) ako rizikový faktor vzniku spontánnej karotickej disekcie (OR 1,33).^{27,28}

Kolagénové vaskulárne poruchy

Ako je uvedené vyššie, typické ochorenia spoja spĺňajúce diagnostické a genetické kritériá sa u pacientov s disekciou ACI vyskytujú len zriedkavo. Avšak izolované mierne abnormality spojivového tkaniva prejavujúce sa ako hypermobilita kĺbov, ľahká tvorba modrín, zlé hojenie rán sú pozorované často (50–96 %).^{26,30}

Pacienti so subklinicky zvýšenou vaskulárnou tortuozitou, resp. zväčšeným priemerom bulbu aorty sú tiež náchylnejší pre vznik disekcie ACI.³¹ Preto mnoho prípadov disekcie ACI sa pravdepodobne vyskytuje pri systémových, ale nedostatočne definovaných miernych poruchách spojivového tkaniva.¹⁵ Fibromuskulárna dysplázia (FMD), neaterosklerotická a nezápalová arteriopatia je jedno z významných ochorení, ktoré môžeme zaradiť do tejto skupiny rizikových faktorov. Má významnú súvislosť s disekciou ACI. Zistilo sa, že viac ako 10 % pacientov s diagnostikovanou FMD je súčasne postihnutých aj disekciou ACI. Disekcia tepny reprezentuje jeden zo znakov FMD, pričom viac ako 90 % prípadov disekcií tepien pri FMD postihuje karotické, menej často vertebrálne tepny.³² Bolo tiež zistené, že takmer u 40 % pacientov s disekciou ACI sa súčasne vyskytuje aj FMD.³³

Nedávne infekcie

Nedávne infekcie horných dýchacích ciest, chrípka a gastrointestinálne infekcie sú popisované častejšie u pacientov s disekciou ACI, hoci základný mechanizmus a príčina súvislosť nie sú jasné. Táto asociácia bola nezávislá od kašľania a kýchania.^{20,34}

Kardiovaskulárne, biochemické a ďalšie rizikové faktory

V etiopatogenéze vzniku karotickej disekcie bol potvrdený aj vplyv artériovej hypertenzie, fajčenia,^{35,36} hyperhomocysteinémie³⁷ a antikoncepcie.³³

Tabuľka 1 prehľadne zobrazuje potenciálne rizikové faktory zohrávajúce úlohu v etiopatológii izolovanej karotickej disekcie.

Patogenéza

Disekciu ACI podľa patomechanizmu vzniku môžeme rozdeliť na **spontánnu a traumatickú**. Disekcia ACI najčastejšie vzniká spolupôsobením viacerých rizikových fak-

torov a traumatický inzult je identifikovateľný len u časti z nich.^{15,38}

Traumatická disekcia postihuje asi 2,6 % pacientov s ťažkou tupou traumou a 2,7 % pacientov s polytraumou. Vzniká pri nadmernom natiahnutí tepny alebo je výsledkom priameho úderu do anterolaterálnej časti krku. K nadmernému natiahnutiu tepny zvyčajne dochádza počas nadmernej hyperextenzie a kontralaterálnej rotácie hlavy.

Diagnostika ochorenia

Pre často nešpecifickú povahu symptómov je diagnostika karotickej disekcie náročná, najmä pri absencii ischemických symptómov a znakov (cievna mozgová príhoda). Diagnostika je tak založená na kombinácii špecifických nálezov zobrazovacích metód, podrobnej anamnéze (symptómov) a dôsledného neurologického vyšetrenia (znaky).

Zobrazovacie metódy

V diagnostickom procese karotickej disekcie môžeme využiť tieto modalitty: CT angiografia, MR angiografia, ultrasonografia a karotická angiografia/DSA.

■ Zobrazovacie diagnostické kritéria podľa Európskej organizácie pre cievne mozgové príhody

EKD je charakterizovaná niektorými z nasledujúcich nálezov (**obr. 1**): intramurálny hematóm, disekujúca aneurizma, tiahla stenóza, intimálny flap, dvojúlumen, uzáver ACI viac ako 2 cm distálnejšie od bifurkácie arteria carotis communis, ktorý sa neskôr demaskuje ako disekujúca aneurizma a/alebo tiahla stenóza po rekanalizácii.³⁹

Obrázky 3–11 zobrazujú CT angiografické vyšetrenie a angiografické vyšetrenie a. carotis interna u pacienta A, B, C a D.

IKD je potvrdená prítomnosťou aspoň jedného z nálezov (**obr. 2**): (i) stenóza alebo uzáver intrakraniálnej tepny so sekundárnou fuziformnou alebo nepravidelnou aneuryzmatickou dilatáciou v časti tepny bez vetiev (ii)

Tabuľka 1 – Rizikové faktory v etiopatológii izolovanej karotickej disekcie

1) Mechanické

- Anatómia – Eaglov syndróm^{9–12}
- Manipulácia s krčnou chrbticou – rehabilitačné techniky¹³
- Zranenia (autonehody, zranenia v športe, pády, napadnutie, obesenie)^{15–20}
- Zdravotné výkony – iatrogénna disekcia¹⁵

2) Genetické faktory

a) Monogénne ochorenia a disekcia a. carotis interna^{22–26}

- Ehlersov–Danlosov syndróm
- Marfanov syndróm
- Pseudoxanthoma elasticum
- Osteogenesis imperfecta
- Loeysov–Dietzov syndróm

b) Disekcia a. carotis interna ako multifaktoriálne ochorenie s genetickou zložkou

- Alela A genetického variantu (rs9349379) génu *PHACTR1* (phosphatase and actin regulator 1 gene)²⁷

3) Kolagénové vaskulárne poruchy^{15,36,30,31}

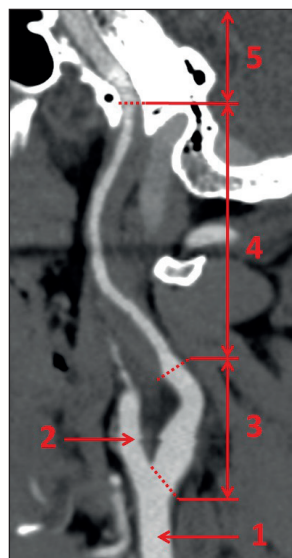
- Fibromuskulárna dysplázia^{31–33}

4) Recentné infekcie^{20,34}

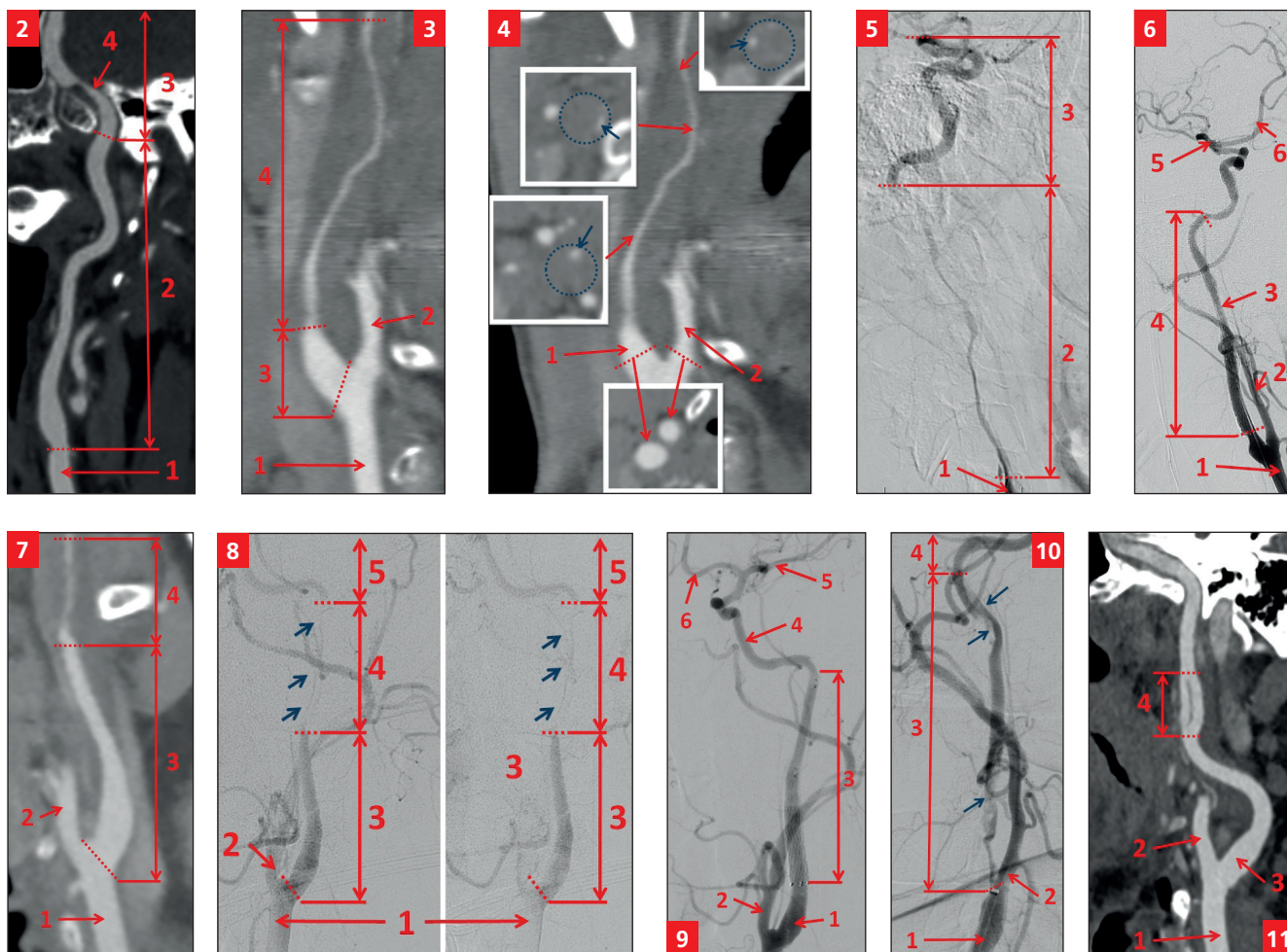
- Horných dýchacích ciest
- Chrípka
- Gastrointestinálne infekcie

5) Kardiovaskulárne, biochemické a ďalšie rizikové faktory^{33,35–37}

- Artérová hypertenzia
- Fajčenie
- Hyperhomocysteinémia
- Antikoncepcia



Obr. 1 – CT angiografické vyšetrenie karotického riečiska zobrazujúce disekciu extrakraniálneho úseku a. carotis interna. 1. A. carotis communis; 2. odstupový úsek a. carotis externa; 3. odstupový úsek a. carotis interna, ktorý nie je postihnutý stenózou/disekciou; 4. extrakraniálny úsek a. carotis interna postihnutý disekciou, ktorá sa manifestuje ako tiahla špirálovitá stenóza po lebečnú bazu; 5. intrakraniálny úsek a. carotis interna, ktorý už nie je postihnutý karotickou disekciou.



Obr. 2 – CT angiografické vyšetrenie karotického riečiska zobrazujúce disekciu intrakraniálneho úseku a. carotis interna. 1. A. carotis communis; 2. extrakraniálny úsek a. carotis interna, ktorý nie je postihnutý disekciou; 3. intrakraniálny úsek a. carotis interna; 4. disekcia intrakraniálneho úseku a. carotis interna, ktorá sa manifestuje ako závažná stenóza.

Obr. 3 CT angiografické vyšetrenie karotického riečiska u pacienta A zobrazujúce disekciu extrakraniálneho úseku a. carotis interna. 1. A. carotis communis; 2. odstupový úsek a. carotis externa; 3. odstupový úsek a. carotis interna, ktorý nie je postihnutý stenózou/disekciou; 4. extrakraniálny úsek a. carotis interna postihnutý disekciou, ktorá sa manifestuje ako ťahla špirálovitá stenóza po lebečnú bazu.

Obr. 4 – CT angiografické vyšetrenie karotického riečiska u pacienta A zobrazujúce disekciu extrakraniálneho úseku a. carotis interna v modifikovanom koronárnom reze (následne spracovaný obraz), do ktorého sú zapracované aj axiálne rezy pre lepšiu ilustráciu pomeru medzi pravým a falošným lúmenom na jednotlivých úrovniach a. carotis interna distálnym smerom. 1. A. carotis interna; 2. odstupový úsek a. carotis externa. Modré kruhy s prerušovanou čiarou zobrazujú teoretický prierez a. carotis interna po jej adventícii. Modré šípky znázorňujú lúmen, ktorý sa plní – ide o pravý lúmen disekcie, falošný sa neplní.

Obr. 5 – Angiografické vyšetrenie karotického riečiska zobrazujúce disekciu extrakraniálneho úseku a. carotis interna u pacienta A. 1. Odstupový úsek a. carotis interna; 2. úsek a. carotis interna, ktorý je postihnutý stenózou/disekciou; 3. intrakraniálny úsek a. carotis interna, ktorý už nie je postihnutý karotickou disekciou.

Obr. 6 – Angiografické vyšetrenie karotického riečiska zobrazujúce výsledok po implantácii stentu do extrakraniálneho úseku a. carotis interna u pacienta A. 1. A. carotis communis; 2. a. carotis externa; 3. a. carotis interna; 4. stenty implantované do extrakraniálneho úseku a. carotis interna; 5. a. cerebri media; 6. a. cerebri anterior.

Obr. 7 – CT angiografické vyšetrenie karotického riečiska u pacienta B zobrazujúce disekciu extrakraniálneho úseku a. carotis interna niekoľko cm po odstupe až po lebečnú bazu. 1. A. carotis communis; 2. odstupový úsek a. carotis externa; 3. odstupový úsek a. carotis interna, ktorý nie je postihnutý stenózou/disekciou; 4. extrakraniálny úsek a. carotis interna postihnutý disekciou, ktorá sa manifestuje ako stenóza po lebečnú bazu.

Obr. 8 – Angiografické vyšetrenie karotického riečiska v rôznej fáze dotekania kontrastnej látky zobrazujúce disekciu extrakraniálneho úseku a. carotis interna u pacienta B. 1. A. carotis communis; 2. odstupový úsek a. carotis externa; 3. odstupový úsek a. carotis interna, ktorý nie je postihnutý disekciou; 4. extrakraniálny úsek a. carotis interna, ktorý je postihnutý disekciou, modré šípky ukazujú na disekciu, ktorá sa manifestuje ako ťahla preokluzívna stenóza s chabým plnením intrakránia; 5. intrakraniálny úsek a. carotis interna, ktorý už nie je postihnutý karotickou disekciou.

Obr. 9 – Angiografické vyšetrenie karotického riečiska zobrazujúce výsledok po implantácii stentu do extrakraniálneho úseku a. carotis interna u pacienta B. 1. Odstupový úsek a. carotis interna; 2. a. carotis externa; 3. extrakraniálny úsek a. carotis interna prekrytý stentom; 4. intrakraniálny úsek a. carotis interna, ktorý je bez disekcie; 5. a. cerebri media; 6. a. cerebri anterior.

Obr. 10 – Angiografické vyšetrenie karotického riečiska u pacienta C zobrazujúce disekciu extrakraniálneho úseku a. carotis interna. 1. A. carotis communis; 2. a. carotis externa; 3. úsek a. carotis interna, ktorý je postihnutý disekciou, modré šípky ukazujú na disekciu; 4. intrakraniálny úsek a. carotis interna, ktorý už nie je postihnutý karotickou disekciou.

Obr. 11 – CT angiografické vyšetrenie karotického riečiska u pacienta D zobrazujúce krátku disekciu distálneho extrakraniálneho úseku a. carotis interna. 1. A. carotis communis; 2. odstupový úsek a. carotis externa; 3. a. carotis interna; 4. krátky extrakraniálny úsek a. carotis interna postihnutý disekciou, ktorá sa manifestuje typickým dvojlúmenom.

intimálny flap, dvojlúmen, intramurálny hematóm, (iii) intrakraniálna disekcia potvrdená patológom.³⁹

Ultrazvukové vyšetrenie cievneho systému prináša oproti klasickým zobrazovacím metódam ako napr. angiografia, CT angiografia alebo MR angiografia unikátnu možnosť posúdenia hemodynamickej závažnosti lézie meraním rýchlosti priamo v lézii za predpokladu, že je možné cieľovú oblasť cievy vyšetriť ultrazvukovou sondou. Typické aterosklerotické lézie sú zvyčajne fokálne, lokalizované proximálne, teda v odstupe a. carotis interna, a sú preto zväčša veľmi dobre prístupné pre ultrazvukové vyšetrenie. V prípade karotickej disekcie to už tak celkom neplatí. Disekcie sú lokalizované distálnejšie a postihujú dlhší úsek tepny (nie fokálne).

Ultrazvukové vyšetrenie v diagnostike disekcie karotických tepien je tak významne limitované len na krátky, proximálny, extrakraniálny úsek, a nemusí tak zachytiť disekcie lokalizované distálnejšie, respektíve celú dĺžku disekcie.

Medzi ultrasonografické znaky karotickej disekcie pri jej priamej vizualizácii môžeme zaradiť: chýbajúca alebo len mierna ateroskleróza (kalcifikáty); zhrubnutie steny tepny nízkej echogenicity spôsobené intramurálnym hematómom s príľahlým trombotickým materiálom, čo vedie k stenóze tejto artérie; „dvojité lúmen“ (ktorý je ale vidieť len zriedka).

Klinická manifestácia

Klinická manifestácia závisí od lokalizácie disekcie, rozlišujeme tak **symptómy extrakraniálnej a intrakraniálnej karotickej disekcie**.

■ Klinické prejavy EKD

Klinicky sa extrakraniálna disekcia zvyčajne prejavuje „lokálnymi“ symptómami a znakmi, ktoré sú zapríčinené útlakom okolitých štruktúr. Patria medzi ne **bolesti hlavy, krku, Hornerov syndróm, obrna hlavových nervov**. Medzi najzávažnejšie prejavy EKD patria **prejavy cerebrálnej ischémie**.

Bolesť hlavy alebo bolesť krku patrí medzi najčastejšie symptómy (65–95 % prípadov). Bolesť hlavy spojená s EKD je zvyčajne silná. Má charakter podobný migrenóznym bolestiam, aj keď boli hlásené aj bolesti hlavy charakteru „cluster headache“ (v preklade klastrová bolesť hlavy) a „thunderclap headache“ (v preklade prudko nastupujúca – blesková bolesť hlavy).^{40,41} **Hornerov syndróm** sa vyskytuje asi u jednej štvrtiny pacientov s EKD.⁴² **Pulzujúci tinitus** bol pozorovaný asi u 8 % pacientov s EKD.⁴³ **Obrna hlavových nervov** komplikuje približne 12 % prípadov extrakraniálnej karotickej disekcie,⁴⁴ pričom nervus hypoglossus je postihnutý najčastejšie.⁴⁵

Približne u dvoch tretín až troch štvrtín pacientov v publikovaných sériách je EKD komplikovaná aj **cerebrálnou ischémiou** (ischemická cievna mozgová príhoda a TIA) alebo zriedkavejšie ischémiou sietnice či miechy.^{1,39}

■ Klinické prejavy IKD

Medzi dva hlavné klinické prejavy IKD patrí **subarachnoidálne krvácanie** (asi u 50–60 % pacientov) a **cerebrálna ischémia** (30–78 %), výnimočne oboje. Asi u 80 % pacientov s IKD sa vyskytne prodromálna bolesť hlavy.^{40,46}

Liečba

Medzi liečebné možnosti ochorenia patrí: **systémová trombolytická liečba, antitrombotická liečba (antikoagulačná alebo antiagregačná) a endovaskulárna (mechanická trombektómia alebo karotický stenting) alebo chirurgická revaskularizácia**. Jednotlivé liečebné možnosti sa môžu kombinovať a ich voľba je podmienená predovšetkým klinickou situáciou, teda či je karotická disekcia príčinou ischemickej cievnej mozgovej príhody/TIA. Voľbu liečebných možností ďalej ovplyvňuje etiopatogenéza disekcie a časové hľadisko. Nedávno Európska organizácia pre cievne mozgové príhody (European Stroke Organization, ESO) vypracovala komplexné odporúčania manažmentu extra- aj intrakraniálnej disekcie, ktoré je možné považovať za prvé svojho druhu. Je však nutné dodať, že uvedené odporúčania sa zameriavajú na spontánnu karotickú disekciu.

Spontánnu karotickú disekciu

Liečba spontánnej karotickej disekcie závisí predovšetkým od toho, či je komplikovaná **akútnou ischemickou CMP**, a tiež od **časového okna**.

● Liečba pacientov so spontánnou karotickou disekciou a ischemickou CMP

Z časového hľadiska, ako aj hlavných úloh a cieľov môžeme liečbu tejto skupiny pacientov rozdeliť na dve fázy: **fáza emergentnej liečby a fáza prevencie rekurencie CMP**.

Emergentná liečba

Emergentná liečba sa uskutočňuje v akútnej fáze, do niekoľkých hodín od vzniku symptómov a znakov ischemickej CMP. Je podobná liečbe a manažmentu ischemickej CMP z iných príčin. Jej hlavným terapeutickým cieľom je **zmiernenie/odstránenie už prebiehajúcej akútnej mozgovej ischémie**. Na tento účel je možné použiť **systémovú trombolytickú liečbu a endovaskulárnu revaskularizáciu**.

■ Systémová trombolytická liečba

Ak je časový interval medzi vznikom ťažkostí v zmysle ischemickej CMP a diagnostikou kratší ako 4,5 hodiny, je potrebné uvažovať o podaní systémovej trombolytickej liečby. Podanie trombolytickej liečby je okrem vyššie uvedeného podmienené aj anatomicou lokalizáciou disekcie.

U pacientov s EKD navrhuje ESO podanie systémovej trombolytickej liečby. IKD asociovaná s akútnou ischemickou CMP je zriedkavejšia a dôkazy na poskytnutie odporúčania sú nedostatočné. Avšak na základe konsenzu odborníkov by sa u takýchto pacientov malo zvážiť podanie systémovej trombolytickej liečby.³⁹ Je možné povedať, že sa má vo veci ordinácie systémovej trombolytickej liečby u pacientov s karotickou disekciou vedúcou k akútnej ischemickej CMP postupovať rovnako ako u pacientov s každou inou ischemickou CMP.³⁹ Cieľom systémovej trombolytickej liečby je zmiernenie už prebiehajúcej akútnej ischémie mozgu.

■ Endovaskulárna revaskularizácia

Pozostáva z endovaskulárnych techník: **mechanickej trombektómie uzáveru veľkej intrakraniálnej tepny (aspirácia alebo stent retriever) a stentingu karotickej disekcie**.

Ak EKD vedie k ischemickej CMP a uzáveru veľkej tepny prednej cirkulácie (a. cerebri media alebo anterior), potom je voľba jednoduchá, má sa realizovať mechanická trombektómia (MTE) – samozrejme ak je dodržané časové okno a ďalšie podmienky indikácie MT ako pri každej inej ischemickej CMP.³⁹

Nejasnou však zostáva odpoveď na otázku, čo v prípade, ak sa jedná o tandémovú léziu, teda oklúziu veľkej tepny prednej cirkulácie a léziu karotídy (ACI) na podklade EKD.

V roku 2020 bola publikovaná štúdia (súhrnná analýza TITAN a ETIS), ktorá študovala bezpečnosť a klinické výsledky emergentného karotického stentingu u pacientov s akútnou ischemickou CMP a tandemovou léziou. Karotický stenting bol prídavnou endovaskulárnou terapeutickou modalitou k mechanickej trombektómii intrakraniálnej tepny u časti pacientov v súbore. Štúdia nepreukázala benefit emergentného karotického stentingu.

Autori však pripúšťajú, že emergentný karotický stenting by sa mohol zväziť najmä v prípade reziduálnej stenózy extrakraniálneho úseku ACI vysokého stupňa po intrakraniálnej revaskularizácii, nedostatočnej priechodnosti Willisovho okruhu alebo pri prítomnosti endoluminálneho trombu s embolizačným potenciálom.⁴⁷ Podobne, aj iné novšie štúdie nepreukázali benefit emergentného stentingu karotickej disekcie ako prídavnej modality k mechanickej trombektómii u pacientov s tandemovou léziou.^{48,49}

Podľa názoru expertov participujúcich na tvorbe odporúčaní ESO je potrebné endovaskulárne (stenting) ošetriť EKD u pacientov s akútnou ischemickou CMP a tandemovou léziou len v prípade, ak je uzavretá veľká tepna prednej mozgovej cirkulácie a súčasne nepriechodný Willisov okruh alebo v prípade rekurentných embólií.³⁹

Na vytvorenie odporúčaní pre manažment IKD u pacientov s akútnou ischemickou CMP chýba dostatok dôkazov, ale podľa názoru expertov sa má endovaskulárna revaskularizácia lézie (stenting) realizovať len v hyperakútnej fáze po zvážení pomeru risk/benefit na základe lokalizácie a rizika krvácania.³⁹

Prevenca rekurencie CMP

Základnou terapeutickou metódou v tejto fáze je **antitrombotická liečba**, ktorá môže byť vhodne doplnená aj **revaskularizáciou** v istých špecifických klinických situáciách. Táto fáza **plynulo nadväzuje na fázu emergentnej liečby** (ak bola realizovaná).

U pacientov, ktorí z nejakého dôvodu nespĺnili kritéria pre indikáciu a realizáciu metód emergentnej fázy liečby, je prevencia rekurencie CMP samostatnou a hlavnou liečebnou fázou.

■ Antitrombotická liečba

Hlavným cieľom antitrombotickej, t.j. antikoagulačnej alebo antiagregačnej liečby je zníženie rizika rekurencie ischemickej CMP.

Odporúčania týkajúce sa danej liečby sa opierajú o dve štúdie: CADISS a TREAT-CAD. Štúdia CADISS (Cervical Artery Dissection in Stroke Study) porovnávala účinnosť a bezpečnosť antikoagulačnej a antiagregačnej liečby u pacientov s akútnou symptomatickou (neurologické príznaky/ischemická CMP) EKD. Štúdia nepreukázala sta-

tisticky významný rozdiel v miere recidívy ischemickej CMP po 3 a 12 mesiacoch.^{50,51}

Štúdia TREAT-CAD porovnávala liečbu kyselinou acetylsalicylovou a liečbu warfarínom u pacientov s akútnou ischemickou CMP a EKD. Sledovaným ukazovateľom bola skupina klinických výsledkov (recidíva iCMP, veľké krvácanie a smrť), teda kumulatívny ukazovateľ. Efektivita antiagregačnej alebo antikoagulačnej liečby v prevencii kumulatívneho ukazovateľa bola hodnotená na základe tzv. non-inferiority. Táto štúdia, na rozdiel od predošlej, nepreukázala non-inferioritu kyseliny acetylsalicylovej voči warfarínu.⁵²

Dôležitým poznatkom z oboch štúdií bola skutočnosť, že recidíva ischemickej CMP bola veľmi nízka. Spoločnosť ESO vydala odporúčania ohľadom antitrombotickej liečby pacientov s akútnou symptomatickou EKD, ktoré plne reflektujú nejednoznačný názor na spôsob antitrombotickej liečby, pretože ponechávajú voľbu na ošetrojúceho lekára. Ak sa zvolí antikoagulačná liečba, môže sa podľa konsenzu odborníkov použiť DOAK namiesto warfarínu. Dostatočné dáta k vytvoreniu odporúčaní pre manažment intrakraniálnej symptomatickej disekcie chýbajú, preto nie je možné vytvoriť aj patričné odporúčania. Avšak podľa konsenzu odborníkov sa má v takomto prípade preferovať antiagregačná liečba pred antikoagulačnou.³⁹

Nekončiacu dilemu voľby najvhodnejšej formy antitrombotickej liečby u pacientov s karotickou disekciou a ischemickou CMP sa pokúsila vyriešiť recentne publikovaná štúdia STOP-CAD.

Štúdia ukázala nižší výskyt ischemickej CMP u pacientov s neoklúznou symptomatickou karotickou disekciou liečených antikoagulačnou liečbou – aj keď bol štatisticky nevýznamný a štatisticky významne nižší výskyt ischemických CMP u pacientov s oklúznou symptomatickou karotickou disekciou liečených antikoagulačnou liečbou v porovnaní s antiagregačnou.⁵³ Štúdia však bola ihneď skritizovaná za nesprávny dizajn a závery, nakoľko sa jednalo o retrospektívnu štúdiu a autori využili inverznú pravdepodobnosť na hodnotenie liečby, čo môže byť nebezpečné v prípade retrospektívnej štúdie.⁵⁴

Otázka najvhodnejšej liečby u pacientov s akútnou EKD po ischemickej CMP tak naďalej zostáva nezodpovedaná a je delegovaná na zváženie ošetrojúceho lekára. Mala by trvať minimálne 6–12 mesiacov. Následne by sa mala ukončiť za predpokladu, že u pacienta nedošlo k recidíve ischemickej CMP a že je disekcia kompletne rekanalizovaná.

V opačnom prípade by po uplynutí 6–12 mesačného liečebného okna mala pokračovať dlhodobá mono-antiagregačná liečba.³⁹

Americké odporúčania z roku 2021 od dvoch spoločností AHA/ASA (American Heart Association/American Stroke Association) odporúčajú, podobne ako ESO, v prevencii rekurencie ischemickej CMP u pacientov s EKD komplikovanej CMP antitrombotickú liečbu o trvaní minimálne tri mesiace.⁵⁵

■ Revaskularizácia

Cieľom revaskularizácie karotickej disekcie v subakútnej fáze (po skončení emergentnej fázy liečby) je zníženie rizika rekurencie ischemickej CMP. V prípade EKD je miera rekurencie po akútnej fáze pomerne nízka, napríklad

3,1 % medzi 3. a 6. mesiacom v kombinovanej štúdii (CADISP + zmiešaná francúzsko-švajčiarska kohorta);⁵⁶ 2 % po 3 mesiacoch a 2,4 % po 1 roku v štúdii CADISS.^{51,57} Je vo všeobecnosti nižšia ako v prípade aterosklerotických lézií. Vzhľadom na vyššie uvedené by sa podľa konsenzu odborníkov nemala rutinne realizovať revaskularizácia reziduálnej stenózy alebo disekujúcej aneurizmy na podklade EKD, a to ani endovaskulárne, ani chirurgicky. Revaskularizácia by sa mala obmedziť len na tieto situácie: **opakujúce sa ischemické príhody napriek optimálnej antitrombotickej liečbe, nárast priemeru disekujúcej aneurizmy spôsobujúcej útlak okolitých štruktúr.**³⁹

Približne rok po zverejnení odporúčaní ESO bol publikovaný systematický prehľad a meta-analýza o úlohe stentingu karotickej disekcie.

Štúdia, okrem iného, hodnotila výsledky karotického stentingu pomocou vybraných klinických parametrov, t.j. mortalita, cerebrovaskulárna udalosť (TIA alebo ischemická CMP), dobrý funkčný stav hodnotený ako mRS (modifikovaná Rankinova škála) 0–2 body medzi skupinou pacientov s karotickou disekciou bez neurologickej symptomatológie a skupinou pacientov s karotickou disekciou a rekurenciou neurologických symptómov napriek inicializácii antitrombotickej liečby.⁵⁸

Mortalita bola podobná u oboch skupín avšak stentovanie po zlyhaní farmakoterapie preukázalo superiorné výsledky pre dobrý funkčný stav (94,12 % vs. 88,46 %); in-stent trombózu (0 % vs. 5,24 %) a cerebrovaskulárnu príhodu (3,33 % vs. 5,02 % pre CMP) a (0 % vs. 2,72 % pre TIA) oproti pacientom s EKD bez neurologickej symptomatológie. Výsledky tejto práce kopírujú odporúčania ESO a sú proti rutinnému stentovaniu karotickej disekcie.⁵⁸

Podobne, americké odporúčania AHA/ASA z roku 2021 odporúčajú zvážiť karotický stenting len u tých pacientov s EKD a ischemickou CMP, u ktorých došlo k recidíve ischemickej CMP napriek optimálnej antitrombotickej liečbe.⁵⁵ Americká spoločnosť AHA v roku 2024 vydala ďalšie vedecké stanovisko k manažmentu karotickej disekcie, pričom karotický stenting v subakútnej fáze by sa mal zvážiť len zriedkavo v prípade klinicky symptomatickej cerebrálnej ischemie napriek maximálne vyťaženej konzervatívnej medikamentóznej liečbe.⁵⁹

● Liečba pacientov so spontánnou karotickou disekciou bez ischemickej CMP

Liečba tejto skupiny pacientov sa riadi rovnakými cieľmi, princípmi a postupmi ako fáza **prevencia rekurencie CMP** u pacientov s karotickou disekciou a ischemickou CMP.

Traumatická karotická disekcia

Optimálny manažment pacientov s traumatickou disekciou je zriedkavo jednoznačný a zvyčajne je potrebný premyslený multidisciplinárny prístup. Oproti spontánnej karotickej disekcii je traumatická spojená s určitými špecifikami. U pacientov s traumou sú často v popredí symptómy a znaky traumatických lézií, karotická disekcia tak môže byť ľahko prehliadnutá. Navyše sú takíto pacienti často v bezvedomí alebo intubovaní v celkovej anestéze. Neurologický deficit tak nie je možné zhodnotiť, čo má za následok jednak prehliadnutie karotickej disekcie ako aj prekročenie časového okna špecifickej liečby – mechanickej trombektómie. Navyše, liečba musí byť zohľadnená

v kontexte celého rozsahu polytraumy. Použitie antiagregačnej alebo antikoagulačnej liečby môže byť komplikované krvácaním zo sprievodných nevaskulárnych poranení. Správna liečba týchto pacientov si často vyžaduje nájdenie rovnováhy medzi léziami, ktoré majú protichodné stratégie manažmentu.

Základnými prvkami manažmentu traumatickej disekcie karotídy sú: **(1) antitrombotická liečba na prevenciu ischemickej cievnej mozgovej príhody, (2) pozorovanie a (3) endovaskulárna liečba vo vybraných prípadoch.**

■ Antitrombotická terapia

Tromboembolizmus je primárnym mechanizmom ischemickej cievnej mozgovej príhody u pacientov s traumatickou disekciou ACI, preto antitrombotická liečba predstavuje základnú liečebnú stratégiu. V rámci antitrombotickej liečby sa môžu použiť antiagregancia aj antikoagulancia. Antiagregancia ponúkajú výhody oproti systémovej antikoagulácii jednoduchším podávaním a zdá sa, že sú aj relatívne dobre tolerované u pacientov s polytraumou. Navyše, antiagregancia majú teoretickú výhodu, pretože aktivácia krvných doštičiek je významnou zložkou protrombotického stavu spojeného s tupou traumou. Antitrombotická liečba nesporne znižuje riziko cievnej mozgovej príhody aj mortalitu.

Na druhej strane môže zvyšovať riziko krvácania najmä pri poranení mozgu a solídnych orgánov. Toto riziko sa však zdá relatívne nízke oproti výhodám, ktoré táto liečba prináša.^{60–64}

■ Mechanická trombektómia

Endovaskulárne odstránenie trombu z intrakraniálnych tepien je potrebné zvažovať u pacientov s ischemickou CMP, traumatickou disekciou karotídy a intrakraniálnym uzáverom tepny, ak sú splnené časové, anatomicke a klinické kritéria, nakoľko je podanie systémovej trombolýzy u pacientov s traumou nemožné.^{60–64}

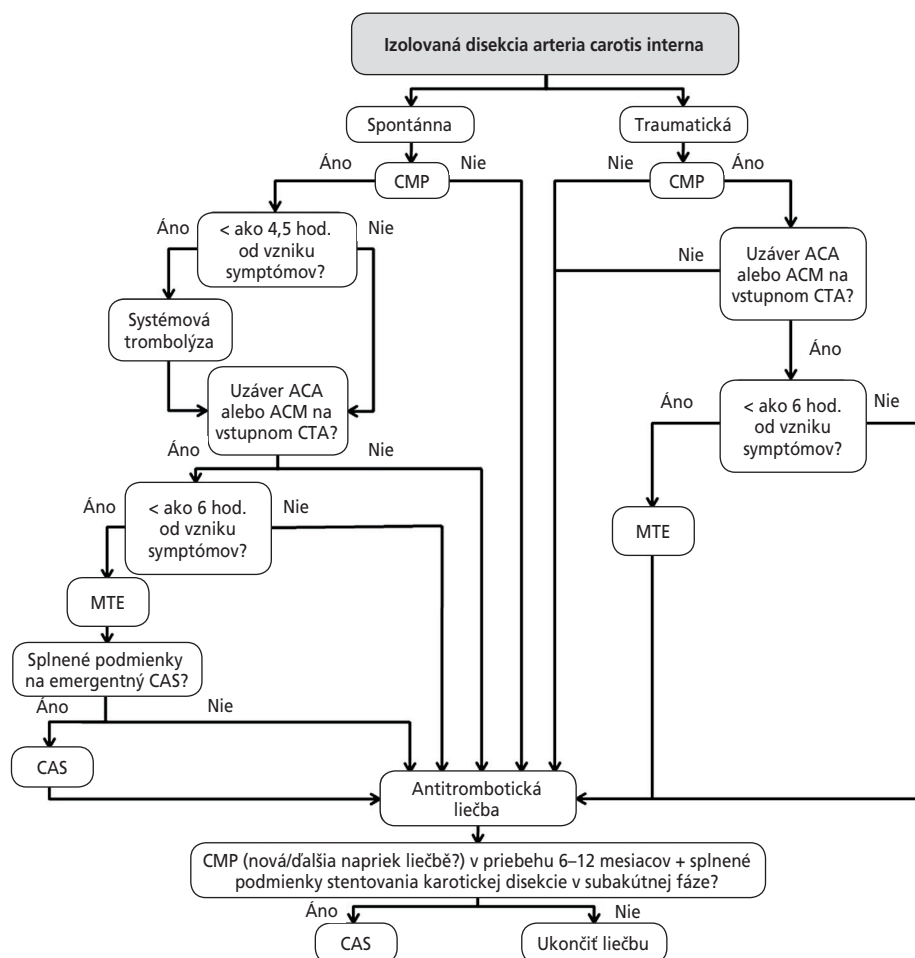
■ Stenting

Rutinná implantácia stentu ako prídavná liečba k antitrombotickej terapii traumatickej disekcie ACI sa v prevencii ischemickej CMP neodporúča. Implantácia stentu je podmienená podávaním duálnej antiagregačnej liečby čo zvyšuje riziko krvácania. Mono-antiagregačná liečba zasa zvyšuje riziko trombózy stentu s následnou rozsiahlou mozgovou ischemiou. Stenting traumatickej karotickej disekcie sa môže zvážiť u: (i) pacientov s opakujúcimi sa symptómami napriek medikamentóznej liečbe, (ii) pacientov s hemodynamickou hypoperfúziou (postihnutím viacerých ciev alebo slabým kolaterálnym obehom), (iii) pacientov s expandujúcou alebo symptomatickou pseudoaneurizmou.^{60–64}

Obrázok 12 schematicky znázorňuje manažment izolovanej karotickej disekcie v jednotlivých krokoch. **Tabuľka 2** zobrazuje indikácie k stentingu disekcie extrakraniálneho úseku a. carotis interna.

Prognóza a prirodzený priebeh disekcie

Ak má EKD charakter stenózy, potom dochádza časom k redukcii závažnosti stenózy – remodelácii alebo ku



Obr. 12 – Schematický manažment izolovanej disekcie extrakraniálneho úseku a. carotis interna. ACA – a. cerebri anterior; ACM – a. cerebri media; CAS – karotický stenting; CMP – cievná mozgová príhoda; CTA – CT angiografia; MTE – mechanická trombektómia.

Tabuľka 2 – Indikácie k stentingu disekcie extrakraniálneho úseku a. carotis interna

Karotický stenting spontánnej karotickej disekcie v emergentnej fáze^{39,47–49}

- Významná reziduálna stenóza extrakraniálneho úseku karotídy po intrakraniálnej revaskularizácii (MTE)^{47,48}
- Endoluminálny trombus s embolizačným potenciálom^{47,48}
- Nedostatočná priechodnosť Willisovho okruhu⁴⁷
- Uzáver veľkej tepny prednej cirkulácie (ACA, ACM) a súčasne uzáver vnútornej karotídy (na podklade disekcie) pri nepriechodnom Willisovho okruhu alebo v prípade rekurentnej embólie (odporúčanie založené na „Konsenzuálnej dohode“)³⁹

Karotický stenting spontánnej karotickej disekcie po emergentnej fáze^{39,55,58,59}

U pacientov s reziduálnou stenózou po disekcii alebo s disekujúcou aneuryzmou a/alebo:

- S opakujúcimi sa ischemickými príhodami napriek optimálnej antitrombotickej liečbe (trieda odporúčaní: 2b, úroveň dôkazov: C podľa AHA/ASA 2021)⁵⁵
(Kvalita dôkazov: Veľmi nízka +; Sila odporúčania: –; odporúčanie založené na „Konsenzuálnej dohode odborníkov“)³⁹
- S nárastom priemeru disekujúcej aneuryzmy spôsobujúcej útlak okolitých štruktúr
(Kvalita dôkazov: Veľmi nízka +; Sila odporúčania: –; odporúčanie založené na „Konsenzuálnej dohode odborníkov“)³⁹

Stenting traumatickej karotickej disekcie v subakútnej fáze^{60–64}

- Opakujúce sa symptómy CMP napriek medikamentózne liečbe
- Významná hemodynamická hypoperfúzia (postihnutie viacerých ciev alebo slabý kolaterálny obeh)
- Expandujúca alebo symptomatická pseudoaneuryzma

ACA – a. cerebri anterior; ACM – a. cerebri media; AHA/ASA – American Heart Association / American Stroke Association; CMP – cievná mozgová príhoda; MTE – mechanická trombektómia.

kompletnej rekanalizácii (vyhojeniu) v 33–90 % prípadov v priebehu 6 mesiacov od vzniku disekcie.^{65,66} EKD charakteru kompletneho uzáveru sa môže spontánne zrekanalizovať (vyhojiť) asi v 30–60% prípadov v priebehu 6 mesiacoch, medián sú asi 4 mesiace,^{67,68} pričom hojenie disekcie môže prebiehať až do 12 mesiacov od jej vzniku. Po tomto intervale je už vyhojenie raritné.⁶⁹

Disekujúca aneuryzma je ďalšou komplikáciou karotickej disekcie, ktorá môže kompletne zaniknúť alebo sa môže zmenšiť u 40–50 % pacientov, ale môže dôjsť aj k zväčšeniu.^{57,70} V štúdií CADISS bola jej incidencia 14,5 % po 3 mesiacoch.⁵⁷ V priebehu ďalšieho sledovania sa výskyt zvyšuje na 19,4 % pri mediáne 6 mesiacov.⁷¹

Disekujúca aneuryzma karotickej tepny má benígnu prognózu^{57,70} a nie je spojená so zvýšeným rizikom recidívy CMP alebo ruptúry.⁷²

Záver

Karotická disekcia je závažné ochorenie pre riziko rozvoja ischemickej cievnej mozgovej príhody, a to najmä u mladých pacientov. Jej manažment si preto vyžaduje skúsených odborníkov. Základným terapeutickým pilierom je antitrombotická (antiagregačná alebo antikoagulačná) liečba u všetkých pacientov postihnutých karotickou disekciou. Systémová trombolytická liečba a endovaskulárna mechanická trombektómia intrakraniálnych vetiev a. carotis interna je indikovaná v emergentnom režime u pacientov s karotickou disekciou komplikovanou ischemickou CMP, ak sú splnené všetky indikačné kritéria k danej liečbe (časové, klinické, zobrazovacie). Karotický stenting sa u pacientov s karotickou disekciou nemá vykonávať rutinne, ale len v špecifických indikáciách (klinických situáciách), a to ani u pacientov s karotickou disekciou komplikovanou ischemickou CMP.

Prehlásenie autorov o možnom stretnutí záujmov

Autori prehlasujú, že nemajú žiaden konflikt záujmu týkajúci sa tohto článku.

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The LACE Index: A Predictor of Mortality and Readmission in Cardiovascular Diseases

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SOUHRN

Index LACE je predikční nástroj používaný ve zdravotnictví pro odhad rizika opětovné hospitalizace pacientů po jejich propuštění z nemocnice. Zkratka LACE vznikla spojením slov (v angličtině) délka pobytu v nemocnici (length of stay), oprávněnost příjmu (acuity of admission), zátěž komorbiditami (comorbidity burden) a počet návštěv oddělení akutního příjmu (emergency department [ED] visits). Jedná se o jednoduchý skórovací systém, ve kterém se přidělují body za každý z uvedených čtyř faktorů podle jejich přítomnosti/nepřítomnosti a závažnosti; sečtením bodů vznikne skóre indexu LACE. Index LACE často používají poskytovatelé zdravotních služeb pro vyhledávání pacientů s potenciálně vyšší pravděpodobností opětovného příjmu do nemocnice po jejich propuštění. Identifikaci pacientů s vyšším skóre LACE umožňuje poskytovatelům zdravotních služeb reagovat a poskytovat dodatečnou podporu nebo finanční prostředky, které by pomohly snižovat počty opětovných hospitalizací. Index LACE může být užitečný při změnách v léčbě a poskytování péče a při plánování propuštění pacienta; lze jej začlenit do rozhodovacích procesů v klinické praxi s cílem optimalizovat výsledný stav pacientů. Celkové skóre indexu LACE lze využít ke stratifikaci pacientů do různých kategorií rizika, například nízkého, středně vysokého a vysokého rizika opětovného příjmu do nemocnice. Tyto informace mohou pomoci poskytovatelům zdravotní péče při stanovování priorit v intervencích a při účinném přidělování finančních prostředků s cílem snižovat počty opětovných hospitalizací a zlepšovat péči o pacienty. Nicméně je nutno poznamenat, že index LACE je pouze jedním z mnoha podobných nástrojů a při rozhodování v této oblasti je třeba použít i klinický úsudek a provést individuální vyšetření pacienta s kardiovaskulárním onemocněním.

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ABSTRACT

The LACE index is a predictive tool used in healthcare to estimate the risk of hospital readmission for patients who have been discharged from the hospital. LACE stands for length of stay, acuity of admission, comorbidity burden, and emergency department (ED) visits. It is a simple scoring system that assigns points to each of these four factors based on their presence and severity and then sums up the points to calculate the LACE index score. The LACE index is often used by healthcare providers to identify patients who may be at higher risk of being readmitted to the hospital after discharge. By identifying patients with higher LACE scores, healthcare providers can potentially intervene and provide additional support or resources to help prevent readmission. The LACE index can be useful in guiding care transitions and discharge planning and can be incorporated into clinical decision-making processes to optimise patient outcomes. The total score calculated from the LACE index can be used to stratify patients into different risk categories, such as low, moderate, or high risk of hospital readmission. This information can help healthcare providers prioritise interventions and allocate resources effectively to prevent hospital readmissions and improve patient care. However, it's important to note that the LACE index is just one tool among many, and clinical judgement and individualised assessment of cardiovascular patients should also be considered in making care decisions.

Keywords:

Comorbidity burden

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LACE index

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Introduction

Canada, Australia, and the UK employ the US-created readmission rate figure for quality and cost reduction. The Affordable Care Act's (ACA's) Hospital Readmission Reduction Programme (HRRP) penalises 30-day readmission rates over the US average. Local healthcare quality improvement may lower readmission rates and save money, benefiting the global economy. More advanced methods are needed to predict readmission risk before discharge.^{1,2} Unexpected hospital readmissions are costly. 30-day unplanned readmission shows the initial method failed. The Centers for Medicare and Medicaid Services (CMS) reports \$17 billion in hospital readmissions. CMS included chronic disorders with high hospitalisation rates in the 2010 Hospital Readmission Reduction Programme (HRRP).³

Several methods predict readmissions.^{3,4} The US and Canada use LACE extensively. The LACE score predicts 30-day readmission or death for medical and surgical patients. Administrative data confirmed the model. Acuity, duration, comorbidities, and six-month Emergency Department (ED) visits are included. 30-day readmission risk is 0–19 and 10+.³ High scores predict rehospitalization. Straightforward, therapeutically helpful.^{5–9} 30-day unplanned readmissions assessed acute care quality. UK hospitals needed emergency readmission 28 days following discharge.¹⁰ The Western Australian Ministry of Health judged quality by unplanned 30-day surgical and all-cause hospital readmissions.¹¹ Its application to diverse populations and locations is unknown.

South Korea's healthcare system is shown in the unplanned 30-day readmission after hospital discharge.¹² Nonetheless, mortality and administrative statistics can be used to calculate the readmission rate. As a result, the use of the LACE index has increased. Quality and cost depend on the 30-day hospital readmission risk prediction. In our opinion, we have not previously found a review of all cardiovascular diseases in the literature. Therefore, we addressed the value of the LACE score in determining mortality and readmissions in all cardiovascular diseases with this review.

Heart failure (HF)

Readmission plagues American hospitals. Medicare and Medicaid increasingly prioritise readmission rates, treatment quality, and cost. 15% of Medicare-covered hospital patients are readmitted within 30 days, costing \$15 billion, according to the Agency for Healthcare Research and Quality. Addressing and predicting HF readmission, a primary cause of over 65 hospital admissions, reduces cost, morbidity, and death.^{13,14}

Hospital Score, LACE index, and LACE+ index are validated readmission prediction measures; however, little research has explored their usage in HF patients. Yazdan-Ashoori et al. found higher LACE index scores predicted 30-day HF readmission when the threshold was increased to 13. Australian researchers developed a 30-day readmission prediction model for HF with preserved ejection fraction (HFpEF) and HF with reduced EF (HFrEF) patients.

Clinical, administrative, sociodemographic, and mental health data were modelled.^{15,16}

Van Walraven et al.³ created and verified LACE. The Ontario population-based LACE+ index was more discriminating than the LACE index (C-statistic 0.771, 95% CI 0.767–0.775). The LACE+ score did not predict brain tumour patients' 30-day readmissions. Brain tumour patients with the LACE+ score had limited specificity for 30-day readmission (C-statistic = 0.58). HFpEF and brain tumour patients reported similar results. Certain groupings may not be predicted by LACE+. ^{17,18}

ED visits predicted readmissions. ED visits may increase readmissions. They may have greater chronic illnesses. Chronic disease increases ED visits, hospital admissions, and hospitalisations. Extreme age may cause it. Age, Charlson Comorbidity Index (CCI) score, and hospital stay did not impact readmission. Myocardial infarction (MI) and peripheral vascular disease (PVD) patients reported more hospital readmissions due to chronic illnesses. Medicare data suggests diabetes, MI, PVD, and stroke may predict congestive HF (CHF) readmissions. MI and CHF increased readmissions. Both chronic disorders typically co-exist.^{19–23} Wang et al.²⁴ observed that the LACE score may not properly predict 30-day CHF readmissions. High-risk CHF readmissions may be associated with frequent ED visits, MI, or PVD.

Acute myocardial infarction (AMI)

Acute coronary syndrome (6.4%) was the most common index diagnosis in the initial LACE investigation, and the 30-day all-cause unplanned readmission and mortality rate was 6.0%. The most common index procedure was angioplasty or coronary artery bypass graft surgery (4.6% prevalence), with a 4.6% 30-day all-cause unplanned readmission and mortality rate. Rates may vary according to stable angiography patients. So, this apparently healthier group may explain the lower AMI readmission rate.^{3,25}

Duration of stay and number of ED visits in the preceding 6 months drove the logistic regression analysis of LACE index factors. These findings confirm recent studies suggesting that a few fundamental factors may predict complex outcomes like readmission after nonemergent noncardiac surgery. Prediction models may not work in homogenous populations with comorbidities like the Charlson Index. In the prior experiment (with a more heterogeneous cohort), dementia and acquired immunodeficiency syndrome (AIDS) were more common, while this research found few cases. The Charlson Comorbidity Index may have been better.²⁵

Labrosciano et al. discovered that the LACE score predicted post-AMI readmission in angiography patients. Length of stay and past 12-month ED encounters best predict 30-day all-cause unplanned readmission (and combined readmission and death). These two traits are simple to detect and may help doctors identify patients at greater risk of readmission and give extra care, treatments, and therapy to reduce readmissions and deaths, but larger samples are needed to see whether they consistently predict readmission.²⁵

Pulmonary embolism

The LACE index may be used as a tool to assess the risk of readmission or death within 30 days after discharge for patients who have been hospitalised for pulmonary embolism, along with other relevant clinical information. However, the LACE index should be used in conjunction with clinical judgement and other assessment tools to make appropriate healthcare decisions for individual patients. It is always important to consult with a qualified healthcare professional for an accurate assessment and management of patients with pulmonary embolism or any other medical condition.

Stroke

The LACE index is not typically used in the context of assessing patients with stroke. For stroke, there are other risk prediction tools that are more commonly used, such as the CHADS₂ and CHA₂DS₂-VASc scores, which are used to estimate the risk of stroke and guide anticoagulation therapy in patients with atrial fibrillation, a common risk factor for stroke. The LACE index, which stands for length of stay, acuity of admission, comorbidity, and emergency department visits, is specifically designed for patients with CHF and is not directly applicable for assessing the risk of stroke or stroke-related outcomes. Stroke risk assessment typically involves evaluating factors such as age, sex, hypertension, diabetes, smoking status, prior history of stroke or transient ischemic attack (TIA), and other relevant clinical information to determine the risk of stroke and guide appropriate management strategies.

Diabetes

The LACE index is not typically used in the context of assessing patients with diabetes. There are other risk prediction tools that are commonly used in the management of diabetes, such as the American Diabetes Association (ADA) Risk Calculator, which estimates the risk of developing diabetes in the next 5 years based on factors such as age, sex, body mass index (BMI), family history of diabetes, blood pressure, and others. In the management of diabetes, healthcare professionals also use various other tools, guidelines, and clinical judgment to assess and manage patients, including glycemic control, blood pressure management, lipid management, lifestyle modifications, and other relevant interventions based on individual patient characteristics and clinical considerations.

Peripheral vascular disease

It may not be directly applicable to assessing patients with vascular disease, as it is specifically designed for CHF. Vascular disease refers to a group of conditions that affect the blood vessels, including arteries and veins, throughout the body. This can include conditions such as PVD, carotid artery disease, aortic aneurysm, deep vein thrombosis (DVT), and others. In the management of vascular

disease, healthcare professionals may use other specific risk assessment tools and guidelines that are relevant to the specific condition being evaluated. For example, in the case of PAD, the Fontaine or Rutherford classification systems may be used to assess the severity of the disease and guide management decisions. In the case of carotid artery disease, the degree of stenosis (narrowing) of the carotid artery, as determined by imaging studies such as carotid ultrasound or angiography, is often used to determine the risk of stroke and guide management decisions.

Recent studies

LACE index values of 4 are related to higher COVID-19 hospital admissions and deaths, consistent with non-COVID-19 studies. COVID-19 patients have a greater risk. As it predicts mortality, the LACE score should identify high-risk COVID-19 patients.²⁶ Unplanned 30-day readmission after stroke was increased in high LACE+ index groups. This verifies the LACE+ stroke readmission prediction approach.²⁷ Cho et al.²⁸ showed that national cohort data may identify older people at high risk for all-cause mortality using the LACE score. These findings influence post-discharge patient management.

The HOSPITAL score and LACE index predicted 30-day and 1-year death in older multimorbid polypharmacy patients. These simple parameters may predict post-hospitalisation mortality in older multimorbid people.²⁹ Belouali et al.³⁰ identified social determinants of health variables that governments and healthcare systems might address to prevent readmissions. Sun et al.³¹ discovered that only specific comprehensive geriatric assessments, mobility disabilities, and gender components independently predicted readmission. LACE and HOSPITAL scores did not discriminate 30-day hospitalisation in all and subgroup participants. To predict 30-day readmissions, this patient sample requires additional identifiers.

LACE and HOSPITAL readmission risk-prediction algorithms performed comparably in a diverse patient cohort at two university medical centres in Houston, Texas. These readmission risk factors may help identify in-house patients at high risk for readmission, so early intervention resources may reduce unplanned readmission.³² Regmi et al.³³ discovered that the HOSPITAL score and the RAHF scale predicted 30-day readmissions differentially in HF patients by race and gender, while the LACE index did not. Borja et al.³⁴ discovered the LACE+ score may predict 30- and 90-day readmissions after single-level lumbar fusion.

The LACE score predicts recurrent hospitalisations and short- and medium-term mortality after hospital discharge, particularly in younger adults.³⁵ LACE scores indicate hospital readmission-prone youth. LACE index scores above 4 reduce readmissions.³⁶ The upgraded LACE-Cranial model predicts short-term postdischarge mortality and readmissions better than the unmodified LACE index.³⁷ Lin et al. recommended giving non-linear classification algorithms greater attention since they produce large risk score discrepancies.³⁸ The EQ-5D-3L mobility, self-care, and total sum scores improve the LACE index 30-day readmission prediction and are associated with readmissions

Table 1 – The main topic points of recent studies

Reference no.	Authors	Subjects	Main theme
[26]	Fluck et al.	COVID-19 patients	LACE index values of 4 are related to higher COVID-19 hospital admissions and deaths, consistent with non-COVID-19 studies. As it predicts mortality, the LACE score should identify high-risk COVID-19 patients.
[27]	Jun et al.	Stroke patients	Unplanned 30-day readmission after stroke was increased in high LACE+ index groups. This verifies the LACE+ stroke readmission prediction approach.
[28]	Cho et al.	A nationwide population-based study	National cohort data may identify older people at high risk for all-cause mortality using the LACE score. These findings influence post-discharge patient management.
[29]	Aubert et al.	Older patients	The HOSPITAL score and LACE index predicted 30-day and 1-year death in older multimorbid polypharmacy patients. These simple parameters may predict post-hospitalisation mortality in older multimorbid people
[30]	Belouali et al.	Patients	Social determinants of health variables that governments and health systems might address to prevent readmissions.
[31]	Sun et al.	Older Adults	LACE and HOSPITAL scores did not discriminate 30-day hospitalisation in all and subgroup participants. To predict 30-day readmissions, this patient sample requires additional identifiers.
[32]	Jones et al.	Patients	LACE and HOSPITAL readmission risk-prediction algorithms performed comparably in a diverse patient cohort at two university medical centres in Houston, Texas. These readmission risk factors may help identify in-house patients at high risk for readmission, so early intervention resources may reduce unplanned readmission.
[33]	Regmi et al.	Heart failure patients	The HOSPITAL score and the RAHF scale predicted 30-day readmissions differentially in HF patients by race and gender, while the LACE index did not.
[34]	Borja et al.	Patients with complete information who underwent single-level, posterior-only lumbar fusion	The LACE+ score may predict 30- and 90-day readmissions after single-level lumbar fusion.
[35]	Heppleston et al.	Patients	The LACE score predicts recurrent hospitalisations and short- and medium-term mortality after hospital discharge, particularly in younger adults.
[36]	Han et al.	Children	LACE scores indicate hospital readmission-prone youth. LACE index scores above 4 reduce readmissions.
[37]	Jin et al.	Patients undergoing cranial neurosurgery	The upgraded LACE-Cranial model predicts short-term postdischarge mortality and readmissions better than the unmodified LACE index.
[38]	Lin et al.	Taiwan population	Non-linear classification algorithms greater attention since they produce large risk score discrepancies.

and death.³⁹ The primary care provider's (PCP's) judgement outperforms the LACE score in identifying high-risk readmission patients. This score may help PCPs identify discharged patients who require more intensive follow-up.⁴⁰ The main topic points of recent studies were shown in Table 1.

Conclusion

Many models predict hospital readmissions. The easy-to-use LACE index discriminates effectively. Therefore, we carried out an updated review of the use of the LACE score to predict mortality and readmission in cardiovascular diseases. Our review addressed firstly the value of the LACE score in determining mortality and readmissions in all cardiovascular diseases. Value-based medical care hos-

pitals may employ the LACE index. This study will help healthcare workers avoid 30-day readmissions by revealing the most effective strategies.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Ethical statement

The work was conducted in accordance with Helsinki declaration.

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Potential of pentoxifylline in preventing reperfusion injury after surgery on limb ischemia: a literature review

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SOUHRN

Kontext: Pro akutní ischemii končetin (acute limb ischemia, ALI) je charakteristická náhlá ztráta průtoku krve v dolních končetinách v důsledku embolie nebo trombózy. Léčba ALI je nesmírně důležitá, protože popsaný stav může vést k těžkým komplikacím včetně ischemicko-reperfučního poškození (IRI) během revaskularizačního výkonu. Při IRI dochází ke složitým funkčním a strukturálním změnám po obnově průtoku krve, vedoucím k rozvoji zánětu a k oxidačnímu stresu. Tyto patologické procesy mohou zhoršit poškození tkání a bránit zotavení. Ukázalo se, že pentoxifylin by mohl dobře sloužit jako potenciální lék díky jeho schopnosti zlepšit průtok krve a snížit zánětlivou odpověď.

Cíl: Tento přehled literatury se zabývá úlohou pentoxifylinu (PTX) při zmírňování ischemicko-reperfučního poškození spojeného s akutní ischemií končetin jako stavu významně ztěžujícího stanovení prognózy a zhoršujícího přežití.

Metody: Tento přehled je syntézou poznatků z četných preklinických a klinických studií zkoumajících ochranné účinky PTX v různých modelech IRI. Mezi primární mechanismy účinku patří inhibice tvorby faktoru aktivujícího krevní destičky (platelet-activating factor, PAF), tlumení zánětu a zlepšování hemoreologických parametrů, které dohromady posilují mikrocirkulaci během reperfuze.

Výsledky: Pomocí modelů ischemie kosterního svalu a mozku se prokázalo se, že PTX účinně omezuje nekrózu tkání a zlepšuje výsledný stav. Navíc se ukázalo, že PTX omezuje poškození plic v důsledku IRI. Tento přehled rovněž vyzdvihuje potenciální přínos kombinace léčby, zvláště ve spojení s antioxidantem jako vitamínem C, která může dále posílit ochranné účinky PTX.

Závěry: Pentoxifylin tak představuje slibný lék pro prevenci reperfučního poškození po ischemických příhodách, jako je ALI. Nicméně – aby bylo možno optimalizovat jeho využití a potvrdit jeho účinnost u různých lidských populací – je zapotřebí dalších klinických studií.

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ABSTRACT

Background: Acute limb ischemia (ALI) is characterized by a sudden loss of blood flow to the lower limbs, often resulting from embolism or thrombosis. Management of ALI is critical, as it can lead to severe complications, including ischemia-reperfusion injury (IRI) during revascularization procedures. IRI involves complex functional and structural changes following restoration of blood flow, leading to inflammation and oxidative stress. These pathological processes can exacerbate tissue damage and impede recovery. Pentoxifylline has emerged as a potential therapeutic agent due to its ability to improve blood flow and reduce the inflammatory response.

Aim: This literature review investigates the role of pentoxifylline (PTX) in reducing ischemia-reperfusion injury associated with acute limb ischemia (ALI), a condition that poses significant challenges to prognosis and survival.

Methods: This review synthesizes findings from multiple preclinical and clinical studies examining the protective effects of PTX across different models of IRI. The primary mechanisms of action include inhibition of platelet-activating factor (PAF) production, reduction of inflammation, and enhancement of hemorheological properties, which collectively improve microcirculation during reperfusion.

Results: PTX has demonstrated efficacy in reducing tissue necrosis and improving outcomes in models of skeletal muscle and cerebral ischemia. In addition, it has been shown to reduce lung damage from IRI. This review also highlights the potential benefits of combination therapy, particularly with antioxidants such as vitamin C, which may further enhance the protective effects of PTX.

Conclusions: Pentoxifylline shows promise as a therapeutic agent to prevent reperfusion injury after ischemic events such as ALI. However, further clinical trials are needed to optimize its application and confirm its efficacy in human populations.

Keywords:

Acute limb ischemia

Antioxidant

Limb ischemia

Pentoxifylline

Reperfusion injury

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Introduction

Acute limb ischemia (ALI) is a lower extremity ischemia that occurs suddenly and has a poor prognosis, not only in the extremities but also in survival. According to research in the UK, the incidence of embolism, thrombosis due to occlusive atherosclerotic lesions, and stent or graft-related thrombosis is quite high.¹ Speed and accuracy in establishing and managing are the keys to successful ALI management. ALI can be classified based on clinical findings and Doppler ultrasound results from related blood vessels. Management can be given according to the ALI classification, ranging from heparinization, revascularization with thrombolytic agents, endovascular management, and surgery to amputation. In revascularization management, side effects are not uncommon, namely vascular reperfusion injury, also known as ischemia-reperfusion injury (IRI).

IRI is a term used to describe functional and structural changes that appear during the recovery of blood flow after a period of ischemia. This may occur as a result of a vicious cycle of vascular, endothelial and mitochondrial dysfunction, with reduced local perfusion, intense dysfunctional changes, edema and many other implications leading to the release of proinflammatory cytokines and free radicals.^{2,3} This occurs after ischemic tissue is reperfused, the influx of molecular oxygen catalyzes xanthine oxidase to degrade hypoxanthine to uric acid and thereby release the highly reactive superoxide anion ($O_2^{\cdot-}$). The main consequence of hydroxyl radical production is peroxidation of the lipid structure of the cell membrane resulting in the production and release of systemic proinflammatory eicosanoids, impaired cell permeability and ultimately cell death.³ Pentoxifylline (PTX), a nonspecific phosphodiesterase derivative of xanthine, has emerged as a promising agent that can attenuate the inflammatory response through several mechanisms.⁴ This drug improves blood flow by reducing viscosity and enhancing red blood cell flexibility.⁵ Pentoxifylline, a non-selective phosphodiesterase inhibitor, has been extensively studied for its potential to mitigate reperfusion injury following ischemic events. This literature review synthesizes findings from various studies focusing on the effects of pentoxifylline in different models of IRI.

Acute limb ischemia

Acute limb ischemia (ALI) is a rapid reduction in lower limb blood flow due to acute occlusion of a peripheral

artery that can result in amputation, regardless of the underlying cause unless appropriate treatment is provided.¹ Acute limb ischemia occurs as a result of an acute (<2 weeks) reduction in blood supply.^{6,7} ALI is a vascular emergency and requires rapid revascularization with an endovascular, surgical, or hybrid approach to avoid limb loss. Sudden ischemia affects all the metabolically active tissues of the limb including skin, muscles, and nerves.

ALI is most commonly caused by arterial thrombosis due to plaque development and complications which account for 40% of total events, followed by arterial embolism (30%), graft thrombosis (20%), popliteal aneurysm thrombosis (5%) and trauma (5%).⁸

The classic term for ALI patients is known as the "6 Ps": pain, pallor, paralysis, pulse deficit, paresthesia and poikilothermia are important keywords for detecting ALI.⁹ Steps for emergency diagnosis are described, emphasizing the role of clinical and imaging data, especially duplex ultrasonography, CT angiography, and digital subtraction angiography. Rutherford criteria are used to assess the severity of ALI (Table 1).

A wide range of therapeutic techniques ranging from pharmacological thrombolysis to interventional techniques to surgical revascularization and minor or major amputation if necessary.⁸ After the diagnosis of ALI, intravenous injection of unfractionated heparin (50–100 units/kg) is given immediately to prevent the development of secondary thrombosis if heparin is not contraindicated. ALI with a severity classification of III is irreversible ischemia and requires amputation. Patients with extensive ischemia due to high occlusion and when time has passed since onset, have a high risk of severe ischemia-reperfusion injury; thus, amputation of the limb may be necessary to prioritize the patient's life.¹

Reperfusion injury

Ischemia-reperfusion injury is an event where reperfusion can worsen cell damage that has been caused by ischemia. Some of the most common pathologies that result in ischemia are sepsis, cerebral infarction, acute coronary syndrome, organ transplantation, and limb injury. A sudden increase in blood and oxygen flow after revascularization can trigger activation of the inflammatory process, release of cytokines, and result in further damage to cells and their membranes. The organs usually involved in vascular reperfusion injury are the heart, brain, liver,

Table 1 – Stages of acute limb ischemia based on Rutherford classification¹⁰

Stage	Prognosis	Findings		Doppler signal	
		Sensory loss	Muscle weakness	Arterial	Venous
I	Limb viable, not immediately threatened	None	None	Audible	Audible
IIa	Limb marginally threatened, salvageable if promptly treated	Minimal (toes)	None	Often inaudible	Audible
IIb	Limb immediately threatened, salvageable with immediate revascularization	More than toes, pain at rest	Mild or moderate	Inaudible	Audible
III	Limb irreversibly damaged, major tissue loss or permanent nerve damage inevitable	Profound, anesthetic	Paralysis (rigor)	Inaudible	Inaudible

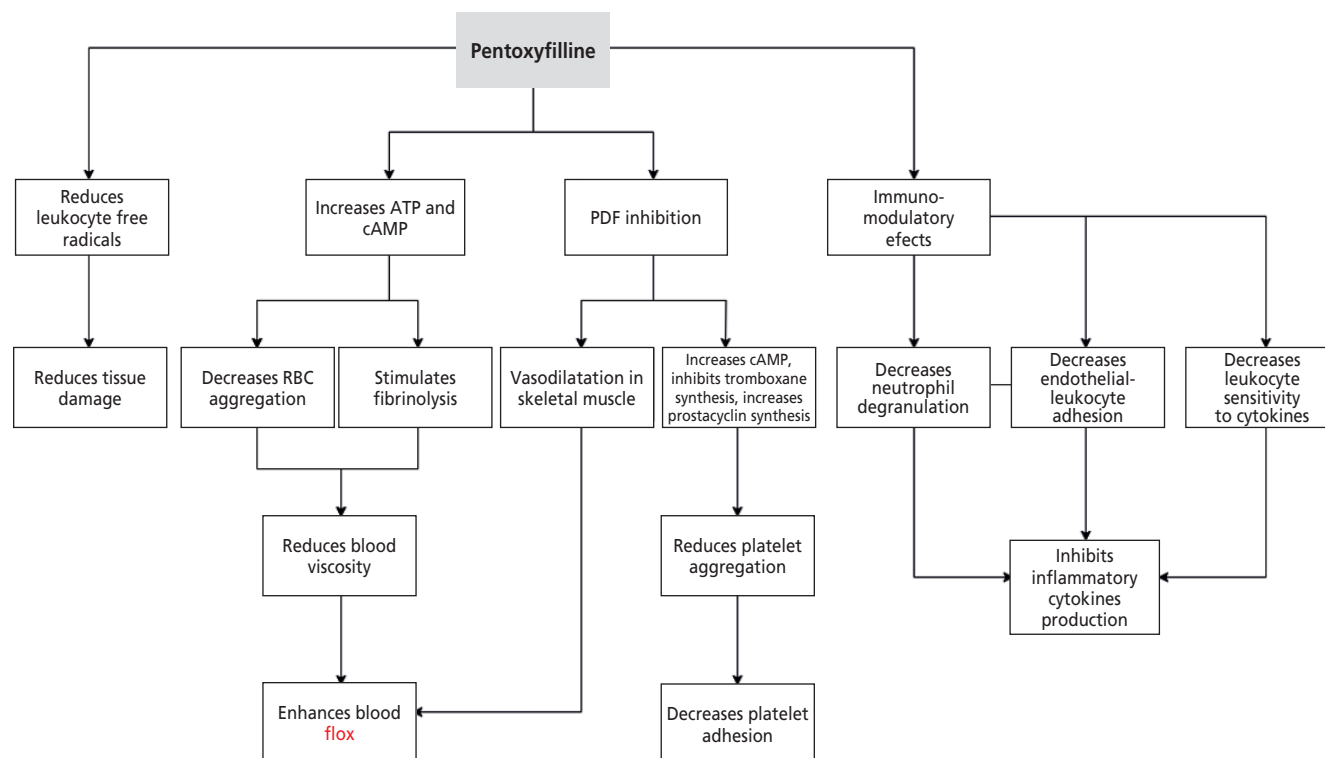


Fig. 1 – Pentoxifylline pathway to prevent reperfusion injury.

skeletal muscle, intestines and kidneys, leading to systemic inflammation, ending in multiorgan failure.¹¹ In some cases after revascularization, the phenomenon of “second hit” where greater damage occurs to cells and membranes that have been damaged often occurs. Early revascularization must be performed to prevent reperfusion injury.

Injury mechanisms involved in vascular reperfusion include increased generation of reactive oxygen species, vasoconstriction of microvasculature, adhesion and activation of neutrophils to the endothelial layer, and release of cytokines. Ischemia results in a lack of oxygen, glucose, and other substances needed for metabolism resulting in anaerobic mitochondrial glycolysis which produces two molecules of adenosine triphosphate (ATP) and lactic acid, which results in a decrease in tissue pH, which then acts through negative feedback to inhibit further ATP production. Ischemia induces the expression of a large number of genes, which play a role in the tissue response to ischemic damage including activating several genes, in particular transcription factors, including activating protein-1 (AP-1), hypoxia-inducible factor-1 (HIF-1) and nuclear factor-kappa B (NF-κB).³

IRI induce the expression of various cytokines, including tumor necrosis factor-α (TNF-α), interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-8) and platelet-activating factor (PAF). TNF-α is a potent chemoattractant and early response cytokine produced by activated macrophages, monocytes, T lymphocytes, natural killer cells and fibroblasts that then induces the expression of IL-1, IL-6, IL-8, and PAF. Several studies in animal models have demonstrated the potential of TNF-α blockade as a therapeutic modality to reduce the severity of IRI.³

Xanthine oxidase shows different distribution and susceptibility to oxidant-mediated IRI. Inhibition of xanthine oxidase activity, prior to ischemia, reduces superoxide production and thereby reduces the severity of reperfusion injury in animal models. Results in humans are also promising.³

Pentoxifylline

Pentoxifylline is a methylxanthine derivative and phosphodiesterase inhibitor (PDEi) with potent hemorheological properties. Pentoxifylline therapy produces various physiological changes at the cellular level. Pentoxifylline acts as an immunomodulator by increasing leukocyte deformability and chemotaxis, reducing leukocyte endothelial adhesion, reducing neutrophil degranulation and superoxide release, reducing the production of monocyte-derived tumor necrosis factor, reducing leukocyte response to interleukin 1 and tumor necrosis factor, inhibiting the activation of T and B lymphocytes, and reduces natural killer cell activity.¹² Pentoxifylline exerts its protective effects through several mechanisms as shown in Figure 1:

1. Inhibition of platelet-activating factor (PAF): Studies have demonstrated that pentoxifylline can significantly reduce the levels of PAF, a key mediator in inflammatory responses during reperfusion. For instance, in a canine model of skeletal muscle ischemia-reperfusion, administration of pentoxifylline prior to reperfusion resulted in decreased PAF levels and reduced muscle necrosis.⁵ Similarly, research involving rabbits indicated that pentoxifylline treat-

ment led to a significant decrease in PAF levels after reperfusion compared to control groups.⁴

2. **Anti-inflammatory effects:** Pentoxifylline has been shown to attenuate inflammation by inhibiting neutrophil activation and adhesion, which are critical processes in the pathophysiology of reperfusion injury, resulting in reduced neutrophil degranulation, decreased leukocyte adhesion to endothelial cells, and diminished leukocyte responsiveness to cytokines.⁵ In a rat model of cerebral IRI, pentoxifylline treatment was associated with reduced neurological deficits and improved neuronal survival, suggesting its role in modulating inflammatory pathways.¹³
3. **Improvement of hemorheological properties:** The drug enhances the deformability of red blood cells and reduces blood viscosity, which can improve microcirculation during reperfusion.^{13,14} It also increases red blood cell flexibility by increasing erythrocyte ATP and cyclic nucleotide levels.⁵ This is particularly important as impaired blood flow can exacerbate tissue damage.
4. Pentoxifylline induces vasodilation in the blood vessels of skeletal muscles by inhibiting phosphodiesterase (PDE) and raising cAMP levels.⁵
5. Pentoxifylline suppresses the production of leukocyte-derived free radicals during peripheral ischemia in patients with peripheral vascular disease. This helps maintain the filterability of unfractionated leukocytes, reducing tissue damage caused by ischemia.¹⁵

The medication may enhance tissue perfusion in these patients by improving blood circulation and reducing signs and symptoms of ischemic pain. However, while it can provide symptom relief, it is not intended to replace standard treatments for peripheral vascular disease.⁵

Pentoxifylline and reperfusion injury

Ischemia-reperfusion (IR) is understood as a complicated series of events that involve interactions among the vascular endothelium, interstitial spaces, circulating cells, and various biochemical components that occur after ischemia. Inflammation plays a crucial role in IR, and the participation of the innate immune system. Ischemia-reperfusion (IR) begins with an episode where blood supply is restricted to an organ, leading to cell death. The return of blood flow exacerbates the damage. Ischemia causes tissue hypoxia, resulting in the accumulation of metabolic intermediates and reactive oxygen species (ROS) such as superoxide, hydrogen peroxide, and hydroxyl radicals. These ROS increase intracellular calcium levels, alter pH, and deplete ATP and nitric oxide (NO), ultimately damaging cell organelles and causing necrotic cell death.¹⁶ That mechanism leads to ischemia-reperfusion injury (IRI).

Influx of activated neutrophils plays a key role in the mediation of IRI.¹⁶ Not surprisingly, pentoxifylline treatment has been reported to lessen such damage in numerous rodent studies, including studies focusing on the heart or brain. From the mechanism of action above, pentoxifylline used because it suppresses production of leukocyte-derived free radicals during peripheral ischemia. Pentoxi-

phylline prevents neutrophil interaction with endothelium and prevents leukocyte degranulation. This will reduce endothelial damage.¹⁷ PDE inhibition by pentoxifylline may reduce the inflammatory response and ischemia-reperfusion damage after lower limb ischemia and reperfusion.¹⁸

In rabbit models of acute limb ischemia, pentoxifylline was shown to attenuate PAF production during reperfusion. The study reported a significant decrease in PAF levels post-treatment, indicating that PTX may effectively mitigate inflammatory responses associated with limb reperfusion injury.⁴ Another study found that administration of PTX at high doses decreased the rate of skeletal muscle necrosis. PTX at a dose of 25 mg/kg immediately before reperfusion decreased the rate of muscle necrosis and PAF levels in venous effluent from isolated gracilis dogs.¹⁹ Endothelial damage following ischemia and reperfusion is marked by increased permeability, cell swelling, and impaired vasorelaxation in response to acetylcholine. In a rabbit hindlimb ischemia model, endothelial cell-dependent vasorelaxation was maintained with intra-arterial administration of PTX during reperfusion, unlike in the control group. The variation in relaxation responses could not be linked to changes in arterial contractility to norepinephrine or histological alterations in the arterial wall. These findings suggest a promising therapeutic approach for minimizing reperfusion injury following acute limb ischemia.²⁰

Pentoxifylline administration also reduced the systemic inflammatory response. In a study with rats that were clamped on their splenic vessels, pentoxifylline was able to significantly reduce serum TNF- α , IL-6 and IL-10.²¹ Administration of pentoxifylline 40 mg/kg dissolved in 0.9% normal saline solution up to 2 ml reduces the inflammatory index in ischemic reperfusion injury.¹⁷

Pentoxifylline in human studies

Pentoxifylline in intermittent claudication at a dose of 400 mg three times a day for 3 month can improve blood rheological properties by reducing plasma and whole blood viscosity, decreasing plasma fibrinogen, increasing erythrocyte distensibility, suppressing erythrocyte aggregation, reducing platelet aggregation, and suppressing neutrophil activation.²²⁻²⁴ Pentoxifylline infusion 1000 mg as an inhibitor of free radical formation resulted in improvement of ischemic damage with an indicator of significant shortening of the half-life of transcutaneous oxygen pressure recovery.²⁵ Peripheral occlusive arterial disease patients receiving 400 mg pentoxifylline four times daily for six weeks showed significant improvements in erythrocyte deformability and a positive impact on microcirculatory blood fluidity.²⁶ Critical limb ischemia patients were treated with pentoxifylline infusion 600 mg twice daily consistently and experienced a significantly decreased pain at rest.²⁷

Combination therapies

Recent studies have explored the efficacy of pentoxifylline in combination with other agents, such as vitamin

C. A study indicated that this combination therapy could further reduce lung damage due to ischemia-reperfusion injury, suggesting enhanced protective effects through synergistic mechanisms.¹⁷

Conclusion

Pentoxifylline appears to be a promising agent in the prevention and treatment of reperfusion injury across various organ systems. Its ability to inhibit PAF production, reduce inflammation, and improve hemorheological properties positions it as a valuable therapeutic option. Further clinical trials are warranted to establish optimal dosing regimens and confirm its efficacy in human subjects suffering from conditions associated with ischemia-reperfusion injury.

Conflict of interest

None to declare.

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None.

Ethical statement

The study was conducted in accordance with Helsinki declaration.

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Abiotrophia defectiva – silent invader and real diagnostic challenge

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Infekčná endokarditída

SÚHRN

Abiotrophia defectiva je bežnou súčasťou mikrobióty dutiny ústnej, tráviaceho a urogenitálneho traktu. Výnimočne, v 1 – 3 % všetkých prípadov, môže táto baktéria spôsobiť infekčnú endokarditídu. Hoci endokarditída spôsobená *Abiotrophia defectiva* nie sú časté, vyznačujú sa vysokou mortalitou a množstvom komplikácií. Zdlhavý, atypický priebeh a zložitá kultivácia vyžadujúca si špeciálne kultivačné médium prispievajú k neskorej diagnostike. Infekčná endokarditída spôsobená *A. defectiva* je známa svojou agresívnou povahou, ktorá sa manifestuje vytváraním veľkých vegetácií vedúcich k devastacným systémovým embolizáciám, deštrukcii srdcových chlopní a v neposlednom rade k progresívnemu srdcovému zlyhaniu. Popisujeme prípad 43-ročného muža s infekčnou endokarditídou mitrálnych chlopní, ktorá sa prejavila nespočetným množstvom embolických príhod.

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ABSTRACT

Abiotrophia defectiva belongs to the normal human microbiome of the oral cavity, gastrointestinal and urogenital tracts. Rarely, about 1–3% of all infective endocarditis, it can be the cause of infective endocarditis. Although uncommon, it is associated with high mortality and complication rates. The chronic course and difficult isolation requiring specialized culture media are contributing to a delayed diagnosis. Moreover, infective endocarditis by *A. defectiva* is known for its aggressive nature characterized by the development of large vegetations leading to massive, life-threatening systemic embolizations, valves destructions, and progressive heart failure. Here, we report a serious case of 43 y.o. previously healthy man diagnosed with *A. defectiva* infective endocarditis presenting with multi-organ septic embolizations.

Keywords:

Abiotrophia defectiva

Embolization

Infective endocarditis

Introduction

Infective endocarditis (IE) due to *Abiotrophia* species, previously referred to as nutritionally variant streptococci, occurs rarely, only between 1–3% of all IE and typically presents with indolent or prolonged course.^{1,2} *Abiotrophia defectiva* is a gram-positive coccus, which is a part of the normal flora of the oral cavity, intestinal and urogenital tracts.

Despite its harmless nature, it can lead to severe IE with development of large vegetations (> 10 mm), excessive embolic events, and congestive heart failure due to valve destruction.^{3,4} Endocarditis in general occurs most often in adults over age 60, however patients with *A. defectiva* IE are usually younger (around 48 years old).² The most common risk factors include previous valvular heart disease,

congenital heart disease, heart valve prosthesis or immunodeficiency, on the other hand, 39% of cases showed no evidence of risk factor.¹ Additionally, *A. defectiva* is very difficult to grow and identify under standard laboratory methods, that is why it is often associated with blood-negative cultures. The incidence of serious complications, delayed diagnosis and treatment failure cause high mortality and need for valve replacement (around 50%).⁵ Our patient, a previously healthy man, with no risk factors, developed insidious course of infective endocarditis with valve destruction and multiple embolizations.

Case presentation

A 43-year-old male reported ongoing sporadic fevers, fatigue, night sweats, joint swelling, pain and substan-

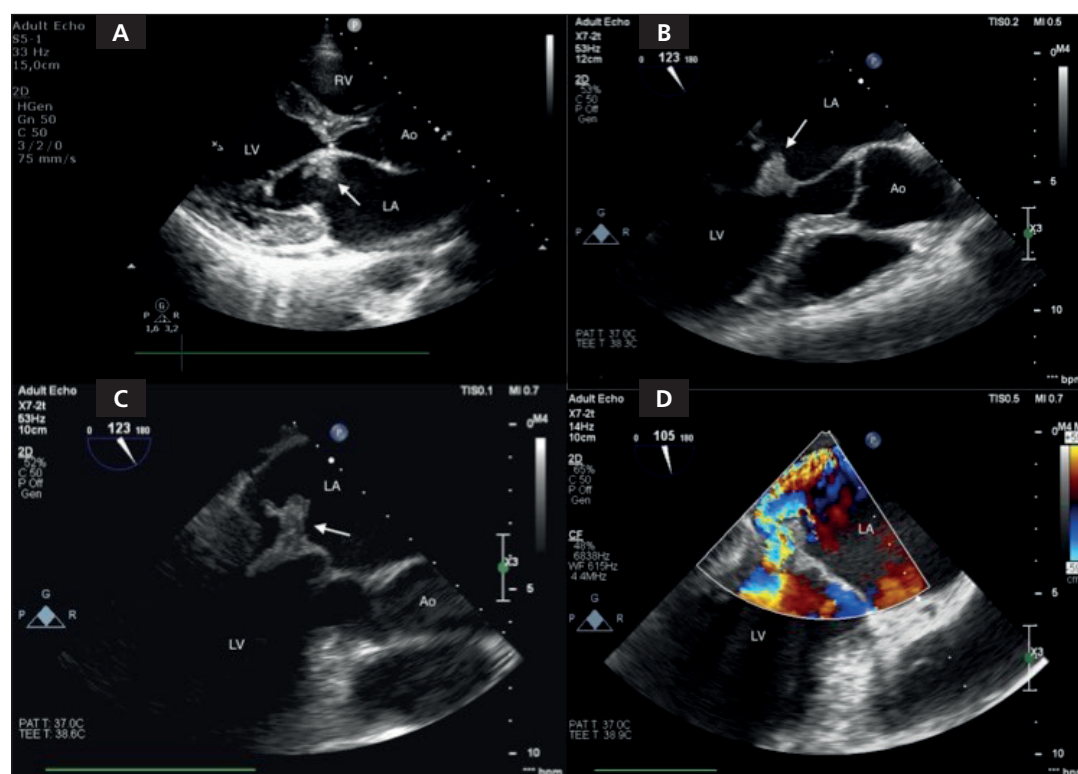


Fig. 1 – Echocardiography. (A) Transthoracic echocardiography apical three-chamber view and transesophageal echocardiography long-axis view (B) show large vegetation (arrow) on the anterior leaflet of the mitral valve on the atrial side (C). The vegetation measures 20 mm in length (arrow). (D) Color flow image shows severe mitral regurgitation.

Ao – aorta; LA – left atrium; LV – left ventricle; RV – right ventricle.

tial weight loss of 11 kg over a year. Following multiple rounds of antibiotic treatment with inadequate response, a systemic rheumatic disease was suspected.

After suffering with a sudden onset of left-sided leg pain and left-sided vision loss, the patient was admitted to department of internal medicine. An arterial Doppler ultrasound revealed embolic occlusion of the left popliteal artery. Upon eye examination, left-sided retinal hemorrhage and right-sided macular hemorrhage was detected. On the fourth day following admission, *A. defectiva* was identified from blood cultures. Under the suspicion of infectious endocarditis, transthoracic echocardiography was performed and large vegetations on mitral valve were found. According to antimicrobial susceptibility testing, an initial antibiotic regimen comprising ceftriaxone and gentamicin were administered, and the patient was referred to our medical centre.

On admission to our hospital, a physical examination revealed a slight underweight and multiple Janeway lesions on the left palm and on the right sole. A laboratory analysis showed an elevated inflammatory response with moderately elevated white blood cell counts ($12 \times 10^9/l$) and C-reactive protein (81 mg/l), elevated NT-proBNP (902 ng/l) and mild microcytic anaemia (Hgb 112 g/l). Transthoracic and transesophageal echocardiography showed normal systolic function of the left ventricle, severe mitral regurgitation with multiple vegetations on the mitral valve predominantly in the anterior leaflet (Fig. 1). Coronary angiography presented a subtotal embolic occlu-

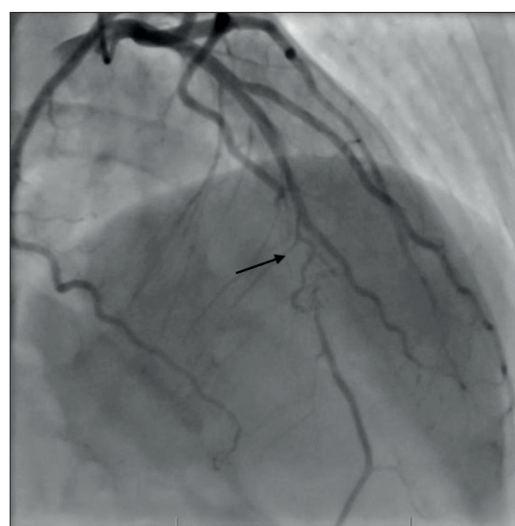


Fig. 2 – Coronary angiography. A subtotal embolic occlusion (arrow) of the left anterior descending coronary artery.

sion of the left anterior descending coronary artery (LAD) (Fig. 2). Abdominal computed tomography (CT) revealed splenic infarction and bilateral renal infarction (Fig. 3). A head CT discovered fusiform aneurysm of the right medial cerebral artery, intracerebral hemorrhage in the right parietooccipital lobe and infarction in the left fron-

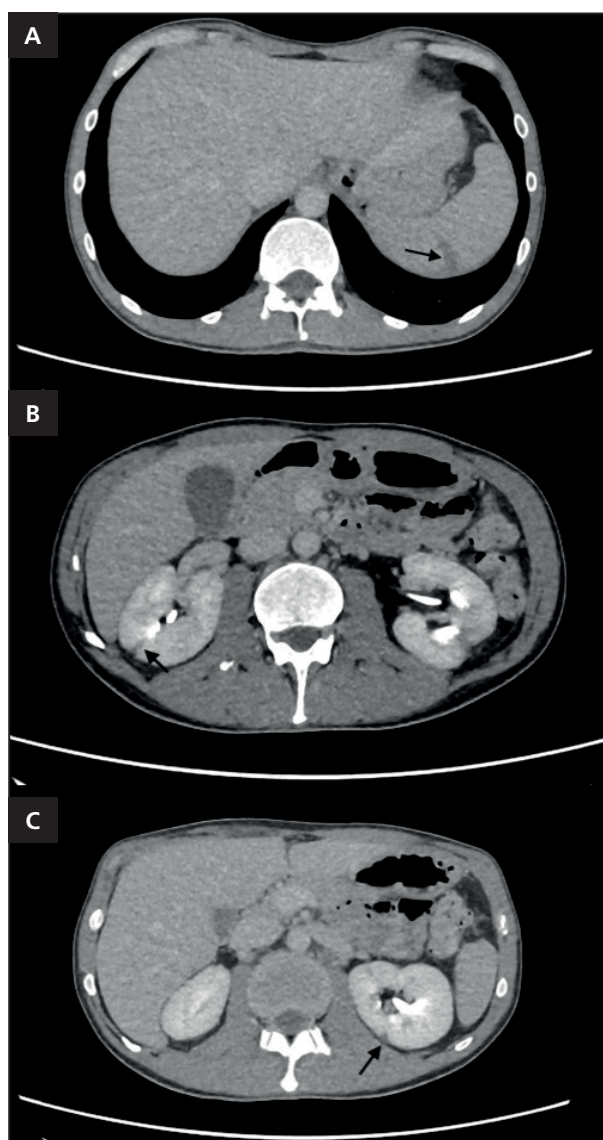


Fig. 3 – Computed tomography of abdomen. (A) Splenic infarction. (B,C) Bilateral renal infarction

tal lobe. The fusiform aneurysm was successfully treated by seven coils placed inside the aneurysm (Fig. 4). After a week, the patient's health condition deteriorated with new neurological symptoms and progression of mitral regurgitation and size of vegetations despite adequate antibiotic therapy worsened. Mitral valve replacement using a 29 mm biological valve (C-E Perimount PLUS) and LIMA to LAD bypass grafting were performed. The post-operative course was uneventful, he was discharged 3 weeks after surgery after completing 6 weeks of antibiotic therapy. No relapse of IE was observed during the 2 years of follow-up at our cardiovascular center.

Discussion

A. defectiva infective endocarditis usually occurs in patients with congenital or preexisting heart disease, a history of previous cardiac surgery or immunocompromised state. Additional risk factors that can also predispose the patients to IE include: older age, indwelling cardiovascular devices, intravenous catheter, intravenous drug use, chronic hemodialysis, poor dentition and invasive dental, gastrointestinal or genitourinary tract procedures.⁷ In our case, the patient had neither of predisposing factors nor the history of dental or any other invasive procedure. However, not only oral procedures, such as tooth extractions, but also routine oral hygiene activities, such as brushing or flossing can facilitate bacterial entry into the bloodstream, which could potentially lead to the development of IE.⁶

The leading cause of difficulty in the diagnosis is related to indolent course, atypical presentation, and difficult isolation. *A. defectiva* IE should be considered in patients with unusual manifestation of infection. Some patients do not even develop fever, but they suffer from nonspecific symptoms, such as weight loss, fatigue or functional decline over a prolonged period of time. Laboratory findings often include anemia and slightly elevated inflammatory markers.⁸ In these cases, use of echocardiography and blood cultures are crucial.

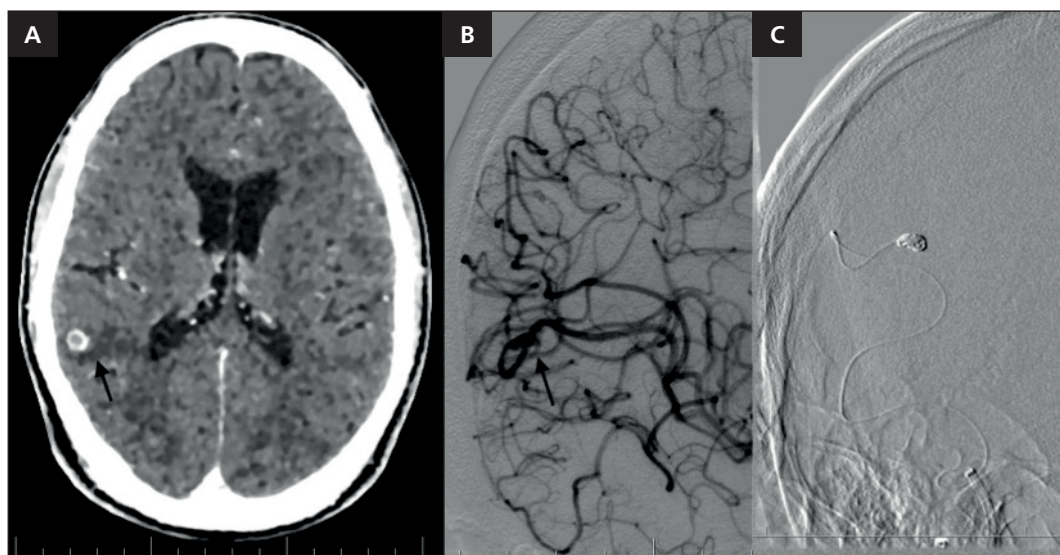


Fig. 4 – Brain imaging. (A) Head computed tomography shows fusiform aneurysm of the right medial cerebral artery and intracerebral hemorrhage in parietooccipital lobe (arrow) on axial view. (B) Digital subtraction angiography (DSA) shows aneurysm (arrow) of the right medial cerebral artery. (C) Seven coils were inserted into the aneurysm.

The name “Abiotrophia” literally means life nutrition deficiency which refers to the species requirements for enhanced culture media for growth. Nowadays, it seems that some isolates may have adapted to grow without the addition of vitamin B₆ or cysteine and can be grown on routine media (as with our patient). Unfortunately, using routine media may not always identify *Abiotrophia* species because of overgrowth of other bacteria or limited growth due to insufficient nutrients. Therefore, enriched media allow selective growth and are more reliable in isolating *A. defectiva*.^{9,10}

According to the current ESC guideline-recommended antibiotic therapy, penicillin G, ceftriaxone, or vancomycin should be used for 6 weeks combined with an aminoglycoside for at least the first 2 weeks. Despite the use of appropriate antibiotics, approximately 50% of cases also need surgical management. Surgical treatment combined with concurrent antimicrobial therapy result in better prognoses, and the main indications for surgery are: recurrent emboli, persistent sepsis, mobile vegetations, and severe heart failure.^{4,11} In our case, despite antibiotic therapy, the patient's condition was deteriorating rapidly due to progressing valve destruction and heart failure, new vegetation development, and recurrent brain embolization. Surgical resection of vegetations and complete mitral valve replacement were inevitable to save the patient.

IE caused by *A. defectiva* is known for its embolization potential. Embolic events are frequent and often life-threatening complications. Several previous studies recognized many predictors for embolic event. The vegetation size (>10 mm), mobility, location and even shape (globular) all increase the risk of embolic complications. Also, the vegetation on the mitral valve has a significantly higher embolic potential. The size of the anterior leaflet, its rapid and forceful movement during valve closure, and the production of negative pressure on the valve by atrial contraction may lead to destabilizing attached vegetations.^{12,13} In the presented case, the size of the vegetation exceeded 20 mm, the embolic rate was higher than usual and caused harm to many organs.

Conclusion

IE caused by *A. defectiva* is rare and easy to miss, but aggressive and leads to a poor prognosis. Atypical manifestation of infection, negative blood cultures and adjunct embolic events should always raise suspicion of *A. defectiva* endocarditis. Role of echocardiography and use of specialized culture media for blood culture is critical in making the right diagnosis.

Conflict of interest

The authors declare that there is no conflict of interest.

Funding

None.

Ethical statement

Approval for the publication was granted by the Ethical Committee of the hospital where the patient underwent evaluation.

Informed consent

We obtained the patient's relative consent in order to publish the article. Any information concerning the patient's identity has been omitted.

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Memorandum o vzájemné spolupráci

Memorandum o vzájemné spolupráci mezi

1. Společností lékařské genetiky a genomiky České lékařské společnosti Jana Evangelisty Purkyně

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a

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Zastoupenou: prof. MUDr. Petrem Ošťádalem, Ph.D., FESC, předsedou ČKS

Se sídlem: Netroufalky 6b, 625 00 Brno

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3. Českou asociací preventivní kardiologie České kardiologické společnosti, z.s.

Zastoupenou: prof. MUDr. Milošem Tábořským, CSc., FESC, FACC, MBA, předsedou ČAPK

Se sídlem: Netroufalky 6b, 625 00 Brno

(společně dále jen „smluvní strany Memoranda“)
uzavřeli níže uvedeného dne, měsíce a roku Memorandum o vzájemné spolupráci
(dále jen „Memorandum“)

I.

Preamble

Smluvní strany, podpisem tohoto Memoranda, deklarují společný zájem o vzájemnou spolupráci, a to především v oblasti diagnostiky a léčby kardiovaskulárních geneticky podmíněných onemocnění, v problematice kardiovaskulární prevence, vzdělávání odborné a laické veřejnosti a v dalších segmentech, s cílem dosáhnout optimální dostupnosti specializovaných genetických vyšetření pro indikované pacienty, metodiky vzájemného předávání pacientů včetně definice standardů reference a podpory obou odborností. Cílem je dlouhodobá kultivovaná odborná spolupráce obou odborností ve prospěch pacientů a cesty pacienta systémem zdravotní péče.

II.

Obecné principy spolupráce založené na EBM datech:

1. Dědičná kardiovaskulární onemocnění se dělí do tří hlavních skupin onemocnění myokardu: 1. dědičné kardiomyopatie, 2. dědičné arytmiické syndromy spojené s normálním strukturálním nálezem na srdci a 3. dědičné aortální syndromy často spojené s chlopenními vadami typu bikuspidální aortální chlopeč nebo prolaps mitrální chlopeč.

2. Společným jmenovatelem dědičných kardiovaskulárních onemocnění je riziko náhlé srdeční smrti, zejména u jedinců mladších 50 let. Náhlá srdeční smrt je dle současných znalostí prvním a často posledním projevem dědičného onemocnění, a to až v polovině případů, a v případě kardiomyopatií často předchází rozvoji jednoznačných strukturálních změn srdečního svalu.

III.

Logistika genetické péče v kardiologii:

1. Klinickou indikaci ke genetické konzultaci stanoví ošetřující kardiolog, pokud zjistil možnou diagnózu některé z forem dědičného kardiovaskulárního onemocnění.
2. Vlastní indikace ke genetickému vyšetření musí být potvrzena a vedena lékařským genetikem, který odpovídá za adekvátní interpretaci výsledků vyšetření. V budoucnosti se subjekty tohoto memoranda budou snažit o zjednodušení tohoto schématu u některých klinicky jasných diagnóz.
3. Genetickou péči v kardiologii chápeme v principu jako mezioborové komplexní vyšetření. Jeho součástí je klinickogenetická konzultace se získáním podrobné

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osobní a rodinné anamnézy. V rámci osobní anamnézy je nutné se zaměřit na zjištění všech průvodních neurologických, jaterních, renálních a jiných onemocnění, která se mohou vyskytovat v rámci syndromového postižení. Součástí konzultace je také sestavení rodokmenu alespoň ve třech generacích s určením dalších rodinných příslušníků v riziku onemocnění. Těmto by mělo být nabídnuto kardiologické screeningové vyšetření s cílem dosáhnout primární prevence závažných komplikací na principech kaskádového rodinného vyšetření.

4. Prosazujeme koncepci multidisciplinárního týmu. Péče o pacienty a jejich příbuzné s dědičným kardiovaskulárním onemocněním předpokládá úzkou multidisciplinární spolupráci dětských i dospělých kardiologů/arytmologů/kardiochirurgů s lékařskými a molekulárními genetiky, patologi, soudními lékaři a lékaři intenzivní medicíny či akutní kardiologie, neurology, praktickými lékaři a psychology aj.
5. Důležitou oblastí genetického vyšetření v kardiologii s ohledem na riziko náhlé srdeční smrti je i komplexní posmrtné vyšetření zemřelého a jeho pozůstalých v riziku. Nezbytné je standardizované provedení pitvy náhle zemřelé osoby, včetně spektra doplňujících laboratorních vyšetření, a následná úzká spolupráce klinických lékařů s patologi, resp. soudními lékaři. Příklad aktivity: www.nahleumrti.cz/kontakt.

IV.

Principy spolupráce subjektů v rozšíření povědomí a dostupnosti kardiogenetického vyšetření:

Odborné společnosti se dohodly, že primárním cílem je dlouhodobá spolupráce zajišťující kontinuitu, rozšíření povědomí a dostupnosti genetického vyšetření v léčbě pacientů s dědičným kardiovaskulárním onemocněním.

Cílem společných aktivit je především zajištění regionální dostupnosti genetických vyšetření pro indikované pacienty. Prosazujeme společně koncepci genetického poradenství, které by mělo být dostupné v každém kardiovaskulárním centru dle Věstníku MZČR KV centra (Seznam-center-vysoce-specializované-kardiovaskulární-péče.pdf) (gov.cz). Tato skutečnost je i součástí Národního kardiovaskulárního plánu (Národní kardiovaskulární plán České republiky na období 2025–2035).

Vytvoříme mapu specializovaných kardiologických pracovišť, která spolupracují v rámci multidisciplinárních týmů s lékařským genetikem a akreditovanou molekulárněgenetickou laboratoří. Tato mapa bude zveřejněna transparentně na webu Národního zdravotnického informačního portálu (NZIP) a také bude dostupná na webových stránkách obou společností a sociálních sítích s cílem informovat jak lékaře, tak pacienty. Tato síť bude průběžně aktualizována na základě dohody obou odborných společností. Aktivně spolupracujeme s patientskými organizacemi, dominantně s Českou aliancí kardiovaskulárních onemocnění, z.s., (ČAKO) a se zainteresovanými patientskými organizacemi sdruženými v České asociaci pro vzácná onemocnění, z.s., (ČAVO).

Budeme vytvářet společná odborná stanoviska a publikovat je jako mezioborové dokumenty o spolupráci. Budeme spolupracovat se zainteresovanými Evropskými referen-

čními sítěmi pro vzácná onemocnění dle Věstníku 1/2022. Průběžně budou dle nových poznatků a studií tyto dokumenty aktualizovány.

V.

Základní odborné dokumenty spolupracujících subjektů:

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VI.**Závěrečná ustanovení:**

1. Smluvní strany Memoranda vyjadřují svou vůli vzájemně spolupracovat v oblasti vymezené tímto Memorandem způsobem uvedeným v čl. I.–V.
2. Memorandum je projevem skutečné, svobodné a vážné vůle smluvních stran Memoranda.
3. Memorandum je vyhotoveno ve třech stejnopisech, z nichž každá smluvní strana Memoranda obdrží po jednom stejnopise.
4. Memorandum nabývá platnosti a účinnosti dnem podpisu všemi smluvními stranami Memoranda.

V Praze dne 26. října 2025

Prof. MUDr. Milan Macek jr., DrSc, MHA

Ústav biologie a lékařské genetiky,
2. lékařská fakulta Univerzity Karlovy
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ČESKÁ KARDIOLOGICKÁ SPOLEČNOST
THE CZECH SOCIETY OF CARDIOLOGY



ČESKÁ SPOLEČNOST
KARDIOVASKULÁRNÍ
CHIRURGIE

Kardio

Ze života společnosti

Zprávy o knize

Prof. MUDr. Eliška Sovová, Ph.D, MBA, slaví významné životní jubileum



Paní profesorka Eliška Sovová se narodila 3. 11. 1960 v Olomouci do lékárnické rodiny, její otec, matka, dva strýcové, teta a sestřenice byli farmaceuti. V mládí chtěla být učitelkou, pak novinářkou, ale nakonec zvolila medicínu, která byla podle rodičů méně závislá na politické příslušnosti. Nicméně se jí nakonec podařilo propojit všechny její představy o povolání – spojení medicíny, psaní popularizačních knih i výuku mediků. Po promoci na Lékařské fakultě v Olomouci, kde absolvovala s vyznamenáním a za výborné studijní výsledky obdržela cenu rektora, nastoupila v nemocnici v Bruntále na interní oddělení, odkud přešla na interní oddělení v Přerově. Zde pracovala do první atestace z vnitřního lékařství. Velmi ráda vzpomíná na přerovského primáře MUDr. Josefa Švejdu, CSc., který byl pro ni po zbytek života velkým vzorem. Praxe, kterou získala v okresní nemocnici, jí dala velmi mnoho zkušeností do života a byla pro její další medicínský život velmi důležitá. V roce 1992 vyhrála konkurs na místo na I. interní klinice Fakultní nemocnice Olomouc, na níž byl přednostou prof. MUDr. Jan Lukl, CSc., který ji naučil, že kardiologie je královnou medicíny. V rámci práce na klinice se věnovala neinvazivní diagnostice, kontrole kardio-stimulátorů a založila oddělení preventivní kardiologie, nejprve jako samostatné oddělení, později jako součást I. interní kliniky – kardiologické a prevence se stala pro její odbornou dráhu tou nejlepší charakteristikou. Postupně, jak šel čas, složila pět atestačních zkoušek (atestace 1. a 2. stupně z vnitřního lékařství, z kardiologie, veřejného zdravotnictví a tělovýchovného lékařství) a okolí se ptá, kdy bude šestá?

Je autorkou více než 150 odborných článků a knih. Byla řešitelkou nebo spoluřešitelkou několika grantových projektů a klinických studií. V roce 2001 obhájila titul Ph.D, v roce 2006 byla jmenována docentkou vnitřního lékařství a v roce 2014 jí prezident republiky udělil titul profesorka vnitřního lékařství. V rámci zvyšování manažerských kompetencí vystudovala MBA na VŠE v Praze. Od roku 2010 pracuje jako přednostka Kliniky tělovýchovného lékařství a kardiovaskulární rehabilitace Fakultní nemocnice Olomouc. Klinika se pod jejím vedením věnuje nejen tělovýchovnému lékařství, ale i léčbě obezity (akreditované centrum pro léčbu obezity) a kardiovaskulární rehabilitaci. Pracoviště je jedním ze čtyř českých center sportovní kardiologie. Pod jejím vedením obhájilo dizertační práci v rámci doktorského studia osm studentů. Je členkou tří oborových rad. V rámci působení jako náměstek pro léčebnou péči Fakultní nemocnice Olomouc zaváděla systém kvality léčebné péče a byla členkou Rady kvality MZ ČR. Od roku 1994 do roku 2023 působila ve správní radě Nadačního fondu Pro srdce Hané, který se zasloužil o vybudování Kliniky kardiovaskulární a transplantační chirurgie ve Fakultní nemocnici Olomouc a od roku 2002 se věnuje hlavně popularizaci prevence srdečních onemocnění (pravidelné popularizační akce na náměstí v Olomouci „Zdravé srdce Hané“, několik českých rekordů v nordic walking chůzi, pokus o Guinnessův rekord Srdce srdcí...). Osm let působila jako proděkanka Lékařské fakulty Univerzity Palackého v Olomouci (UPOL), kde stála u zrodu centra pro simulační medicínu CENTESIMO. V gesci měla dále specializační vzdělávání a byla členkou celostátní koordinační rady. Byla opakovaně členkou akademického senátu LF a UPOL. Byla členkou vědecké rady LF UPOL, Fakulty zdravotnických věd UPOL a v současné době je členkou vědecké rady Fakulty tělesné kultury UPOL.

Je členkou několika odborných společenství, kde působila nebo působí opakovaně v různých výborech. Je členkou Mezioborové komise pro pohybové aktivity MZ ČR. V rámci České lékařské komory pracuje již čtvrté období jako členka čestné rady Okresního sdružení v Olomouci. Byla dvakrát zvolena do Zastupitelstva statutárního města Olomouc, kde působila hlavně v oblasti zdravotnictví a ekologie.

Tolik souhrn dosavadního profesionálního života paní profesorky, při výčtu všech jejích činností se mi v mysli objevila otázka: nemá paní profesorka dvojče? Všechno, co dosud dokázala, je pro jednu osobu až neuvěřitelné! Ale ne, je na to sama, je to všechno podloženo ohromnou pracovitostí a láskou k oboru, který v řadě oblastí naprostoto zásadně ovlivnila. Její prezentace na odborných akcích je vždy dokladem hlubokých znalostí oborů, kterým se věnuje, a všechno k tomu provází její přirozené a noblesní vystupování.

Je jistě správné dodat, že k tomu vychovala dvě děti, které následovaly její profesní dráhu – syn Milan je profesor vnitřního lékařství a působí jako přednosta Kliniky



nemocí plicních a tuberkulózy ve FN Brno a dcera Markéta má atestaci z vnitřního lékařství a tělovýchovného lékařství a je v současné době na mateřské dovolené. Paní profesorka nejraději relaxuje s manželem Milanem a s vnukem, na kole a na lyžích.

Dovolte mi na závěr, abych za výbor ČKS i za celou kardiologickou společnost i osobně paní profesorce velmi po-

děkoval nejen za všechny ty roky náročné a úspěšné práce jak pro naši společnost, tak pro všechny nemocné, ale také za angažovanost v oblasti regionální politiky, jež je pro zdravotnictví tolik potřebná. Přejeme pevné zdraví a mnoho dalších úspěchů a radosti z těch, kteří jí jsou nejbližší.

Srdečně, Michael Aschermann za výbor ČKS

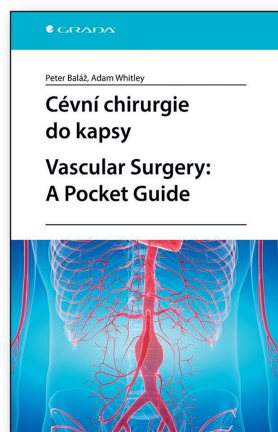
Mgr. Klára Procházková, odpovědná redaktorka *Cor et Vasa*, slaví životní jubileum



Redaktorka našeho časopisu Klára Procházková, nesmírně pracovitá a milá dáma, se narodila 1. 11. 1975 a po maturitě složila v roce 1995 státní jazykovou zkoušku z angličtiny. Dále se věnovala studiu českého jazyka a literatury na Filozofické fakultě UK – státní zkoušky absolvovala v září 2001. Po promoci pracovala nejdříve jako učitelka angličtiny a češtiny pro cizince, od roku 2002 se pak začala více věnovat práci redaktorské, nejprve jako korektorka a editorka *Medical Tribune* a od roku 2010 jako redaktorka *Cor et Vasa*. Máme tedy v letošním roce 15 let výročí společné práce na hlavním časopisu České kardiologické společnosti. Klára Procházková je pro *Cor et Vasa* neviditelnou, ale naprosto nepostradatelnou duší, obdivuhodným způsobem zvládá nejen rutinu nekonečného příběhu

tvorby časopisu, ale přátelsky a citlivě řeší situace obtížné a nečekané. Jsem přesvědčen, že precizní práce Kláry na každém čísle časopisu přispívá k jeho kvalitě a byla jedním z faktorů, které přivedly *Cor et Vasa* k získání tolik potřebného impakt faktoru. Ještě dodám, že spolu s manželem Honzou mají dceru Hanu a ve volném čase se věnuje literatuře a všichni spolu pak výletům do přírody a za poznáním. Dovolte mi, abych za nás všechny čtenáře *Cor et Vasa* Kláře Procházkové od srdce poděkoval a popřál především pevné zdraví a radost s blíznými, nám pak přání, aby její spolupráce s *Cor et Vasa* byla i nadále tak skvělá jako dosud.

Michael Aschermann
za výbor ČKS



Peter Baláž, Adam Whitley: Cévní chirurgie do kapsy. Vascular Surgery: A Pocket Guide

Vydala Grada Publishing, a.s., 2025, 154 stran.

První vydání, barevný výtisk, měkká vazba.

ISBN: 978-80-271-8048-6 (ePub).

ISBN: 978-80-271-8047-9 (pdf).

ISBN: 978-80-271-5210-0 (print).

Cena: 349 Kč

Monografie má 154 stran, text knihy je v dvoujazyčné mutaci (česky a anglicky), kniha byla podpořena projektem Programu rozvoje vědních oblastí Univerzity Karlovy Cooperatio 207029 Cardiovascular Science.

Autory monografie jsou prof. MUDr. Peter Baláž, Ph.D., FEBS, MPH, (3. lékařská fakulta Univerzity Karlovy, Praha) a MUDr. Adam Whitley (původem z Oxfordu, Velká Británie, nyní 3. lékařská fakulta Univerzity Karlovy v Praze).

Monografie má celkem 15 kapitol:

1. Pacient s ischemickou chorobou dolních končetin,
2. Stenóza arteria carotis interna,
3. Akutní ischemie horní končetiny,
4. Syndrom horní hrudní apertury,
5. Aneuryzma hrudní aorty,
6. Aneuryzma abdominální aorty,
7. Disekce aorty,
8. Aneuryzma viscerálních tepen,
9. Chronická mezenterická ischemie,
10. Akutní mezenterická ischemie,
11. Chronická ischemie dolní končetiny,
12. Akutní ischemie dolní končetiny,
13. Aneuryzma zákolenní tepny,
14. Diabetická noha,
15. Chronická venózní nedostatečnost.

Stejně kapitoly jsou v druhé polovině knihy v angličtině, což jistě ocení především studenti medicíny ze zahraničí, také česká část knihy bude jistě oceněna mediky a lékaři, kteří vstupují do praxe a potřebují znát základy popsané závažné angiologické problematiky.

Patnáct kapitol je shrnuto na 50 stranách, text obsahuje ve zkratce zásadní otázky klinické manifestace, diagnostiky a léčby a prognózy uvedených patnácti klinických stavů. Je možné konstatovat, že zkušeným autorům se podařilo minimalizovat text bez ztráty přehledu o jednotlivých klinických situacích. Text je doplněn algoritmy, obrázky a piktogramy, jež usnadňují orientaci v problematice, je možné konstatovat, že autoři připravili výjimečnou publikaci, která bude v praxi jistě užitečná, a to jak pro obory chirurgické, tak interní. Rejstřík, seznam zkratek a stručný souhrn literatury jsou samozřejmým doplňkem monografie.

Zpracování drobné monografie od týmu Grada Publishing je vysoce kvalitní.

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Jiří Vítovec, Monika Špinarová, Anna Chaloupka, Karel Lábr: Farmakoterapie srdečního selhání

Praha, Grada Publishing, a.s., 2025, 190 stran.

Vydání první, formát 120 × 205 mm, měkká (brožovaná) vazba, barevný výtisk.

ISBN: 978-80-271-7874 (ePub).

ISBN: 978-80-271-7873 (pdf).

ISBN: 978-80-271- 5516-3 (print).

Cena: 357 Kč.

Všichni autoři této knihy jsou pracovníky I. interní kardiologické kliniky Lékařské fakulty Masarykovy univerzity v Brně a Fakultní nemocnice u sv. Anny v Brně. Profesor Lékařské fakulty Masarykovy univerzity, hlavní autor (a zřejmě iniciátor napsání) prof. MUDr. Jiří Vítovec, CSc., je i pracovníkem Ústavu farmakologie a toxikologie Farmaceutické fakulty Masarykovy univerzity. Jde o drobnou knihu kapesního formátu. Je monotematická, věnuje se problematice srdečního selhání. Odborný obsah je rozdělen do šesti kapitol. Po krátké předmluvě (autorka profesorka MUDr. Lenka Špinarová, Ph.D. – strany 9–11) následují kapitoly v tomto pořadí. První kapitola: Historie farmakologie chronického srdečního selhání (strany 11–17), druhá kapitola: Farmakologie léků pro srdeční selhání (strany 17–60). Třetí kapitola je věnována akutnímu srdečnímu selhání (strany 60–78), čtvrtá kapitola (strany 78–101) srdečnímu selhání chronickému a pátá kapitola (strany 101–118) kardiomyopatiím. Odbornou část zakončuje šestá kapitola o léčbě přidružených onemocnění u srdečního selhání (strany 124–169). Na straně 176 je uvedeno devět názvů monografií o srdečním selhání. Textovou část ukončují český a anglický souhrn s následným seznamem zkratk (strany 177–182). Úplně konečným je dvousloupcový rejstřík (strany 181–187). Odborný text je (od strany 31) doplněn řadou dvou- i polybarevných obrázků a tabulek. Na konci každé kapitoly je různě dlouhý seznam literatury.

Srdeční selhání je velmi závažný stav, v němž může vyústit řada kardiopatií. Končí jím nejen téměř všechny formy ischemické srdeční choroby, ale i řada neischemických kardiomyopatií. Ve statistice příčin úmrtí trvale figuruje srdeční selhání na jednom z předních míst. Obrovský pokrok přinesly do diagnostiky nové zobrazovací metody (echokardiografie, CT, MR) a endomyokardiální biopsie, v terapii betablokátory inhibitory angiotenzin konvertujícího enzymu, sartany, antagonisté mineralokortikoidních receptorů, neprilysinu a glifloziny.

Tato „malá“ kniha přináší řadu významných moderních faktů. Malý kolektiv autorů pod vedením zkušeného internisty, kardiologa a farmakologa profesora Vítovice přinesl řadu moderních poznatků jak z oblasti diagnostiky, tak (především) terapie a napsal kvalitní knihu.

Komu knihu doporučit?

Všem lékařům, kteří léčí pacienty se srdečním selháním. Především kardiologům, gerontologům a rehabilitačním lékařům.

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v Praze, e-mail: petrjanv@email.cz*



Libor Jelínek, Samuel Genzor, Jan Václavík a kolektiv: Adherence k medikaci kardiovaskulárních onemocnění v praxi

Praha, Grada Publishing, a.s., 2025, 171 stran.

Vydání první, formát 224 × 167 mm, měkká (brožovaná) vazba, barevný výtisk.

ISBN: 978-80-271-7877-3 (ePub).

ISBN: 978-80-2717876-6 (pdf).

ISBN: 978-80-271-5494-4 (print).

Cena: 390 Kč.

Tři editoři, ale i současní autoři několika kapitol přizvali k napsání této knihy dalších deset spoluautorů. Byli to především pracovníci Lékařské fakulty Univerzity Palackého v Olomouci a Lékařské fakulty Ostravské univerzity.

Odborný text je rozdělen na obecnou a speciální část. Obecnou část tvoří šest kapitol (48 stran), speciální část devět kapitol (114 stran). Do obecné části bylo zařazeno šest kapitol: 1. kapitola: Definice a terminologie (strany 5–8), 2. kapitola: Historie adherence (strany 9–10), 3. kapitola: Měření adherence (strany 11–22), 4. kapitola: Patologie adherence a základní principy komunikace s non-adherentním pacientem (strany 23–25), 5. kapitola: Intervence ke zlepšení adherence (strany 26–42), poslední, šestá kapitola obecné části se věnuje psychologickým aspektům adherence (strany 43–48). Speciální část odborného textu začíná v pořadí sedmou kapitolou: Adherence k medikaci u srdečního selhání (strany 49–63), následována druhou významnou osmou kapitolou Adherence u arteriální hypertenze (strany 64–77). Devátá kapitola je o adherenci k hypolipidemické terapii (strany 78–90), předchází desátou kapitolu Adherence k režimovým opatřením u kardiovaskulárních onemocnění (strany 91–102). Zřejmě k nejkratším patří jedenáctá kapitola, jež se zabývá adherencí k antiarytmické terapii (strany 103–114). Dvanáctá kapitola nese název Adherence k přímo působícím antikoagulanciím (strany 115–128). Třináctá kapitola se věnuje adherenci u osob s chlopenní vadou nebo protetickou náhradou (strany 129–137), čtrnáctá kapitola adherenci k dechové rehabilitaci (138–143). Celkově je čtrnáctá kapitola nejkratší kapitolou celé knihy. Patnáctá je kapitola o adherenci u syndromu spánkové apnoe (strany 144–154). Šestnáctá a poslední kapitola Adherence a kardiovaskulární komplikace u chronické

obstrukční plicní nemoci (strany 155–162) textovou odbornou část knihy uzavírají. Dost rozsáhlá literatura je na konci každé speciální kapitoly a sumárně pro kapitoly 1–5. Oživením standardního obsahu jsou krátké odstavce „take-home message“ umístěné ke konci všech kapitol, jejichž text je růžově podbarven. Následují seznam zkratek (stránky 163–167), jednostránkový český souhrn, jednostránkové anglické summary a příliš stručný (strany 170 a 171) dvousloupkový rejstřík (např. zmiňovaný odstavec „take-home message“, ačkoliv je v textu uvede šestnáctkrát, v rejstříku chybí).

Téma knihy se v naší literatuře objevuje poprvé, ačkoliv knih s kardiologickou problematikou je velká řada. Je nutné ocenit i skutečnost, že každé téma je na počátku kapitoly představeno stručným úvodem a na konci kapitoly dokumentováno krátkou kazuistikou ukazující jeho využití v praxi. Odborný text knihy zaslouží pochvalu, i když jen dva z autorů jsou kvalifikovaní pedagogové. Jako vždy se osvědčily barevné ilustrace. Nakladatelství Grada obohatilo domácí knižní trh kvalitním kardiologickým titulem.

Komu knihu doporučit?

Tato „malá monografie“ přináší informace o zvláště důležité a zajímavé problematice, s níž se všichni lékaři setkávají, bez rozdílu specializace, v každodenní praxi. Zvláště pro mladé lékaře by to měla být povinná četba.

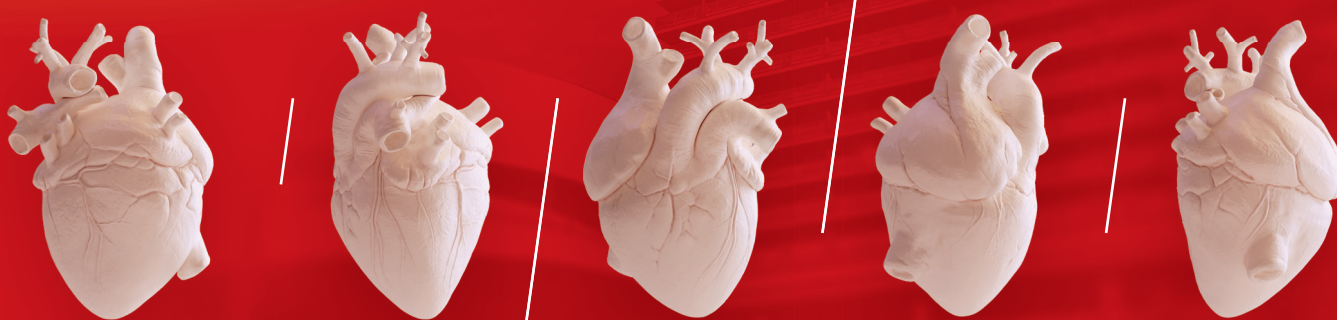
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ČESKÁ
KARDIOLOGICKÁ
SPOLEČNOST



Česká asociace
akutní kardiologie



23. KONFERENCE ČESKÉ ASOCIACE AKUTNÍ KARDIOLOGIE

30. 11.–2. 12. 2025 | HOTEL THERMAL, KARLOVY VARY

Bohatý program, zaměřený na akutní a intenzivní kardiologickou péči, bude doplněn pěti workshopy pro lékaře a jedním pro sestry. Paralelně s lékařskými bloky bude probíhat sesterská sekce.

Program pokryje všechny zásadní aspekty akutní kardiologické péče a my doufáme, že Vás zaujme.

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