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Cor et Vasa

Minimally invasive thoracoscopic vs. sternotomy approach in mitral valve surgery

Stent Overlapping and Clinical Outcomes

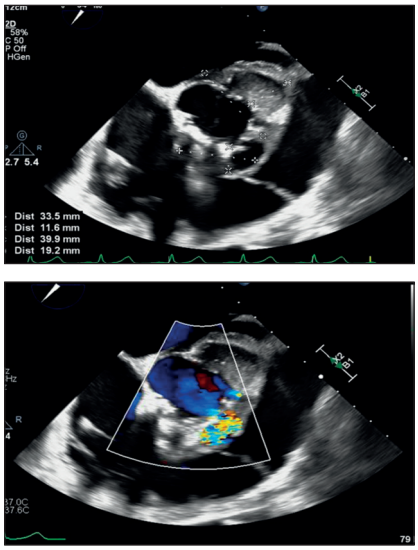
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Machine Learning and Survival after CABG



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Cor et Vasa

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

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

Inzerce
Mgr. Denisa Ebelová
Tel.: +420 725 777 880
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Prof. MUDr. Michael Aschermann, DrSc., FESC, FACC (Editor-in-Chief)
2nd Department of Internal Medicine – Cardiology and Angiology
School of Medicine I, Charles University and General University Hospital
U Nemocnice 2, 128 08 Prague 2, Czech Republic
E-mail: Aschermann@seznam.cz, Aschermann@e-coretvasa.cz

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

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

Advertising information
Mgr. Denisa Ebelová
Tel.: +420 725 777 880
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Minimally invasive thoracoscopic vs. sternotomy approach in mitral valve surgery

Jana Čobejová, Tomáš Toporcer, Peter Šafár, Štefánia Mižáková, Lukáš Vajda, Štefan Lukačín, Adrián Kolesár

Department of Heart Surgery, East Slovak Institute of Cardiovascular Diseases and Medical Faculty, Pavol Jozef Šafárik University, Košice, Slovakia

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SÚHRN

Úvod: V posledných desaťročiach sa popri štandardnom prístupe k mitrálnej chlopni pomocou úplnej strednej sternotómie stáva minimálne invazívna srdcová chirurgia (MIMVS) čoraz populárnejším chirurgickým prístupom. Cieľom tejto štúdie bolo retrospektívne porovnať výsledky operácií mitrálnej chlopne prístupom z video-asistovanej torakoskopie (VATS) a štandardnej sternotómie (ST).
Metódy: Retrospektívna analýza bola vykonaná na pacientoch, ktorí podstúpili operáciu mitrálnej chlopne. Pacienti boli rozdelení do skupiny operovanej prístupom ST a skupiny operovanej prístupom VATS. Skúmané boli predoperačné, chirurgické a pooperačné parametre, vrátane prežívania a závažných kardiovaskulárnych príhod (MACE), ktoré zahŕňali mozgovú príhodu, infarkt myokardu, závažnú arytmiu a smrť. Pooperačné echokardiografické parametre boli hodnotené na podskupinách pacientov podstupujúcich jednotlivými prístupmi výhradne záchovnú operáciu mitrálnej chlopne.
Výsledky: V skupine bolo 123 pacientov, z ktorých 69 bolo operovaných prístupom ST a 54 prístupom VATS. Predoperačne bolo hlavným rozdielom EuroScore, pričom skupina ST bola rizikovejšia (0,94 vs. 0,73 $p < 0,0001$). V skupine VATS prevažovala záchovná operácia (94 % vs. 55 %, $p < 0,0001$). Pacienti po VATS mali dlhší čas kardiopulmonálneho bypassu (CPB) a aortálnej svorky (146 vs. 91,8 min; $p < 0,0001$; 110 vs. 75,5 min; $p < 0,0001$). Echokardiograficky neboli v podskupine mitrálnych záchovných výkonov štatisticky významné rozdiely v pooperačných tlakových gradientoch na mitrálnej chlopni ani v parametroch remodelácie ľavej komory. Miera prežívania a MACE boli v skupinách podobné. V pooperačnom období bol v ST skupine zistený vyšší výskyt evakuácie perikardiálnej efúzie (12 vs. 0 %, $p < 0,01$) a podania krvnej plazmy (1,17 vs. 0,46, $p < 0,001$). Sledovanie pooperačných komplikácií ako revízia, infekcia rany, punkcia fluidothoraxu, drenáž pneumothoraxu, implantácia kardiostimulátora, vznik predsieňovej fibrilácie, dĺžka hospitalizácie, neurologické komplikácie, nutnosť eliminačnej terapie nezaznamenalo medzi skupinami štatisticky významné rozdiely.
Záver: Údaje naznačujú, že VATS ponúka porovnateľné chirurgické výsledky ako ST pri operáciách mitrálnej chlopne s dodatočnými kozmetickými výhodami.

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Keywords:
Minimally invasive surgery
Mitral regurgitation
Mitral valve
Sternotomy

ABSTRACT

Introduction: In recent decades, minimally invasive cardiac surgery (MIMVS) has become an increasingly popular surgical approach alongside the standard approach to the mitral valve using complete median sternotomy. The aim of this study was to retrospectively compare the results of mitral valve surgery using video-assisted thoracoscopy (VATS) and standard sternotomy (ST).
Methods: A retrospective analysis was performed on patients (n = 123) who underwent mitral valve surgery. They were divided into ST (n = 69) and VATS (n = 54) groups. Various preoperative, surgical, and postoperative parameters were examined, including survival and major adverse cardiac events (MACE), which included stroke, myocardial infarction, severe arrhythmia and death.
Results: Preoperatively, the main difference was in EuroScore, with the ST group being at higher risk (0.94 vs. 0.73, $p < 0.0001$). In the VATS group, conservative surgery prevailed (94 vs. 55%, $p < 0.0001$), while in the ST group, valve replacements prevailed (45 vs. 6%, $p < 0.0001$). Patients after VATS had longer cardiopulmonary bypass (CPB) and aortic clamp times (146 vs. 91.8 min; $p < 0.0001$; 110 vs. 75.5 min; $p < 0.0001$). Echocardiographically, there were no statistically significant differences in postoperative pressure gradients across the mitral valve or in left ventricular remodeling in the mitral valve repair (MVP) subgroup. Survival rates and

Address: MUDr. Jana Čobejová, Department of Heart Surgery, East Slovak Institute of Cardiovascular Diseases and Medical Faculty, Pavol Jozef Šafárik University, Ondavská 8, 04001 Košice, Slovakia, e-mail: cobejovaj@gmail.com
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MACE were similar. In the postoperative period, the ST group had a higher incidence of pericardial effusion evacuation (12 vs. 0%, p <0.01) and blood plasma administration (1.17 vs. 0.46, p <0.001). Monitoring of postoperative complications such as revision, wound infection, fluidothorax puncture, pneumothorax drainage, TKS implantation, atrial fibrillation, length of hospitalisation, neurological complications, and the need for CVVHD did not reveal any statistically significant differences.
Conclusion: The data suggest that VATS offers comparable surgical results to ST in mitral valve surgery with additional cosmetic advantages.

Introduction

Mitral valve diseases are one of the most common cardiac pathologies and include two primary disorders: mitral stenosis and mitral regurgitation. Mitral regurgitation is the second most common valvular defect after aortic stenosis requiring intervention.[1,2] The epidemiological profile has changed significantly over the last decade, with degenerative pathology coming to the fore in developed countries ahead of rheumatic pathology, which was dominant in the past.[3] European ESC/EACTS guidelines state that mitral valve repair (especially when indicated early) has a positive effect on preserving/restoring the elasticity of the left ventricle and on ejection fraction compared to late indication or inappropriate replacement.[4]

The standard surgical approach in cardiac surgery is generally median sternotomy, which allows easy access to the heart, flexibility in myocardial protection, multiple approaches to the mitral valve, and high-quality cardiac ventilation. However, the invasiveness of sternotomy is associated with a delayed return to preoperative physical function and an increase in postoperative complications.[5] In recent decades, there has been a significant progress in the development of minimally invasive procedures in cardiac surgery thanks to advances in surgical instruments, telemanipulation, and perfusion technology. VATS, performed through a 4 to 7 cm lateral thoracotomy, is a less invasive alternative with comparable quality and safety to standard sternotomy (**Fig. 1**).[6]

The aim of this study was to compare the standard sternotomy and minimally invasive approaches to the mitral valve in terms of intraoperative parameters, postoperative complications and short-term postoperative outcomes, and to evaluate the results of mitral valve repair using the ST vs. VATS approach.

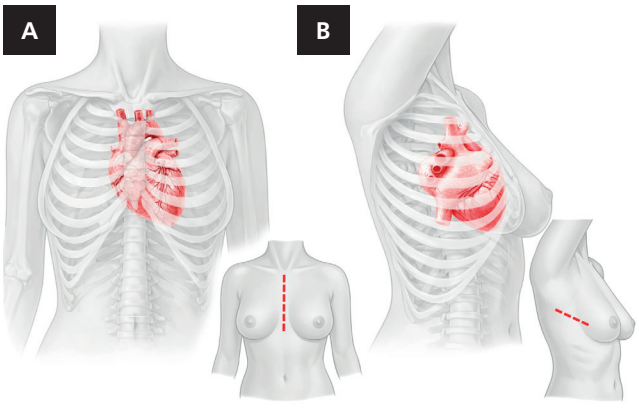


Fig. 1 – Topographic relationship between surgical access and the anatomical position of the heart (A – median sternotomy; B – left thoracotomy).

Material and methods

This study presents a retrospective analysis of data from patients who underwent primary mitral valve surgery at the Department of Heart Surgery of VÚSCH a.s. Košice between January 2016 and December 2025. The inclusion criteria were isolated mitral valve surgery. Exclusion criteria included combined surgery, reoperation, and acute surgery. The following preoperative data were recorded for all patients: age, sex, type of valve disease (stenosis, regurgitation, infective endocarditis), body surface area (BSA), body mass index (BMI), risk of death during hospitalization (EuroScore II), left ventricular ejection fraction (LVEF), effective regurgitant orifice area (EROA), end-systolic and end-diastolic volumes (ESV, EDV), left ventricular size in systole and diastole (LKs, LKd), and regurgitant volume (RV).

The following perioperative and postoperative data were also recorded: type of surgical approach (complete sternotomy or video-assisted thoracoscopy), type of mitral valve procedure selected (replacement or repair), length of cardiopulmonary bypass, duration of cardioplegic arrest, early revision due to bleeding, evacuation of pericardial effusion, development of wound infection, development of emphysema, need for drainage or puncture of the pleural space, renal failure requiring CVVHD, development of neurological deficit, postoperative atrioventricular block (AVB), need for pacemaker implantation (PPM), persistent and paroxysmal postoperative atrial fibrillation, pressure gradient and residual regurgitation on the valve, length of stay in the intensive care unit (ICU), length of hospitalization, survival, and occurrence of major adverse cardiovascular events (MACE). Patient survival was recorded on the basis of a contract with the health insurance provider using the ÚDZS portal. Within the MACE, the postoperative incidence of stroke, myocardial infarction and death was monitored during the study period and was determined electronically based on e-health data.

Subsequently, patients undergoing valve replacement were excluded from the group for further analysis in order to objectively compare the effectiveness of mitral valve preservation surgery using ST vs. VATS. In the subgroups created, a comparison of postoperative echocardiographic parameters was performed between patients who underwent surgery using the ST and VATS approach.

Quantitative data are expressed in the statistical analysis as mean ± standard deviation. Qualitative data are

expressed as a percentage of positive cases. A two-sample t-test was used to compare the ST and VATS patient groups (for quantitative parameters), and the chi-square and Fisher's exact tests were used to compare qualitative parameters. Survival outcomes and MACE incidence in the two patient groups (ST and VATS) were compared using Kaplan–Meier survival curves and the log-rank test. Statistical analysis was performed using SPSS version 20. Parameters with a *p*-value <0.05 were considered statistically significant in each evaluation.

Results

A total of 123 patients were included in the analysis and divided into two groups based on the surgical approach chosen: patients with ST (n = 69) and VATS (n = 54). The average age of the patients was 55 years. The cohort included 40/123 (32.5%) women.

The average left ventricular ejection fraction (LVEF) for the entire group was 60% ± 7.9%, the mean effective regurgitant orifice area (EROA) was 0.57 ± 0.2 , regurgitant volume (RV) was 84 ± 33.7 ml, left ventricular size in systole (LVs) 38.8 ± 6.9 mm, left ventricular size in diastole (LVd) 56.2 ± 7.4 mm, end-diastolic volume (EDV) 151.3 ± 51 ml, end-systolic volume (ESV) 63 ± 27 ml. The average body surface area (BSA) was 1.9 ± 0.3 , the average body mass index (BMI) was 26.8 ± 4.7 kg/, and the in-hospital mortality parameter (EuroScore II) was 0.85 ± 0.35. The indication for surgery was mitral regurgitation in 85.4% of cases, stenosis in 3.3%, a combination of both in 3.3% and infectious endocarditis in 8% of cases. The primary minimally invasive thoracoscopic approach was chosen in 54/123 (43.9%) patients, with no cases requiring conversion to sternotomy.

The average duration of cardiopulmonary bypass (CPB) for the entire group was 116 ± 43.7 minutes and the duration of aortic clamping was 90.8 ± 27.5 minutes. The valve was replaced in 27.6% of patients. The length of stay in the intensive care unit was 5.1 ± 3.5 days and the total length of hospitalization was 12 ± 6.7 days. After surgery, 4% of patients were diagnosed with new atrioventricular block requiring pacemaker implantation, early revision due to bleeding was necessary in 3.3% of patients, and late revision due to pericardial effusion was necessary in 6.5% of patients. Paroxysmal atrial fibrillation was detected in 34.2% of patients, with a transition to persistent atrial fibrillation in 20.3%. Surgical wound infection was reported in 5.7% of patients. The need for elimination therapy (CVVHD) was reported in 6.5% and neurological complications in 4.9% of patients.

Comparison of the ST and VATS groups revealed a difference in preoperative parameters in terms of surgical risk (EuroScore). Patients who underwent surgery via ST were at higher risk, with a statistical significance of $p < 0.001$. The difference in patient age, BMI, and BSA was not statistically significant (**Table 1**).

Surgery due to valvular stenosis was more prevalent in the ST group, but with no statistical significance (4% vs. 0%, $p = 0.255$), same as for infectious endocarditis (12% vs. 2%, $p = 0.08$). Surgery due to valvular insufficiency was statistically significantly more common in the VATS group (98% vs. 77%, $p = 0.001$). In the ST group, valve replacement prevailed over repair surgery (45 vs. 55%), while in VATS, repair surgery prevailed (94 vs. 6%).

A comparison of perioperative parameters showed statistically significant longer CPB time and aortic clamp time in the VATS group, by 54 resp. 34 minutes ($p < 0.0001$ for both). A statistically significant difference in the amount of blood plasma administered (1.2 vs. 0.5, $p = 0.001$) and pericardial effusion evacuation (12 vs. 0%, $p < 0.01$) was demonstrated to the ST group. When comparing the need for revision, wound infection, fluidothorax puncture, drainage for pneumothorax, PPM

Table 1 – Comparison of pre-operative parameters

Parameter	ST (n = 69)	VATS (n = 54)	*p*-value
EuroScore	0.94	0.73	<0.0001
Age	56.61	52.94	0.186
BMI	27.35 kg/m^2	26.15 kg/m^2	0.20
BSA	1.91 m^2	1.97 m^2	0.05
Stenosis	4%	0%	0.255
Regurgitation	77%	98%	0.001
Stenosis + regurgitation	7.2%	0%	0.07
Infective endocarditis	12%	2%	0.08

Table 2 – Surgery, hospitalization and follow-up parameters – comparison

Parameter	ST (n = 69)	VATS (n = 54)	*p*-value
CPB	91.85 min	146.3 min	<0.0001
Aortic clamp	75.54 min	110 min	<0.0001
Atrial fibrillation	37.7%	29.6%	0.444
Permanent fibrillation	21.7%	18.5%	0.822
AVB	8.7%	1.9%	0.134
PPM	7.2%	0%	0.067
Wound infection	4.3%	7.4%	0.525
Hospitalization	12 days	11.9 days	0.461
ICU hospitalization	5.2 days	5.0 days	0.946
Neurological complication	3%	7%	0.403
Pneumothorax (right)	10.1%	22.2%	0.081
Pneumothorax (left)	5.8%	0%	0.13
Pericardial evacuation	11.6%	0%	0.01
Emphysema	4.3%	14.8%	0.058
Pleural puncture	5.8%	9.3 %	0.504
Erytrocytes	2.01	1.41	0.094
Plasma	1.17	0.46	0.001
Trombocytes	0.04	0.09	0.46
Protrombin	0.12	0.15	0.46
Revision	3%	4%	1.0
CVVHD	9%	4%	0.30

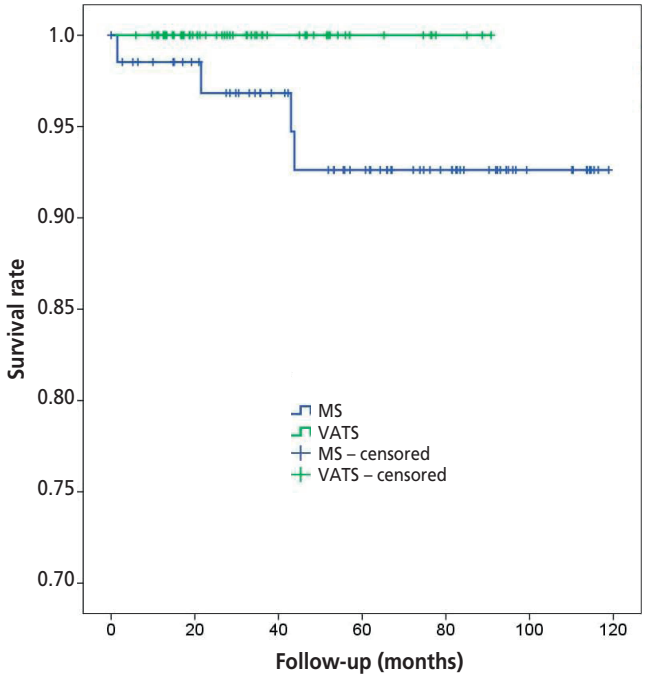


Fig. 2 – Kaplan–Meier analysis of postoperative survival.

Table 3 – Echocardiographic parameters after mitral valve repair surgery

Parameter	ST (n = 37)	VATS (n = 51)	*p*-value
Pre-operative			
LVEF	59.6%	60.6%	0.74
LKd	56.0 mm	58.5 mm	0.12
LKs	38 mm	39.6 mm	0.42
3 months post-OP			
LVEF	54.2%	55.5%	0.50
LKd	50 mm	51 mm	0.13
LKs	37.50 mm	37.52 mm	0.48
Regurgitation	0.61	0.76	0.40
Mean gradient	3.1	2.9	0.25
1 year post-OP			
LVEF	55.7%	56.3%	0.77
LKd	49.6 mm	51.4 mm	0.03
LKs	35.53 mm	35.46 mm	0.35
Regurgitation	0.66	0.68	0.88
Mean gradient	3.1	3.3	0.17

implantation, development of atrial fibrillation, length of hospitalization, neurological complications or need of CVVHD, no differences were observed between the groups (**Table 2**).

Survival was monitored for an average of 3 years in the VATS group with a survival rate of 100% and in the ST group for 5.2 years with a survival rate of 94%. Kaplan–Meier survival analysis and log-rank test showed no statistically significant difference in survival (p = 0.12) (**Fig. 2**). The median follow-up for MACE incidence in the ST group was 4.9 years with an incidence of 13%, and in the VATS group it was 2.8 years with an incidence of 6%, with no statistically significant difference (p = 0.71) (**Fig. 3**).

In the subgroup after exclusion of patients who underwent mitral valve replacement, no significant differences in ECHO parameters were found preoperatively. In the subsequent comparison of postoperative parameters, a larger left ventricular diameter in diastole was recorded one year after surgery in the VATS group (51.4 vs. 49.6 mm; p = 0.03). No other parameters showed statistically significant differences (**Table 3**).

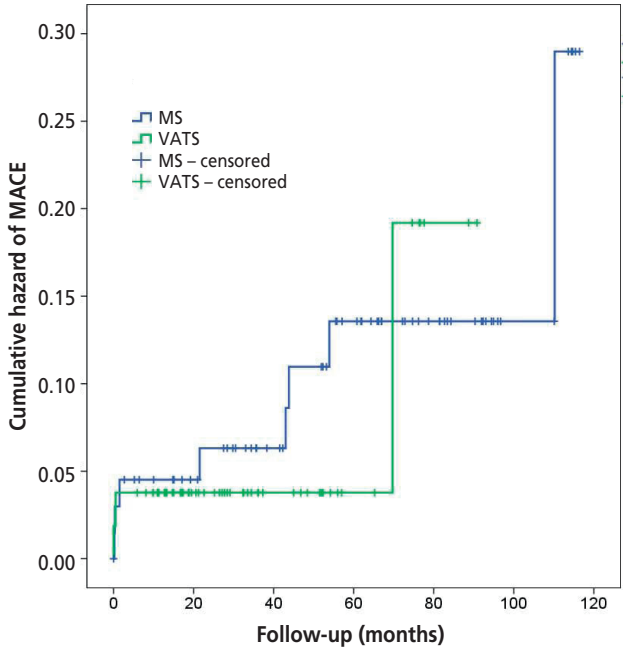


Fig. 3 – Kaplan–Meier analysis of MACE event.

Discussion

An interesting finding of the study is the difference in preoperative risk between the groups, with patients in the ST group having a higher EuroScore. This observed selection of patients probably reflects natural tendencies in surgical practice, where more complex or higher-risk patients are treated using a standard approach. A similar trend was described in a retrospective analysis by Pojar et al.[7] with a higher EuroScore in the case of sternotomy by an average of 1.7, and in a British observational study by Jackson et al.[8] by as much as 3.2. In contrast, in randomized and propensity score-matched studies that specifically balanced baseline characteristics, including EuroScore, no difference in preoperative risk between ST and VATS was demonstrated. In the multicenter UK Mini Mitral randomized clinical trial, the average EuroScore was identical in both groups (1.7 ± 1.6 vs. 1.7 ± 1.4).[5]

The incidence of infective endocarditis was higher in the ST group (12% vs. 2%), but the difference was not statistically significant (p = 0.08). This trend is consistent with the literature, according to which valve with infective endocarditis has long been considered a relative con-

traindication to a minimally invasive approach, and many centers have therefore preferred sternotomy.[9] However, recent studies show that with careful patient selection, MIMVS is technically feasible in native infective endocarditis and provides comparable or even better results, including shorter ventilation and ICU stay, compared to sternotomy.[9,10]

In the VATS group, we describe a valve-sparing surgery rate of 94%, compared to 55% in the ST group. Data from the STS and Euro Heart Survey databases indicate that the valve repair rate in the US and Europe was 41% and 46.5%, respectively.[11,12] A study by Gammie et al. reports a 67% repair rate with ST and an 85% repair rate with VATS.[13]

Our echocardiographic follow-up found that, when valve replacements were excluded and only preservation surgeries (MVP group) were evaluated, there were no statistically significant differences in mitral valve pressure gradients between the two approaches throughout the follow-up period. This comparable medium-term valve function is clinically important because it shows that the quality of conservative surgery is not compromised by the minimally invasive approach.

The only statistically significant echocardiographic difference in the MVP subgroup was a larger end-diastolic left ventricular dimension (LVd) in the VATS group one year after surgery (51.4 mm vs. 49.6 mm, $p = 0.033$). Although this difference is statistically significant, its clinical impact is likely to be marginal (a difference of 1.8 mm), and it has not been shown to result into differences in left ventricular ejection fraction, other echocardiographic parameters, or patient survival. Longer-term follow-up would be useful to characterize this phenomenon.

In our study, we found no statistically significant differences between ST and VATS in terms of the need for surgical revision, wound infection, complications requiring fluidothorax puncture or pneumothorax drainage, the occurrence of atrial fibrillation, neurological complications or the need for CVVHD, with all these parameters ranging within the values described in larger studies.[7,14]

The statistically significant longer CPB and aortic clamp times in the VATS group (by 54 and 34 min, respectively; $p < 0.0001$) is consistent with most published studies describing an increase in both of these times in MIMVS compared to sternotomy, reflecting the technical difficulty and longer learning curve of minimally invasive techniques. In the analysis by Iribarne et al.[15], the CPB time in VATS was approximately 22–25 minutes longer and the clamp time was 9–14 minutes longer; similar differences are also reported in other comparative studies and meta-analyses.[7,14] In the presented group, the prolongation of CPB and aortic clamp time is even more significant, which may be related to both the learning curve during the introduction of the VATS program and the higher complexity of procedures (higher incidence of repair operations) in the minimally invasive group. Nevertheless, this difference did not lead to a deterioration in survival, longer hospitalization or a higher incidence of renal failure or reoperations for bleeding, which is consistent with meta-analyses that do not consider longer operating times in MIMVS to be clinically significant.[14,16,17]

The meta-analysis by Spadini et al.[17] reports a shorter length of hospital stay after VATS compared to ST, which was not statistically significant in our study (VATS 5.0 vs. ST 5.2 days in the ICU, VATS 11.9 vs. ST 12 days of hospital stay). This result may be due to similar postoperative care and patient management protocols in both groups at our center.

In our cohort, the average number of red blood cell units administered between the ST and VATS groups differed only slightly (ST 2.01 vs. VATS 1.41 units), with the difference not reaching statistical significance ($p = 0.09$). This result is consistent with published studies with smaller and medium-sized patient cohorts, in which MIMVS does not show a clear reduction in the consumption of erythrocyte concentrates, or the differences are only marginal and often not statistically significant.[18,19] In contrast, meta-analyses with several hundred to thousands of patients more often demonstrate a slightly lower need for transfusions in MIMVS.[20]

In the context of our data, there is a lower incidence of MACE in the VATS group (6% vs. 13% in ST), with no statistical significance ($p = 0.71$), in line with several studies reporting a long-term absence of MACE at a level of approximately 85–95% in both groups during medium- to long-term follow-up.[14,18] The fact that no significant difference was demonstrated between the groups despite different median follow-up times suggests that even with longer follow-up, there is no accumulation of MACE in the ST group that would fundamentally disadvantage this approach, but at the same time supports the hypothesis of the long-term safety of VATS.

In the medium-term follow-up, the survival analysis in our cohort reached 100% after 3 years in the VATS group and 94% after an average follow-up of 5.2 years in the ST group ($p = 0.12$), which is consistent with several large studies where 5-year survival is most often around 93–96% in both groups, with no significant difference between MIMVS and sternotomy.[7,21,22]

Conclusion

Our results show that video-assisted thoracoscopic mitral valve surgery provides clinical results comparable to standard median sternotomy. Despite longer cardiopulmonary bypass and aortic cross-clamp times, no increase in serious postoperative complications was observed. The minimally invasive group had a higher proportion of mitral valve repairs and similar echocardiographic results in the repair surgery subgroup. Long-term survival and the incidence of major adverse cardiac events (MACE) did not differ between the two approaches. Our findings support the position of the minimally invasive VATS approach as a safe and effective alternative to sternotomy in specialized centers with sufficient experience.

Conflict of interest
The authors declare that there are no financial or personal relationships that could inappropriately influence (bias) the work reported in this manuscript. The authors

confirm that they have no conflicts of interest relevant to the content of this article.

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Ethical statement
The processing of the retrospective study was approved by the Ethics Committee in compliance with the principles of the Declaration of Helsinki and ICH Guidelines for Good Clinical Practice and applicable regulatory requirements (protocol code: 2026003 and date of approval: February 13, 2026).

Informed consent
During hospitalization, patients provided written consent for the healthcare received. According to the recommendation of the Ethics Committee, due to the retrospective nature of the study, no further patient consents were required.

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Původní sdělení | Original research article

Systemic Immune-Inflammation Index Levels in Patients with Coronary Slow Flow: A Case-Control Study

Okan Tanriverdi[a], Husna Sengul Askin[b], Lutfu Askin[c], Mustafa Polat[d], Esra Polat[d]

[a] *Department of Cardiology, Adiyaman Education and Research Hospital, Merkez/Adıyaman, Turkey*
[b] *Department of Infectious Disease, Gaziantep City Hospital, Gaziantep, Turkey*
[c] *Department of Cardiology, Gaziantep Islamic Science and Technology University, Gaziantep, Turkey*
[d] *Department of Cardiology, Gaziantep City Hospital, Gaziantep, Turkey*

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Zánět

SOUHRN

Kontext: Termínem pomalý koronární průtok (coronary slow flow, CSF) se při angiografickém vyšetření označuje protrahovaná distální opacifikace koronárních tepen v nepřítomnosti významné stenózy. I když přesná patogeneze tohoto jevu dosud nebyla zcela objasněna, přibývající důkazy ukazují na jistý podíl systémového zánětu a mikrovaskulární dysfunkce. Za spolehlivý ukazatel systémového zánětu je v poslední době uznáván index systémového zánětu a imunitní odpovědi (systemic immune-inflammation index, SII), založený na počtech buněk v periferní krvi.
Cílem této studie bylo zhodnotit korelaci mezi hodnotami SII a pomalým koronárním průtokem u pacientů s pocitem tlaku či bolesti na hrudi.
Metody: Do studie bylo zařazeno celkem 300 pacientů ve věku 30 až 70 let, kteří byli dopraveni na urgentní příjem nebo na ambulanci s bolestí na hrudi. Na základě výsledku koronarografického vyšetření byli pacienti rozděleni do dvou skupin: skupina s CSF (n = 150) a skupina s normálním koronárním průtokem (n = 150). Ze studie byli vyřazeni pacienti s významnou stenózou koronární tepny, chlopenní vadou, nádorovým onemocněním nebo se systémovým zánětem. Hodnota SII se vypočítávala jako (počet neutrofilů × počet trombocytů) / počet lymfocytů. Statistické analýzy se prováděly s použitím softwaru SPSS verze 25.0.
Výsledky: Průměrné hodnoty SII byly ve skupině CSF vyšší než u kontrol (728 ± 242 vs. 418 ± 165; $p < 0{,}001$). Pacienti s CSF vykazovali zvýšené poměry neutrofilů k lymfocytům (neutrophil-to-lymphocyte ratio, NLR) a trombocytů k lymfocytům (platelet-to-lymphocyte ratio, PLR). V multivariační logistické regresní analýze představovala zvýšená hodnota SII nezávislý prediktor CSF (OR = 2,41; 95% CI 1,64–3,53; $p < 0{,}001$). Analýza křivky operační charakteristiky přijímače (receiver operating characteristic, ROC) prokázala vhodnou mezní hodnotu SII ve výši 560 s výslednou 80% senzitivitou a 75% specificitou (AUC = 0,84).
Závěr: Zvýšené hodnoty SII statisticky významně korelují s pomalým koronárním průtokem, což ukazuje na zásadní roli systémového zánětu v patofyziologii uvedeného jevu. Hodnoty SII tak mohou představovat nákladově účinný a snadno dostupný biomarker pro stanovení rizika u pacientů s podezřením na CSF.
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Keywords:
Biomarkers
Coronary sluggish flow
Inflammation
Microvascular dysfunction
Systemic immune-inflammation index

ABSTRACT

Background: Coronary slow flow (CSF) is an angiographic occurrence marked by the protracted distal opacification of coronary arteries without the presence of substantial stenosis. While its precise pathogenesis is not fully elucidated, mounting evidence substantiates the involvement of systemic inflammation and microvascular dysfunction. The Systemic Immune-Inflammation Index (SII), based on peripheral blood counts, has lately been recognised as a reliable indicator of systemic inflammation.
The objective of this study was to assess the correlation between SII levels and coronary sluggish flow in patients experiencing chest discomfort.
Methods: A total of 300 patients, aged 30 to 70 years, presenting to the emergency department or outpatient clinic with chest pain were enrolled. All individuals underwent coronary angiography and were categorised into two groups: the CSF group (n = 150) and the normal coronary flow group (n = 150). Patients with substantial coronary stenosis, valve disease, cancer, or systemic inflammatory conditions were excluded. The SII was computed as (Neutrophil count × Platelet count) / Lymphocyte count. Statistical analyses were conducted with SPSS version 25.0.

Address: Lutfu Askin, MD, Gaziantep Islamic Science and Technology University, 2700 – Gaziantep, Turkey, e-mail: lutfuaskin23@gmail.com
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Results: Mean SII levels were markedly elevated in the CSF group relative to controls (728 ± 242 vs. 418 ± 165, p <0.001). Patients with CSF exhibited elevated neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). In multivariate logistic regression, increased SII was an independent predictor of CSF (OR = 2.41, 95% CI: 1.64–3.53, p <0.001). An examination of the receiver operating characteristic (ROC) curve indicated an appropriate SII cutoff of 560, resulting in 80% sensitivity and 75% specificity (AUC = 0.84).
Conclusion: Increased SII levels are significantly correlated with coronary sluggish flow, indicating that systemic inflammation is crucial in its pathophysiology. The SII may function as a cost-effective and readily available biomarker for risk evaluation in patients with suspected CSF.

Introduction

Coronary slow flow (CSF) is delayed opacification in the coronary arteries without occlusion. Initially documented by Tambe et al. in 1972.[1] The incidence varies from 1% to 5% in angiograms, although the underlying mechanisms are not fully comprehended.[2] Proposed aetiologies encompass microvascular dysfunction, endothelial inflammation, and heightened small-vessel resistance.[3,4] The Systemic Immune-Inflammation Index (SII) is a composite biomarker derived from the counts of neutrophils, lymphocytes, and platelets. It harmonises the equilibrium between inflammatory and immunological responses.[5] Originally established as a prognostic marker in oncology,[6] the SII has lately been linked to several cardiovascular disorders, including cardiovascular diseases (CVDs).[7–9] Considering that CSF is regarded as a low-grade inflammatory condition, evaluating the role of SII may yield new insights into its pathophysiology and clinical applicability.[10] This study sought to assess SII levels in CSF patients relative to people with normal coronary flow.

Materials and methods

Study design and population

This case-control study was performed from January 2024 to June 2025 at a tertiary cardiology centre. Three hundred individuals aged 30 to 70 years, who reported with chest discomfort and had coronary angiography, were included in the study. The minimal required sample size, calculated using G*Power 3.1, was determined to be 270 for an effect size of 0.35, α = 0.05, and power = 0.90.

Inclusion criteria: Individuals aged 30 to 70 years presenting with chest pain warranting coronary angiography, with angiographic findings of normal coronary anatomy or coronary spasm (**Table 1**).

Exclusion criteria: Substantial coronary stenosis (>20%), valvular heart disease, heart failure (ejection fraction <50%), malignancy, autoimmune or inflammatory disorders, acute infection, chronic renal or hepatic impairment. Coronary angiography was conducted using the usual Judkins procedure. The TIMI frame count was utilised to establish CSF as a corrected TIMI frame count (CTFC) above 27 frames for a minimum of one major coronary artery.[11]

Laboratory measurements and SII calculation

Venous blood specimens were obtained following an 8-hour fast. The complete blood count was evaluated by an automated haematology analyser. SII = (neutrophil count multiplied by platelet count) divided by lymphocyte count. Routine biochemical parameters were documented as well (**Table 2**).

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 25.0 (IBM Corp., Armonk, NY, USA). The minimal sample size was determined using G*Power 3.1.9.7. For a medium effect size (Cohen's d = 0.35), α = 0.05, and power (1–β) = 0.90, a minimum sample size of 270 people was calculated. To reduce attrition and improve statistical robustness, 300 participants were included. Data normality was determined using Kolmogorov–Smirnov and Shapiro–Wilk tests. Continuous variables with normal distribution were represented as mean ± SD, whereas non-normally distributed data were presented as median (IQR). Categorical variables were reported as numbers and percentages. Both groups were compared using the Student's t-test for normally distributed variables and

Table 1 – Baseline demographic and clinical characteristics of the study population

Parameter	CSF (n = 150)	Control (n = 150)	Total (n = 300)	t / χ^2	*p*-value
Age (years)	54.8 ± 9.6	53.6 ± 10.1	54.2 ± 9.8	1.01	0.31
Male gender, n (%)	85 (56.7%)	77 (51.3%)	162 (54%)	0.85	0.36
Hypertension, n (%)	72 (48%)	68 (45.3%)	140 (46.7%)	0.22	0.64
Diabetes mellitus, n (%)	36 (24%)	33 (22%)	69 (23%)	0.16	0.69
Smoking, n (%)	65 (43.3%)	60 (40%)	125 (41.7%)	0.30	0.58
BMI (kg/m²)	27.9 ± 3.5	27.5 ± 3.7	27.7 ± 3.6	0.88	0.38

BMI – body mass index; CSF – coronary slow flow.
Continuous variables were analyzed using Student's t-test; categorical variables were analyzed using the Chi-square (χ^2) test.

Table 2 – Laboratory parameters and inflammatory indices in study groups

Parameter	CSF (mean ± SD)	Control (mean ± SD)	t-value	*p*-value
Neutrophils (× 10⁹/L)	6.4 ± 1.8	4.8 ± 1.5	5.12	<0.001
Lymphocytes (× 10⁹/L)	1.9 ± 0.6	2.5 ± 0.7	-6.42	<0.001
Platelets (× 10⁹/L)	274 ± 55	252 ± 50	3.38	0.001
SII ([Neut × PLT]/Lymph)	728 ± 242	418 ± 165	9.56	<0.001
NLR	3.1 ± 1.2	2.0 ± 0.8	8.01	<0.001
PLR	145 ± 48	110 ± 40	6.12	0.002
CRP (mg/L)	4.8 ± 1.7	2.9 ± 1.3	8.40	<0.001

CRP – C-reactive protein; NLR – Neutrophil-to-Lymphocyte Ratio; PLR – Platelet-to-Lymphocyte Ratio; SII – Systemic Immune-Inflammation Index.
Continuous variables were analyzed using Student's t-test. A *p*-value <0.05 was considered statistically significant. Significance levels: *p* <0.05. Values are expressed as mean ± standard deviation (SD).

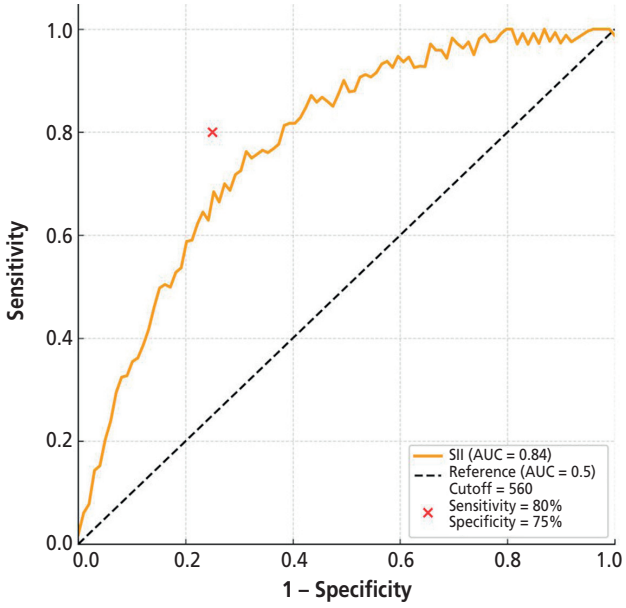


Fig. 1 – ROC curve for SII in predicting coronary slow flow.

the Mann–Whitney U test for non-parametric variables. Categorical data were analysed using chi-square (χ^2) or Fisher's exact test.

SII, TIMI frame count, NLR, PLR, and CRP were correlated. CSF-independent factors were found using binary logistic regression. Variables with a *p*-value <0.10 in univariate analysis were included in the multivariate model. The results were given as ORs with 95% CIs. SII's CSF prediction accuracy was assessed using ROC curve analysis (**Fig. 1**). AUC, optimum cutoff value, sensitivity, and specificity were calculated using the Youden index (J = sensitivity + specificity – 1). All statistical tests are two-tailed, and *p*-values under 0.05 are significant.

Results

Three hundred patients were analysed, evenly divided into the CSF group (n = 150) and the control group (n = 150) exhibiting normal coronary flow. The average age of the entire group was 54.2 ± 9.8 years, with 162 individuals (54%) being male. The baseline demographics, encompassing hypertension, diabetes mellitus, and smoking prevalence, were comparable between the two groups (*p* >0.05). Laboratory results indicated markedly elevated inflammatory markers in CSF patients. The average SII was 728 ± 242 in the CSF group compared to 418 ± 165 in the control group (*p* <0.001). The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were elevated in the CSF group (NLR: 3.1 ± 1.2 vs. 2.0 ± 0.8, *p* <0.001; PLR: 145 ± 48 vs. 110 ± 40, *p* = 0.002).

A correlation study revealed a strong positive association between TIMI frame count and SII (r = 0.46, *p* <0.001). Multivariate logistic regression revealed SII (OR = 2.41, 95% CI: 1.64–3.53, *p* <0.001) and NLR (OR = 1.83, 95% CI: 1.21–2.78, *p* = 0.004) were independent predictors of CSF. ROC curve research determined an appropriate SII threshold of 560, resulting in 80% sensitivity and 75% specificity (AUC = 0.84, *p* <0.001).

Discussion

The current investigation revealed that patients with CSF display markedly elevated levels of the SII, NLR, and PLR in comparison to persons with normal coronary flow. These findings corroborate the concept that systemic inflammation and microvascular endothelial dysfunction are pivotal in the pathogenesis of CSF.[12,13]

Our findings align with numerous other studies that have associated inflammatory indicators with CSF. Increased levels of C-reactive protein and soluble adhesion molecules correlate with compromised coronary flow. Akboga et al.[15] determined that PLR forecasts both the existence and intensity of CSF, whereas Li et al.[14] emphasised NLR as a sensitive marker of microvascular impairment. In our investigation, SII surpassed both NLR and PLR in discriminative capability, indicating that it may offer a more thorough depiction of immunological and inflammatory equilibrium. The increase of SII in CSF can be elucidated through multiple interrelated processes.[16] Activated neutrophils discharge reactive oxygen species (ROS) and proteolytic enzymes, resulting in endothelial damage and

diminished nitric oxide bioavailability, hence elevating microvascular resistance.[17,18]

Concurrently, platelets secrete thromboxane A2, serotonin, and adhesion molecules, thereby enhancing endothelial activation and microvascular constriction.[20] Decreased lymphocyte levels indicate a reduction of the adaptive immune response, leading to an uncontrolled proinflammatory environment.[21] Collectively, these pathways create a detrimental inflammatory loop that may contribute to CSF. This work builds upon prior findings by using SII as a new haematological biomarker in the evaluation of CSF. In our logistic regression study, SII independently predicted CSF (OR = 2.41, 95% CI 1.64–3.53), even after controlling for confounding variables like hypertension, diabetes, and smoking. The ROC analysis exhibited exceptional diagnostic accuracy (AUC = 0.84), akin to values documented in acute coronary syndromes and subclinical atherosclerosis.[19–22]

These findings underscore SII as an accessible, cost-effective, and dependable inflammatory indicator that may be integrated into the clinical risk assessment of chest pain patients with normal angiograms. Our data, moreover, furnish indirect evidence corroborating the continuum between microvascular inflammation and early atherosclerosis. Kaya et al.[17] and Taşolar et al.[18] identified endothelial dysfunction and low-grade inflammation as common mechanisms linking CSF and coronary artery disease (CAD). Oflar et al.[21] and Candemir et al.[19] have shown that SII is associated with atherosclerotic plaque load and instability.

Consequently, CSF may not be a benign angiographic observation, as previously proposed by Ahmed et al.,[25] but instead an early indicator of systemic vascular inflammation and a potential precursor to future coronary events. Clinically, the identification of increased SII in CSF patients may impact therapy options. Anti-inflammatory treatments, including colchicine, statins, and IL-1 inhibitors, have demonstrated efficacy in diminishing vascular inflammation and enhancing endothelial function.[22] The incorporation of SII into standard clinical practice may assist in informing therapeutic choices, assessing treatment response, and stratifying cardiovascular risk in this patient demographic.[23,24]

Notwithstanding its merits – sufficient sample size, exclusion of confounding inflammatory diseases, and standardised angiographic evaluation – this study possesses multiple limitations. The study has a single-centre, cross-sectional design, which prevents causal inference. Secondly, specific inflammatory mediators such as IL-6, TNF-α, and hs-CRP were not assessed. Third, long-term follow-up data about cardiovascular outcomes were unavailable. Future multicentre longitudinal investigations are essential to evaluate the predictive significance of SII and ascertain whether therapies aimed at systemic inflammation can enhance coronary microvascular perfusion and outcomes in CSF patients.

In conclusion, our findings robustly endorse the notion that systemic immune-inflammatory activation plays a substantial role in coronary sluggish flow. The SII is a reliable and effective biomarker for evaluating inflammatory status and forecasting the presence of CSF. Prompt diagnosis of patients with increased SII may provide timely treatment measures to mitigate inflammation, enhance endothelial function, and avert progression to overt atherosclerotic disease.

Conflict of interest
No conflicts of interest

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The funding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

Ethical statement
All procedures in this study comply with ethical standards and are consistent with the Declaration of Helsinki. The Ethics Committee for Clinical Research accepted the study protocol (2024-478).

Informed consent
All participants gave informed permission before the trial.

Contributions of authors
All authors contributed equally to the work, encompassing data collection and analysis, manuscript composition and revision, culminating in final approval of the version for publication. We collectively accept responsibility for all technical and ethical dimensions of the activity.

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Původní sdělení | Original research article

Impact of Stent Overlapping on Clinical Outcomes in Patients with Long Coronary Lesions Undergoing Percutaneous Coronary Intervention

Esma Selva Ateş Ceyhun

Department of Cardiology, Erzurum City Hospital, Erzurum, Turkey

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SOUHRN

Kontext: Perkutánní koronární intervence se běžně provádí jako způsob léčby ischemické choroby srdeční. Dlouhé koronární léze často vyžadují implantaci více než jednoho stentu, což znamená, že se jejich jednotlivé segmenty mohou překrývat. Zvýšená přítomnost kovu a změněné hojení cév v oblasti překrytí mohou přispívat k nežádoucímu výslednému klinickému stavu.
Metody: V této studii jsme hodnotili pacienty po perkutánní koronární intervenci pro dlouhé léze na koronárních tepnách. Pacienti byli rozděleni do dvou skupin podle strategie použité při implantaci stentu: implantace překrývajících se stentů nebo implantace jednoho dlouhého stentu. Během sledování se hodnotily klinické parametry včetně vzniku významných kardiovaskulárních příhod, infarktu myokardu, revaskularizace cílové léze, trombózy stentu a mortalita.
Výsledky: U pacientů s překrývajícími se stenty byl zaznamenán početně vyšší výskyt nežádoucích klinických příhod, který nicméně nedosáhl statistické významnosti. Ve skupině s překrývajícími se stenty byl pozorován zvláště vyšší počet případů revaskularizace cílové léze a trombózy stentu.
Závěr: Implantace překrývajících se stentů v léčbě dlouhých koronárních lézí může být spojena s trendem zvyšujícího se rizika nežádoucích kardiovaskulárních příhod. Zlepšení výsledného klinického stavu u této skupiny pacientů může napomoci uvážlivá volba strategie implantace stentu.

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Keywords:
Coronary artery disease
Drug-eluting stents
Long coronary lesions
Percutaneous coronary intervention
Stent overlap

ABSTRACT

Background: Percutaneous coronary intervention is widely used in the treatment of coronary artery disease. Long coronary lesions frequently require implantation of more than one stent, which may lead to overlapping stent segments. Increased metal burden and altered vascular healing in the overlapping region may contribute to adverse clinical outcomes.
Methods: This study evaluated patients who underwent percutaneous coronary intervention for long coronary lesions. Patients were divided into two groups according to the stenting strategy: overlapping stent implantation and single long stent implantation. Clinical outcomes including major adverse cardiovascular events, myocardial infarction, target lesion revascularization, stent thrombosis, and mortality were assessed during follow-up.
Results: Patients treated with overlapping stents demonstrated numerically higher rates of adverse clinical events without reaching statistical significance. In particular, target lesion revascularization and stent thrombosis were observed more frequently in the overlapping stent group.
Conclusion: Overlapping stent implantation in the treatment of long coronary lesions may be associated with a trend toward increased risk of adverse cardiovascular events. Careful selection of stenting strategy may help improve clinical outcomes in these patients.

Address: Esma Selva Ateş Ceyhun, MD; Department of Cardiology, Erzurum City Hospital, Erzurum, Turkey, e-mail: esmaselva@gmail.com
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Introduction

Coronary artery disease remains one of the leading causes of morbidity and mortality worldwide despite significant advances in diagnostic and therapeutic strategies. Percutaneous coronary intervention has become a cornerstone in the treatment of obstructive coronary artery disease and is widely performed to restore coronary blood flow and improve clinical outcomes. The introduction of drug-eluting stents has significantly reduced rates of restenosis and repeat revascularization compared with bare-metal stents, representing a major milestone in interventional cardiology.[1]

Despite these advances, the treatment of long coronary lesions continues to pose important procedural and clinical challenges. Long lesions are commonly associated with diffuse atherosclerosis, increased plaque burden, and complex vessel morphology. These characteristics have been shown to increase the risk of restenosis, target lesion failure, and other adverse cardiovascular outcomes following percutaneous coronary intervention.[2] Consequently, achieving complete lesion coverage often requires the implantation of multiple stents.

In clinical practice, long coronary lesions frequently necessitate the use of more than one stent, resulting in overlapping stent segments. Stent overlap may increase the total metal burden within the treated vessel and may lead to alterations in local vascular biology. Experimental and pathological studies have suggested that overlapping segments may be associated with delayed endothelial healing, increased inflammatory response, and greater neointimal proliferation.[3] In addition, overlapping regions may disrupt normal coronary flow dynamics, which may further contribute to thrombotic complications.

Several clinical studies have investigated the potential impact of stent overlap on clinical outcomes. Earlier studies suggested that overlapping stents were associated with increased rates of restenosis and stent thrombosis, particularly in the era of first-generation drug-eluting stents.[4] However, with the introduction of newer-generation drug-eluting stents characterized by thinner struts, improved polymers, and enhanced drug delivery systems, the clinical implications of stent overlap remain controversial. Some studies have reported comparable outcomes between overlapping and non-overlapping stenting strategies, while others have continued to demonstrate an increased risk of adverse events in overlapping segments.[5]

Given the increasing complexity of coronary interventions and the frequent need to treat long lesions in contemporary practice, understanding the clinical implications of stent overlap remains highly relevant. Clarifying whether overlapping stent implantation affects long-term clinical outcomes may help guide procedural strategies and optimize patient management during percutaneous coronary intervention.

Therefore, the present study aimed to evaluate the effect of stent overlapping regions on clinical outcomes in patients undergoing percutaneous coronary intervention for long coronary lesions.

Methods

Study design and study population

This study was designed as a single-center retrospective observational study. Consecutive patients who underwent percutaneous coronary intervention for long coronary lesions at the cardiology department between January 2019 and December 2025 were retrospectively screened. Clinical, angiographic, and procedural data were obtained from the hospital electronic medical record system and catheterization laboratory database.

Patients aged 18 years or older who underwent percutaneous coronary intervention for a coronary lesion with a total stent length greater than or equal to 30 mm were included in the study. Patients with previous coronary artery bypass graft surgery, cardiogenic shock at presentation, in-stent restenosis, or incomplete clinical follow-up data were excluded from the analysis.

Definition of long coronary lesion

Long coronary lesion was defined as a coronary stenosis requiring a total stent length of 30 mm or greater during percutaneous coronary intervention. Lesion length was determined based on coronary angiographic assessment performed by experienced interventional cardiologists.

Study groups

Patients were divided into two groups according to the stenting strategy used during the index procedure. The overlapping stent group consisted of patients in whom two or more stents were implanted with overlapping segments to achieve complete lesion coverage. The non-overlapping group included patients treated with a single long stent without overlapping segments.

Percutaneous coronary intervention procedure

All coronary angiography and percutaneous coronary intervention procedures were performed according to standard clinical practice guidelines. Vascular access was obtained through either the radial or femoral artery depending on operator preference. Lesion characteristics, stent diameter, and stent length were determined by the interventional cardiologist based on angiographic findings. Drug-eluting stents were used in all patients. Post-dilatation was performed when considered necessary to optimize stent expansion.

Data collection

Demographic characteristics, cardiovascular risk factors, angiographic findings, procedural details, and follow-up outcomes were collected retrospectively from medical records and the institutional database. Angiographic data included lesion length, target vessel, stent diameter, stent length, and number of implanted stents. Follow-up data were obtained from hospital records and outpatient visits, and when necessary, by telephone contact.

Clinical outcomes and definitions

The primary outcome of the study was the occurrence of major adverse cardiovascular events during 12-month

follow-up. Major adverse cardiovascular events were defined as a composite of cardiovascular death, myocardial infarction, target lesion revascularization, or definite stent thrombosis.

Myocardial infarction was defined according to the Fourth Universal Definition of Myocardial Infarction. Stent thrombosis was defined according to the Academic Research Consortium (ARC) criteria. Target lesion revascularization was defined as repeat percutaneous coronary intervention or coronary artery bypass graft surgery performed due to restenosis or re-occlusion within the previously treated lesion segment. Stent thrombosis was defined according to standard clinical definitions.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation, and categorical variables were presented as numbers and percentages. The normality of data distribution was assessed using the Kolmogorov–Smirnov test. Continuous variables were compared using the Student's t-test or the Mann–Whitney U test as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test when necessary. A two-sided *p*-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using statistical software.

Ethics statement

The study protocol was reviewed and approved by the Scientific Research Ethics Committee of the Faculty of Medicine at Health Sciences University Erzurum City Hospital. Ethical approval was granted on December 10, 2025 (Meeting No: 12, Decision No: 297; Approval No: 2025/297). The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective design of the study, the requirement for informed consent was waived by the ethics committee.

Results

Study population

A total of 214 patients who underwent percutaneous coronary intervention for long coronary lesions were included in the study. According to the stenting strategy, patients were divided into two groups: the overlapping stent group (n = 96) and the single long stent group (n = 118).

Baseline clinical characteristics

Baseline clinical characteristics of the study population are presented in **Table 1**. The mean age of the overall population was 63.4 ± 10.8 years, and 68% of the patients were male. The prevalence of major cardiovascular risk factors, including hypertension, diabetes mellitus, hyperlipidemia, and smoking, was similar between the two groups. No statistically significant differences were observed between the groups with respect to baseline demographic or clinical characteristics.

Angiographic and procedural characteristics

Angiographic and procedural characteristics are summarized in **Table 2**. Lesion length was significantly longer in the overlapping stent group compared with the single stent group (38.6 ± 6.4 mm vs 31.2 ± 4.8 mm, $p < 0.001$). Accordingly, the mean stent length and the number of implanted stents were significantly higher in the overlapping stent group. Drug-eluting stents were used in all patients. Procedural success was achieved in the majority of cases, and post-dilatation rates were comparable between the two groups.

Clinical outcomes

Clinical outcomes during follow-up are presented in **Table 3**. Major adverse cardiovascular events were numerically higher in the overlapping stent group; however, the difference did not reach statistical significance (14.6% vs 7.6%, $p = 0.09$). Target lesion revascularization was significantly higher in the overlapping stent group (8.3% vs 3.4%, $p = 0.048$). Stent thrombosis occurred more frequently in the overlapping stent group; however, the difference did not reach statistical significance.

The rates of myocardial infarction and cardiovascular death were similar between the two groups.

Table 1 – Baseline clinical characteristics

Variable	Overlapping stent (n = 96)	Single stent (n = 118)	*p*-value
Age (years)	64.1 ± 10.2	62.8 ± 11.1	0.38
Male sex, n (%)	66 (68.7)	79 (66.9)	0.77
Hypertension, n (%)	58 (60.4)	69 (58.5)	0.78
Diabetes mellitus, n (%)	34 (35.4)	38 (32.2)	0.63
Hyperlipidemia, n (%)	46 (47.9)	54 (45.8)	0.76
Current smoking, n (%)	29 (30.2)	32 (27.1)	0.61

Table 2 – Angiographic and procedural characteristics

Variable	Overlapping stent (n = 96)	Single stent (n = 118)	*p*-value
Lesion length (mm)	38.6 ± 6.4	31.2 ± 4.8	<0.001
Stent length (mm)	44.8 ± 7.3	34.5 ± 5.6	<0.001
Number of stents	2.1 ± 0.4	1.0 ± 0.0	<0.001
Post-dilatation, n (%)	58 (60.4)	69 (58.5)	0.79
Radial access, n (%)	71 (74.0)	85 (72.0)	0.74

Table 3 – Clinical outcomes during follow-up

Outcome	Overlapping stent (n = 96)	Single stent (n = 118)	*p*-value
Major adverse cardiovascular events, n (%)	14 (14.6)	9 (7.6)	0.09
Myocardial infarction, n (%)	4 (4.2)	3 (2.5)	0.49
Target lesion revascularization, n (%)	8 (8.3)	4 (3.4)	0.048
Stent thrombosis, n (%)	3 (3.1)	1 (0.8)	0.18
Cardiovascular death, n (%)	2 (2.1)	2 (1.7)	0.85

Discussion

In the present study, we evaluated the clinical impact of stent overlapping in patients undergoing percutaneous coronary intervention for long coronary lesions. The main findings of our study were that overlapping stent implantation was associated with a higher rate of target lesion revascularization during follow-up, whereas other major adverse cardiovascular outcomes such as myocardial infarction and cardiovascular mortality were comparable between patients treated with overlapping stents and those treated with a single long stent.

The treatment of long coronary lesions remains one of the most challenging scenarios in contemporary interventional cardiology. Diffuse atherosclerotic disease and increased plaque burden frequently require implantation of multiple stents to achieve complete lesion coverage. Previous studies have demonstrated that lesion length is an important predictor of restenosis and adverse clinical outcomes after percutaneous coronary intervention.[6] It should be noted that lesion length was significantly greater in the overlapping stent group, which may have influenced the observed outcomes. Lesion length is a well-established predictor of adverse events following percutaneous coronary intervention and may act as a confounding factor in the relationship between stent overlap and clinical outcomes.

One of the main concerns regarding stent overlap is the increased metal burden within the vessel wall. Pathological and experimental studies have demonstrated that overlapping stent segments may lead to delayed endothelialization, increased inflammatory response, and excessive neointimal proliferation.[3] These mechanisms may increase the risk of restenosis and thrombotic complications.

Several clinical investigations have evaluated the clinical implications of overlapping stents. Earlier studies conducted during the first-generation drug-eluting stent era demonstrated higher rates of restenosis and repeat revascularization in overlapping segments.[7] Similarly, observational studies have reported that overlapping stent implantation may be associated with an increased incidence of target lesion failure and adverse cardiovascular events.[8]

However, with the introduction of newer-generation drug-eluting stents characterized by thinner struts and improved polymer biocompatibility, the clinical impact of stent overlap remains controversial. Recent studies have suggested that newer-generation stents may mitigate some of the adverse vascular responses associated with overlapping segments.[4]

In our study, we observed a higher rate of target lesion revascularization in patients treated with overlapping stents. This finding is consistent with previous studies reporting that increased metal density and vessel wall injury in overlapping segments may promote neointimal hyperplasia and restenosis.[9]

On the other hand, the rates of myocardial infarction and cardiovascular mortality were similar between the two groups in our study. These findings are consistent with several contemporary studies indicating that although stent overlap may increase repeat revascularization, it does not necessarily translate into higher mortality or myocardial infarction rates during mid-term follow-up.[10]

Overall, our findings emphasize the importance of careful procedural planning when treating long coronary lesions. Whenever technically feasible, minimizing stent overlap or using a single long stent may reduce the risk of repeat revascularization.

Study limitations

This study has several limitations. First, this was a retrospective single-center observational study and therefore may be subject to selection bias. Second, the relatively small sample size may limit the statistical power to detect differences in less frequent clinical outcomes. Third, intravascular imaging techniques were not routinely used, which may have provided additional insights into stent expansion and overlap geometry. In addition, lesion length was significantly longer in the overlapping stent group, which may have confounded the association between stent overlap and clinical outcomes. No multivariable adjustment analysis was performed due to the sample size, and therefore the findings should be interpreted with caution. Finally, the follow-up duration was limited to 12 months.

Conclusion

In patients undergoing percutaneous coronary intervention for long coronary lesions, overlapping stent implantation was associated with a higher rate of target lesion revascularization during follow-up. However, other major adverse cardiovascular outcomes were comparable between overlapping and non-overlapping stenting strategies.

Conflict of interest
The author declares that there is no conflict of interest.

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Author contributions
The author solely contributed to the conception, study design, data collection, analysis, interpretation of data, and writing of the manuscript.

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Původní sdělení | Original research article

Coronary Artery Disease with Isolated Side Branch Lesions: Follow-Up Outcomes with Medical Treatment

Mehmet Ali Maz[a], Fatih Gülçebi[b], İhsan Dursun[c]

[a] *Department of Cardiology, Bayburt State Hospital, Bayburt, Turkey*
[b] *Department of Cardiology, Trabzon Kanuni Training and Research Hospital, Trabzon, Turkey*
[c] *Department of Cardiology, University of Trabzon Ahi Evren Thoracic and Cardiovascular Surgery Training and Research Hospital, Trabzon, Turkey*

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SOUHRN

Cílem této studie bylo vyjasnit klinické dilema týkající se farmakologické versus intervenční léčby pacientů s ICHS, kteří se dostavili k lékaři s izolovanými lézemi na větvích koronárních tepen. Autoři retrospektivně posoudili výsledky všech koronarografických vyšetření provedených na naší klinice v období od ledna 2020 do července 2023. Pacienti byli rozděleni do dvou skupin podle případné progrese lézí na jednotlivých větvích koronárních tepen během farmakoterapie. Z celkového počtu 400 pacientů ve studii nebyla progrese koronárních lézí během farmakoterapie zjištěna u 332 pacientů. Komparativní analýzy koronarografických údajů prokázaly, že průměr jednotlivých větví koronárních tepen během prvního koronarografického vyšetření (p = 0,012), procento stenóz na jednotlivých větvích (p = 0,001), časový interval mezi oběma koronarografickými vyšetřeními (p = 0.049), počty ostiálních lézí na levé marginální větvi 1 (p = 0,006), a počty ostiálních lézí na levé marginální větvi 2 (p = 0,027) se mezi oběma skupinami statisticky významně lišily. Studie ukázala nízkou rychlost progrese lézí u pacientů s ICHS a izolovaných lézí jednotlivých větví při farmakologické léčbě. Uvedená zjištění hovoří ve prospěch provádění farmakoterapie oproti intervenční léčbě u daných pacientů.
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Keywords:
Coronary artery disease
Coronary artery side branch
Obtuse marginal artery

ABSTRACT

This study aimed to eliminate the clinical dilemma between medical and interventional treatments for patients with CAD presenting with isolated side branch lesions. All coronary angiography procedures performed at our clinic between January 2020 and July 2023 were retrospectively reviewed. The patients were categorized into two groups based on whether their coronary side branch lesions progressed under medical treatment. Of the 400 patients included in the study, 332 exhibited no progression in their coronary lesions under medical treatment. Comparative analyses of angiographic data revealed that side branch vessel diameter during the first angiography (p = 0.012), percentage of side branch stenosis (p = 0.001), the time interval between the two angiographies (p = 0.049), ostial lesions in obtuse marginal 1 (p = 0.006), and ostial lesions in obtuse marginal 2 (p = 0.027) statistically significantly differed between the two groups. This study revealed a low rate of lesion progression in patients with CAD and isolated side branch lesions managed with medical treatment. These findings support the clinical feasibility of prioritizing medical therapy over interventional treatment for such patients.

Address: Fatih Gülçebi, MD, Department of Cardiology, Trabzon Kanuni Training and Research Hospital, Kaşüstü, Topal Osman St. Yomra/Trabzon, Turkey, e-mail: fgulcelebi10@gmail.com
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Introduction and objective

Coronary artery disease (CAD) is a major cardiovascular condition and a predominant cause of mortality in both developed and developing countries, significantly affecting the global population. According to the World Health Organization, approximately 17 million deaths annually are attributed to CAD, ranking it as the third leading cause of death globally.[1] While many risk factors contribute to the development of CAD, primary risks include diabetes mellitus, hypertension, hyperlipidemia, smoking, obesity, lifestyle, genetic predispositions, and psychosocial stress.[2] Although CAD-related mortality has declined in recent years, it still accounts for nearly one third of deaths in individuals over 35 years of age. Approximately 50% of this decline can be attributed to advancements in the management of acute coronary syndrome (ACS) and acute heart failure, alongside improved primary and secondary prevention measures. The remaining 50% of the reduction is linked to stricter control of cardiovascular risk factors such as smoking, high cholesterol, sedentary lifestyles, and hypertension.[3]

The primary approach to CAD treatment integrates lifestyle changes, exercise, and dietary modifications into medical therapy. Medical treatment encompasses antiischemic medications (β-blockers, calcium channel blockers, and nitrates), drugs preventing atherothrombotic events (aspirin and $P2Y_{12}$ inhibitors), and agents reducing cardiovascular risks (statins, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers).[4]

Coronary angiography is frequently employed in the diagnosis of CAD. Currently, angiographic interventional procedures constitute a cornerstone of CAD treatment.[5] However, while coronary angiography effectively identifies lesions in epicardial arteries, it fails to visualize the smaller vessels that comprise a substantial portion of the coronary vasculature. This limitation underscores the importance of medical therapy. Furthermore, lesions detected in epicardial arteries sometimes involve side branches rather than main arteries. Since side branches are narrower than main arteries, interventional procedures such as balloon angioplasty or stent implantation are more challenging and carry higher risks, presenting a dilemma for operators. Therefore, while medical and interventional treatments complement each other in the management of CAD, determining the optimal approach remains an active area of research.[6]

In this study, we investigated the follow-up outcomes of patients with CAD and side branch lesions detected through coronary angiography who did not undergo interventional procedures. Since both medical and interventional treatments carry inherent risks for patients in the short and long term, making a definitive decision in the angiography laboratory can be challenging. The primary objective of this study was to evaluate the clinical and angiographic outcomes of medical management in cases of coronary side branch stenosis.

Patients and methods

Study design

In this study, all coronary angiographies performed in the angiography laboratory of the cardiology department of a tertiary care hospital between January 2020 and July 2023 were retrospectively reviewed. Over three and a half years, the medical records of angiographies were examined through the hospital's system, and patients meeting the study criteria were selected. From the initial dataset, 2,562 patients were identified with ≥50% side branch lesions. Among these, 460 patients who underwent angiography twice at an average interval of four years were included. Due to the inability to retrieve angiographic images for 50 patients and incomplete information for 10 patients, the final sample comprised 400 patients.

The patients were contacted via telephone to gather information about the medical treatments they received between the two angiographies and their existing health conditions. Additional data, including blood values, cardiac rhythm, echocardiographic parameters, angiography dates, and angiographic findings, were obtained from hospital records. Patients with ≥50% stenosis in coronary side branches were divided into two groups: those whose stenosis percentage increased and those whose stenosis percentage did not increase between the two angiographies.

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and received approval from the local ethics committee.

Patient selection and method

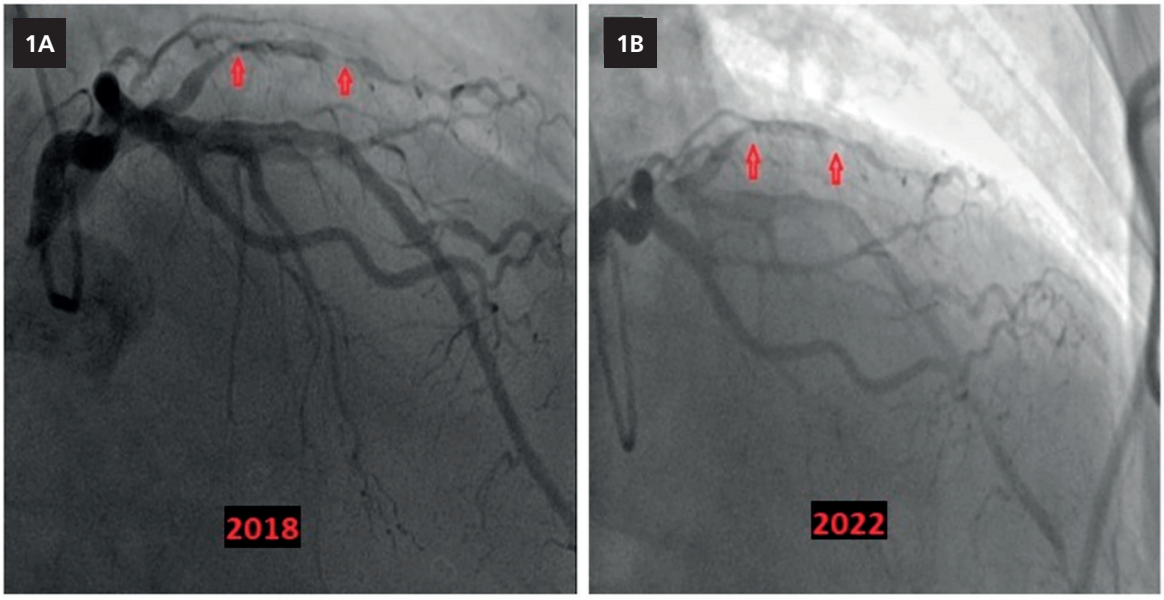
The primary criteria for the target patient group in this study, which aimed to evaluate the follow-up outcomes of coronary artery side branch lesions managed with medical therapy, were the presence of ≥50% stenosis in the coronary artery side branch, independent of any interventional procedure performed on the main artery.

Excluded from the study were patients with <50% stenosis in the coronary artery side branch, those with less than a 12-month interval between the two angiographies, those who did not take at least one antiplatelet agent (aspirin or $P2Y_{12}$ inhibitor) after the index angiography, those who did not receive lipid-lowering therapy (statins) following the index angiography, those with a history of bypass surgery, and those with chronic renal failure requiring dialysis.

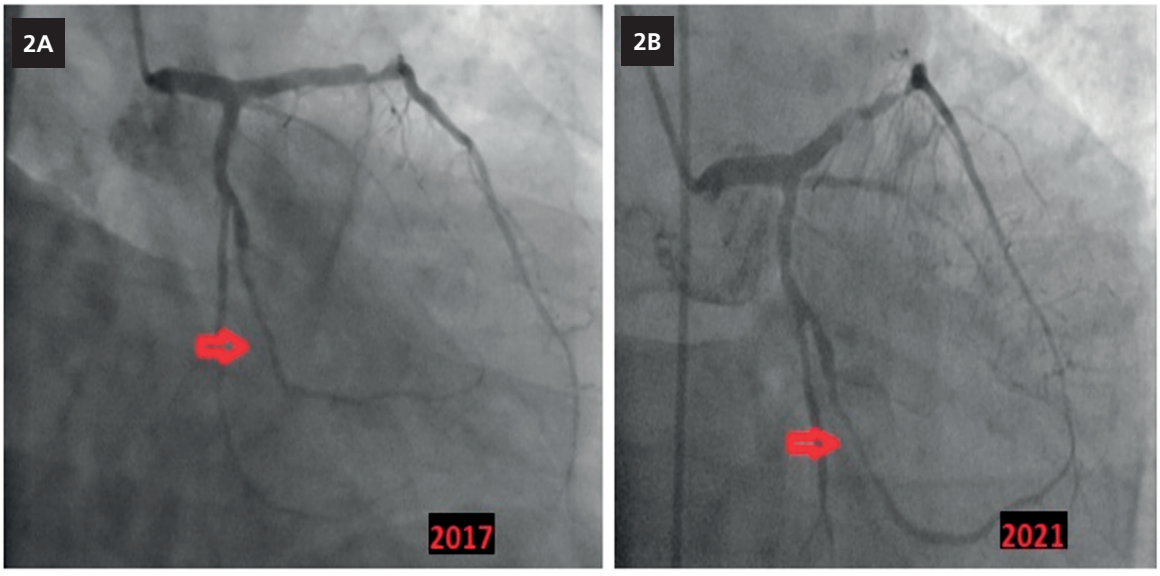
Definitions

The initial angiography, where the presence of ≥50% stenosis in the coronary artery side branch was first identified, was defined as the index angiography, and the angiography conducted within an average of four years was accepted as the second angiography. Angiographic images of patients with ≥50% stenosis in the coronary artery side branch during the first and second angiographies are shown in **Figures 1** and **2**.

Active smokers and individuals with a history of smoking were considered to have significant exposure to smoking. A family history of CAD was deemed significant if first-degree male relatives were diagnosed before the age of 55 and first-degree female relatives before the age of 60. Patients using antihypertensive medications or those with blood pressure >140/90 mmHg during outpatient follow-ups were considered to have significant hypertension. Diabetes mellitus was defined as a clinically significant condition in cases where the patient was un-



Figs 1A–B – Angiography images of a 62-year-old female patient in 2018 and 2022. (A) Proximal and mid-region lesion of the diagonal artery observed in 2018. (B) No progression observed in the same lesion in 2022.



Figs 2A–B – Angiography images of a 69-year-old male patient in 2017 and 2021. (A) Lesion of the obtuse marginal artery observed in 2017. (B) Progression observed in the same lesion in 2021.

dergoing treatment with oral antidiabetic medications or insulin, had a fasting plasma glucose level exceeding 126 mg/dL, or demonstrated a glycated hemoglobin (HbA_{1c}) value of 6.5% or higher, which reflects the average glucose levels over three months. Dyslipidemia, on the other hand, was characterized by a low-density lipoprotein cholesterol level exceeding 116 mg/dL despite effective lifestyle modifications and the use of lipid-lowering medications, such as statins.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 21.0 (SPSS Inc., Chicago, IL, USA) to compare the data of patients with and without an increase in stenosis percentage. The Kolmogorov–Smirnov and homogeneity of variances tests were used to evaluate parametric and non-parametric distributions. The independent-samples t-test was used to compare variables with parametric distributions, while the Mann–Whitney U test was used for non-parametric distributions. Categorical variables were compared using the chi-square test. Parametric continuous variables were expressed as mean ± standard deviation, while non-parametric variables were expressed as median (minimum–maximum) values. Categorical variables were presented as frequencies and percentages. Pearson and Spearman

Table 1 – Baseline parameters of patients included in the study

Variables	Patients with increased stenosis percentage (n = 68)	Patients without increased stenosis percentage (n = 332)	*p*-value
Age (year)	67.95 ± 10.31	65.82 ± 9.76	0.105
Sex (female/male)	14 / 54	64 / 268	0.804
Body mass index (kg/m^2)	27.7 (20–44.9)	27.7 (19–43)	0.887
Hypertension (%)	53	237	0.270
Diabetes mellitus (%)	27	132	0.993
Hyperlipidemia (%)	21	96	0.745
CAD history (%)	27	126	0.786
Smoking (%)	16	110	0.120
Family history (%)	5	22	0.828
ASA (%)	62	292	0.448
Statin (%)	66	326	0.543
ACE inhibitor/RB (%)	44	217	0.918
$P2Y_{12}$ inhibitor (%)	29	160	0.404
Beta blocker (%)	43	224	0.499
Hemoglobin (g/dL)	14.65 (8.3–18.5)	14.5 (8.8–18.5)	0.700
Hematocrit (%)	42 (24–53)	42 (28–53)	0.485
WBC count (× 10^9/L)	8.1 (4.7–14.4)	8.3 (3.9–20)	0.403
Platelet count (× 10^9/L)	221.5 (125–404)	218 (109–520)	0.744
MCV (fL)	88 (72–98)	87 (69–100)	0.321
MPV (fL)	8.42 ± 0.86	8.51 ± 1.13	0.559
Neutrophil count (%)	4.8 (2–11.7)	5 (1.5–16.7)	0.516
Lymphocyte count (%)	2.1 (0.7–5.1)	2.1 (0.4–6.5)	0.685
Glucose (mg/dL)	114 (63–446)	119 (65–434)	0.362
Creatinine (mg/dL)	0.8 (0.54–1.8)	0.8 (0.4–3)	0.800
GFR (ml/min/1,73 m^2)	83.5 (39–124)	90 (14–119)	0.167
CRP (mg/L)	4 (1–99)	4 (1–116)	0.287
Total cholesterol (mg/dL)	202.13 ± 46.4	202.47 ± 52.4	0.960
HDL (mg/dL)	40 (26–78)	40 (23–87)	0.864
TG (mg/dL)	175.5 (41–585)	150.5 (36–580)	0.069
LDL (mg/dL)	140.01 ± 35.37	137.26 ± 40.77	0.605
LDL-2 (mg/dL)	109.13 ± 39.67	108.43 ± 40.81	0.898
Delta LDL (mg/dL)	31.61 ± 48.94	28.30 ± 47.23	0.600

ACEi – angiotensin-converting enzyme inhibitor; ARB – angiotensin receptor blocker; ASA – acetylsalicylic acid; CAD – coronary artery disease; CRP – C-reactive protein; GFR – glomerular filtration rate; HDL – high-density lipoprotein; LDL – low-density lipoprotein; MCV – mean corpuscular volume; MPV – mean platelet volume; TG – triglycerides; WBC – white blood cell.

Table 2 – Echocardiographic and electrocardiographic parameters of patients

Variables	Patients with increased stenosis percentage	Patients without increased stenosis percentage	*p*-value
LV-EF (%)	60 (30–65)	60 (25–65)	0.911
LVEDD (mm)	48 (37–74)	47 (38–69)	0.618
LVESD (mm)	32 (20–50)	30 (21–59)	0.152
Left atrium (mm)	38 (30–51)	38 (30–64)	0.707
Aortic velocity (m/s)	130 (90–461)	137.5 (80–436)	0.446
Ascending aorta (mm)	36 (25–44)	36 (28–48)	0.906
E wave (cm/s)	60 (20–100)	60 (20–158)	0.592
A wave (cm/s)	70 (30–120)	70 (30–158)	0.659
Rhythm (AF/SR)	7/61	21/311	0.243

AF – atrial fibrillation; A wave – late diastolic wave; E wave – early diastolic wave; LVEDD – left ventricular end-diastolic diameter; LV-EF – left ventricular ejection fraction; LVESD – left ventricular end-systolic diameter; SR – sinus rhythm.

correlation analyses were conducted to evaluate correlations. Univariable and multivariable binary logistic regression analyses were performed to identify dependent and independent predictors. A *p*-value of <0.05 was considered statistically significant for all analyses.

Results

Patients' presentation data

A total of 400 patients who underwent coronary angiography twice with an average interval of 36 ± 8 months

Table 3 – Angiographic comparison of stenosis in obtuse marginal and diagonal arteries

Variables	Patients with increased stenosis percentage (n = 68)	Patients without increased stenosis percentage (n = 332)	*p*-value
Index angiography stenosis percentage	80 (60–95)	70 (50–95)	0.001
Side branch diameter (mm)	2.25 (1.5-3)	2.25 (1.5–3)	0.012
Time interval between two angiographies (months)	36 (11–83)	33 (9–86)	0.049
Diagonal 1 artery lesion	34	201	0.108
Ostial	8	52	0.412
Proximal	18	99	0.580
Mid	10	65	0.348
Distal	–	–	–
Diagonal 2 artery lesion	7	49	0.334
Ostial	2	16	0.496
Proximal	3	28	0.258
Mid	2	5	0.411
Distal	–	–	–
Diagonal 3 artery lesion	1	1	0.213
Ostial	–	–	–
Proximal	1	1	0.213
Mid	–	–	–
Distal	–	–	–
Obtuse marginal 1 lesion	27	85	0.018
Ostial	9	15	0.006
Proximal	16	54	0.151
Mid	4	24	0.692
Distal	0	1	0.650
Obtuse marginal 2 lesion	6	18	0.282
Ostial	4	5	0.027
Proximal	2	11	0.875
Mid	0	3	0.431
Distal	–	–	–

Table 4 – Univariable and multivariable regression analyses of factors associated with increased stenosis percentage

	Univariable analysis			Multivariable analysis		
Variables	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Index angiography side branch stenosis percentage	1.047	1.018–1.077	0.001	1.060	1.027–1.093	<0.001
Side branch diameter	2.606	1.167–5.823	0.019	2.534	1.074–5.980	0.034
Time interval between two angiographies	1.014	1.000–1.028	0.047	1.016	1.001–1.031	0.033
Obtuse marginal 1 lesion	1.914	1.110–3.299	0.020			
Obtuse marginal 2 lesion	3.224	1.348–7.709	0.009	4.575	2.715–12.207	0.002
Obtuse marginal 3 lesion	4.087	1.058–15.638	0.040	4.198	1.046–16.857	0.043

CI – confidence interval; OR – odds ratio.

were included in the study. Among these, 68 patients (14 females and 54 males; mean age 67.95 ± 10.31 years) showed an increase in side branch stenosis percentage, whereas 332 patients (64 females and 268 males; mean age 65.82 ± 9.76 years) did not. In 13 of the 332 patients without increased stenosis percentage (four females and nine males; mean age 61.07 ± 11.55 years), a decrease in stenosis percentage was observed.

An examination of the 68 patients with increased stenosis revealed that in 24 cases, the second coronary angiography was indicated solely due to an increased stenosis percentage in the side branch, without any lesions in other arteries. Of these 24 patients, seven were diagnosed with stable angina pectoris, 10 with unstable angina pectoris, and seven with acute subendocardial myocardial infarction. Percutaneous coronary intervention (PCI) was performed in five patients with unstable angina pectoris and four patients with acute subendocardial myocardial infarction. In the remaining 44 patients with an increased stenosis percentage, both side branch lesions and lesions in other major arteries had increased. Among these, PCI was performed in one patient with lateral myocardial infarction, three patients with posterior myocardial infarction, and six patients with subendocardial myocardial infarction.

Comparison of patients' presentation data

The comparison of demographic data, blood parameters, and electrocardiographic and echocardiographic findings between patients with and without an increased stenosis percentage is presented in **Tables 1** and **2**. No statistically significant differences were found between the two groups regarding these parameters.

Comparison of angiographic findings

The comparison of angiographic findings is shown in **Table 3**. Statistically significant differences were found between the two groups in terms of side branch stenosis percentage in the index angiography (p = 0.001), side branch vessel diameter (p = 0.012), time interval between the two angiographies (p = 0.049), obtuse marginal 1 lesions (particularly ostial lesions; p = 0.006), and obtuse marginal 2 lesions (p = 0.027).

To determine the correlation between the side branch stenosis increase and the side branch stenosis percentage in the index angiography, the Spearman correlation test was performed, which yielded a correlation coefficient of 0.167 (p = 0.001). In patients with an increased side branch stenosis percentage, the receiver operating characteristic curve analysis for stenosis percentage revealed a cut-off value of 69.1% for the side branch stenosis percentage in the index angiography, with a sensitivity of 52.7% and a specificity of 77.5% (area under the curve: 0.622, 95% confidence interval: 0.546–0.698, p = 0.002; **Fig. 1**).

To identify predictors of an increased side branch stenosis percentage, univariate and multivariate regression analyses were conducted (**Table 4**). According to the multivariate regression analysis, independent predictors of side branch stenosis progression included the side branch stenosis percentage in the index angiography (p <0.001), side branch vessel diameter (p = 0.034), time interval between the two angiographies (p = 0.033), obtuse marginal 1 ostial lesion (p = 0.002), and obtuse marginal 2 ostial lesion (p = 0.043).

Discussion

In this study, we investigated the outcomes of patients with CAD and isolated significant side branch lesions, as identified through coronary angiography, who were managed with medical therapy. The comparison of demographic data, blood parameters, and electrocardiographic and echocardiographic findings between patients with and without an increase in stenosis percentage revealed no statistically significant differences. However, the comparison of angiographic stenosis values showed statistically significant differences between the two groups concerning side branch vessel diameter, side branch stenosis percentage in the index angiography, the time interval between the two angiographies, and ostial lesions in both obtusemarginal 1 and obtuse marginal 2.

Advancements in medical therapy options for CAD have significantly improved the control of angina symptoms. Patients receive classical conservative treatments (beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, antiplatelet therapy, and statins) as well as antianginal drugs (calcium channel blockers, nitrates, ivabradine, trimetazidine, and ranolazine). For patients with refractory angina under these therapies, PCI may be considered. However, PCI carries risks of early complications such as bleeding, hyperacute stent thrombosis, cerebral embolism, arterial injury, and coronary dissection, as well as late complications such as stent thrombosis, in-stent restenosis, and recurrent myocardial infarction. Compared to major epicardial arteries, coronary side branch lesions are relatively thinner, often involve bifurcation lesions, and supply smaller myocardial territories, making interventional procedures such as balloon angioplasty or stent implantation challenging and risky. These complexities pose considerations for operators regarding treatment decisions. While medical and interventional therapies complement each other in the management of CAD, studies have demonstrated the superiority of one over the other in different contexts.[7]

In our study, among the 332 patients without an increased stenosis percentage, no progression in existing side branch lesions was observed over an average follow-up of four years with medical therapy. Of the 68 patients with increased stenosis percentage, only 19 underwent PCI, as they presented with ACS and the culprit lesion was considered to be in the side branch. The remaining 49 patients continued medical therapy for their coronary side branch lesions. As a result, 381 patients, regardless of stenosis progression, were managed with medical therapy. Similar to our study, a multicenter ORBITA trial conducted by Al-Lamee et al. in 2018 demonstrated no superiority of PCI over medical therapy in patients with significant epicardial coronary artery stenosis.[8] However, unlike Al-Lamee et al., we focused on coronary side branches, which are thinner and supply smaller myocardial territories compared to epicardial coronary arteries, and observed no progression in these lesions under medical therapy.

When determining treatment options for patients with significant coronary artery stenosis, the myocardial territory supplied by the side branch should also be considered. In comparison to epicardial coronary arteries, the area supplied by side branches is smaller. If the affected myocardial territory exceeds 10%, a more detailed evaluation for PCI should be undertaken. In a study by Hyung et al., the impact of ischemia caused by side branch lesions on myocardial territory was assessed, and no correlation was found between fractional flow reserve values and stenosis percentage. However, a side branch vessel length greater than 73 mm was deemed significant. The authors also reported that only 20% of non-left main coronary artery side branch lesions affected more than 10% of myocardial tissue, as determined by fractional flow reserve and coronary computed tomography angiography.[9] Based on these findings and our results, PCI should be reconsidered for side branch lesions that affect less than 10% of the myocardial territory.

In the 2013 COURAGE trial by Spertus et al., the 12-month follow-up outcomes of optimal medical therapy and PCI in epicardial coronary arteries were compared. No significant differences were observed in one-year survival, mortality, or myocardial infarction rates, except for patients whose symptoms could not be controlled with optimal medical therapy, for whom PCI was recommended.[10] In our study, the patients were followed up for an average of 48 months, with medical therapy being the primary treatment strategy. Only 19 patients presenting with ACS and suspected culprit lesions in side branches underwent PCI, while 381 patients with coronary side branch lesions were managed with medical therapy.

Coronary artery side branch lesions are frequently observed in the ostial segment.[11] Ostial coronary side branch lesions are associated with certain serious complications that may arise during interventional procedures. These include the extension of dissection into the distal portion of the main branch during stent implantation, inadequate coverage of the side branch ostium by the stent, and the shifting of the lesion's carina into the main vessel due to insufficient pre-dilatation.[12] Therefore, the decision to treat wide (>2 mm) ostial side branch lesions medically or interventionally remains controversial. In a study conducted by Brueck et al. in 2004, interventional treatment of diagonal artery ostial lesions with >75% stenosis was found to be safe but did not reduce adverse cardiac events or eliminate angina compared to medical therapy.[13] Of the patients included in our study, 111 had ostial side branch lesions, with 78 involving the diagonal artery ostium and 33 involving the obtuse marginal artery ostium. During approximately four years of follow-up, no progression was observed in diagonal ostial lesions (1, 2, or 3), whereas obtuse marginal ostial lesions (1 and 2) demonstrated progression, which was statistically significant. This could be attributed to the steeper angulation of the obtuse marginal artery compared to the diagonal artery and the relatively smaller caliber of the circumflex artery compared to the left anterior descending artery, resulting in reduced blood flow. Yiannis et al. proposed that in bifurcation regions with significant coronary artery expansion, early disruption of intravascular laminar blood flow led to reduced endothelial shear stress, which stimulated atherogenesis, the formation of atherosclerotic plaques, and vascular remodeling.[14] In another study, Peter et al. suggested that the more frequent occurrence of atherothrombotic events in the ostial coronary segment was primarily due to the high shear stress at the bifurcation region. This stress induced the release of nitric oxide and matrix metalloproteinases, which promoted the "outward remodeling" phenomenon, in which the arterial wall remodeled toward the lumen. It is believed that this outward remodeling increases blood flow, flow velocity, and shear stress in the affected vessel, thereby enhancing platelet activation and raising the possibility of thrombosis formation.[15]

A recent study by Torun et al. investigated the medical management of isolated ostial bifurcation lesions and found no statistical differences compared to interventional treatment over an average follow-up of 36.6 months.[16] In our study, we evaluated the outcomes of medical treatment for lesions in the ostial and non-ostial segments of side branches (proximal, mid, and distal). Progression was observed in only the obtuse marginal 1 ostial and obtuse marginal 2 ostial lesions under medical treatment. In the aforementioned study, Torun et al. investigated the follow-up outcomes of side branch ostial lesions with both medical and interventional treatments. In contrast, our research did not include an interventional treatment arm; instead, it focused solely on the follow-up results of patients treated with medical therapy.

Our study has certain limitations. First, the specific coronary artery responsible for the symptoms in patients with ≥50% stenosis in the second angiography was not clearly identified. Second, both the group with increased stenosis percentage and the group with no change in stenosis were initiated on medium-to-high-dose lipid-lowering therapy after the index angiography. However, it was observed that the patients did not fully achieve the current guideline targets during follow-up. Third, as our study was retrospective, only the follow-up results of patients who received medical treatment were examined. Therefore, this study does not provide information on which treatment option is more beneficial for patients with significant coronary side branch lesions.

Conclusion

Our study found that medical therapy generally prevented progression in coronary artery side branch lesions, supporting its use as an appropriate treatment approach for isolated coronary side branch lesions. However, as highlighted by our findings, the follow-up of lesions, particularly those involving the obtuse marginal, varies. Therefore, we defer to interventional cardiologists on whether the obtuse marginal artery should be considered a side branch or a main branch.

Acknowledgments
None.

Data availability
The data that support the findings of this study are available on request from the corresponding author. The data

are not publicly available due to privacy or ethical restrictions.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethical statement

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and received approval from the local ethics committee.

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Původní sdělení | Original research article

Impact of Preoperative Versus Intraoperative and Postoperative Intra-Aortic Balloon Pump Insertion on Mortality and Clinical Outcomes in High-Risk Coronary Artery Bypass Grafting Patients: A Systematic Review and Meta-Analysis

Muhammad Caesar Borni Agustio Putra Hutabarat[a,b], Danang Himawan Limanto[a,b], Mohamad Rizki[a], Yan Efrata Sembiring[a,b]

[a] *Department of Thoracic and Cardiovascular Surgery, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[b] *Department of Thoracic, Cardiac and Vascular Surgery, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia*

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Klíčová slova:
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SOUHRN

Úvod: Optimální načasování zavedení intraaortální balonkové pumpy (intra-aortic balloon pump, IABP) při vysoce rizikovém koronárním bypassu (coronary artery bypass grafting, CABG) zůstává předmětem sporu. Zatímco předoperačně může IABP zajistit časnou stabilizaci hemodynamických poměrů, peroperační nebo pooperační zavedení se typicky provádí jako záchranná léčba při zhoršení hemodynamických poměrů. Cílem této studie bylo zhodnotit vliv předoperačního versus peroperačního/pooperačního zavedení IABP na mortalitu a výsledný klinický stav u pacientů při vysoce rizikovém CABG.
Metody: Systematický přehled a metaanalýza byly provedeny podle metodiky PRISMA 2020. V databázích PubMed a ScienceDirect byly vyhledány studie na dané téma publikované v období mezi lednem 2000 a lednem 2025. Za vhodné byly považovány studie zahrnující pacienty podstupující vysoce rizikový CABG a přímo srovnávající zavedení IABP před operací versus v průběhu operace a po ní. Primárním sledovaným parametrem byla krátkodobá mortalita (nemocniční nebo 30denní). Mezi sekundární sledované parametry patřily závažné nežádoucí kardiovaskulární příhody (major adverse cardiac events, MACE), dlouhodobá mechanická ventilace, pobyt na JIP, pobyt v nemocnici a doba podpory pomocí IABP. Údaje byly hodnoceny metaanalýzou náhodných účinků s použitím softwaru RevMan 5.4.
Výsledky: Do analýzy bylo zařazeno 10 studií s 49 557 pacienty. Předoperační zavedení IABP bylo spojeno se statisticky významně sníženou nemocniční mortalitou (OR 0,52; 95% CI 0,33–0,81; $p = 0,004$) a 30denní mortalitou (OR 0,12; 95% CI 0,05–0,31; $p < 0,001$). Statisticky významně nižší byl i výskyt MACE (OR 0,54; 95% CI 0,39–0,76; $p < 0,001$). Byl zaznamenán nižší počet případů dlouhodobé mechanické ventilace (OR 0,38; 95% CI 0,15–0,96; $p = 0,04$). Žádné statisticky významné rozdíly v délce pobytu na JIP, v nemocnici, délce mechanické ventilace i v délce podpory pomocí IABP nebyly zaznamenány.
Závěr: Předoperační zavedení IABP je spojeno s příznivějším krátkodobým přežitím a se sníženým výskytem perioperačních komplikací u pacientů podstupujících vysoce rizikový CABG; toto zjištění hovoří ve prospěch – u pečlivě vybraných jedinců – spíše aktivní než záchranné strategie.

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Keywords:
Coronary artery bypass grafting
Hemodynamic support
Intra-aortic balloon pump
Meta-analysis
Mortality

ABSTRACT

Introduction: The optimal timing of intra-aortic balloon pump (IABP) insertion in high-risk coronary artery bypass grafting (CABG) remains controversial. While preoperative IABP may provide early hemodynamic stabilization, intraoperative or postoperative insertion is typically performed as rescue therapy after hemodynamic deterioration. This study aimed to evaluate the impact of preoperative versus intraoperative/postoperative IABP insertion on mortality and clinical outcomes in high-risk CABG patients.
Methods: A systematic review and meta-analysis were conducted according to PRISMA 2020 guidelines. PubMed and ScienceDirect were searched for studies published between January 2000 and January 2025. Eligible studies included adult high-risk CABG patients directly comparing preoperative and delayed (intra-

Address: Yan Efrata Sembiring, Department of Thoracic and Cardiovascular Surgery, Faculty of Medicine, Airlangga University, Jl. Mayjend Prof. Dr. Moestopo No. 6-8, Surabaya, East Jawa 60285, Indonesia, e-mail: yan-e-s@fk.unair.ac.id
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operative/postoperative) IABP insertion. The primary endpoint was short-term mortality (in-hospital or 30--day). Secondary outcomes included major adverse cardiac events (MACE), prolonged mechanical ventilation, ICU stay, hospital stay, and duration of IABP support. Random-effects meta-analysis was performed using RevMan 5.4.

Results: Ten studies comprising 49,557 patients were included. Preoperative IABP insertion was associated with significantly reduced in-hospital mortality (OR 0.52; 95% CI 0.33–0.81; $p = 0.004$) and 30-day mortality (OR 0.12; 95% CI 0.05–0.31; $p < 0.001$). Major adverse cardiac events were also significantly lower (OR 0.54; 95% CI 0.39–0.76; $p < 0.001$). Prolonged mechanical ventilation was reduced (OR 0.38; 95% CI 0.15–0.96; $p = 0.04$). No significant differences were observed in ICU stay, hospital stay, ventilation duration, or IABP support duration.

Conclusion: Preoperative IABP insertion is associated with improved short-term survival and reduced perioperative complications in high-risk CABG patients, supporting a proactive rather than rescue strategy in carefully selected individuals.

Introduction

Coronary artery bypass grafting (CABG) remains the standard revascularization strategy for patients with multivessel coronary artery disease, significant left main stenosis, or advanced left ventricular dysfunction.[1] Contemporary surgical techniques and perioperative care have substantially improved outcomes; however, patients classified as high risk, particularly those with reduced left ventricular ejection fraction (LVEF), recent myocardial infarction, cardiogenic shock, or complex coronary anatomy, continue to experience considerable perioperative morbidity and mortality.[2,3] Operative mortality in this subgroup remains clinically significant despite advances in risk stratification models such as the Society of Thoracic Surgeons (STS) scoring system.[4] Optimizing perioperative hemodynamic stability is therefore a critical component of management in high-risk CABG.

Mechanical circulatory support devices are frequently employed to stabilize these vulnerable patients. The intra-aortic balloon pump (IABP) remains the most widely used temporary support device in cardiac surgery due to its relative simplicity, safety profile, and physiologic mechanism of action.[5] Through diastolic counterpulsation, IABP augments coronary perfusion pressure and reduces left ventricular afterload, thereby improving myocardial oxygen supply-demand balance and systemic perfusion.[6] Although its role in cardiogenic shock has evolved with the emergence of alternative support devices, IABP continues to be commonly used in high-risk surgical populations.[7]

The optimal timing of IABP insertion in high-risk CABG remains controversial. Preoperative insertion may provide hemodynamic stabilization before induction of anesthesia and initiation of cardiopulmonary bypass, potentially reducing the incidence of low-cardiac-output syndrome and major adverse cardiovascular events.[8,9] Conversely, intraoperative or postoperative insertion is typically reserved for patients who develop hemodynamic compromise, raising concerns regarding confounding by indication and delayed intervention. Contemporary studies and meta-analyses report heterogeneous findings, with some demonstrating survival benefit and others suggesting neutral outcomes while highlighting device-related complications.[9–13] Given evolving perioperative strategies and variability in defining "high-risk" CABG, an updated systematic review and meta-analysis is warranted to clarify the impact of IABP timing on mortality and major clinical outcomes in contemporary practice.

Materials and methods

Search strategy and data sources

This study was conducted as a systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The study protocol was developed prior to data extraction to minimize selection and analytical bias.

A comprehensive literature search was performed in PubMed and ScienceDirect for studies published between January 1, 2000 and January 31, 2025. The following keywords and Boolean operators were applied: ("intra-aortic balloon pump" OR "IABP") AND ("coronary artery bypass grafting" OR "CABG") AND ("preoperative" OR "intraoperative" OR "postoperative") AND ("mortality" OR "clinical outcomes").

Only studies published in English were considered. Reference lists of eligible articles and relevant reviews were manually screened to identify additional studies.

Eligibility criteria

Studies were included if they met the following criteria: (1) Adult patients undergoing isolated CABG. (2) Classified as high-risk according to study-defined criteria (e.g., reduced LVEF ≤40%, cardiogenic shock, left main disease, recent myocardial infarction, or hemodynamic instability). (3) Direct comparison between preoperative IABP insertion and intraoperative or postoperative insertion. (4) Reported at least one relevant clinical outcome (in-hospital mortality, 30-day mortality, major adverse cardiovascular events, duration of mechanical ventilation, ICU stay, or hospital stay). (5) Observational cohort studies or randomized controlled trials. Exclusion criteria were case reports, editorials, reviews, conference abstracts without full text, pediatric populations, studies without timing comparison, and studies lacking extractable outcome data.

Study selection

Two independent reviewers screened titles and abstracts for eligibility. Full-text review was performed for po-

tentially relevant studies. Disagreements were resolved through discussion and consensus. The following data were extracted using a standardized form: study design, country of origin, publication year, sample size, patient demographics, definition of high-risk status, timing of IABP insertion, operative characteristics, and reported clinical outcomes.

Quality assessment

Methodological quality of observational studies was assessed using the Newcastle–Ottawa Scale (NOS). Studies scoring ≥7 were considered high quality. Risk of bias was independently evaluated by two reviewers.

Outcome measures

The primary endpoint was short-term mortality, defined as in-hospital mortality or 30-day mortality. Secondary endpoints included: Major adverse cardiovascular events (MACE), Prolonged mechanical ventilation, Duration of mechanical ventilation, Length of intensive care unit (ICU) stay, and Length of hospital stay.

Statistical analysis

Meta-analysis was performed using Review Manager (RevMan) version 5.4. Dichotomous outcomes were analysed using risk ratios (RR) with 95% confidence intervals (CI). Continuous variables were pooled using mean differences (MD) with 95% CI.

A random-effects model (DerSimonian–Laird method) was applied due to expected clinical heterogeneity across studies. Statistical heterogeneity was assessed using the I^2 statistic, with values >50% considered indicative of substantial heterogeneity.

Sensitivity analyses were performed by sequential exclusion of individual studies. Publication bias was evaluated using funnel plot inspection when ≥10 studies were available for a given outcome. A p-value <0.05 was considered statistically significant.

Results

Study selection

The systematic search identified 3,606 records from electronic databases, including 3,007 from ScienceDirect and 599 from PubMed. After removal of 360 duplicate records, 3,246 studies remained for title and abstract screening. During initial screening, 3,182 records were excluded due to non-human studies (n = 811), irrelevant topics (n = 1,305), review articles (n = 1,021), and non-English publications (n = 45). A total of 64 full-text articles were retrieved and assessed for eligibility. Of these, 54 studies were excluded for the following reasons: inappropriate study design (n = 2), irrelevant outcomes (n = 2), lack of full-text availability (n = 14), and absence of clearly defined timing of IABP insertion (n = 36). Ultimately, 10 studies met the inclusion criteria and were included in the systematic review and meta-analysis. The study selection process is summarized in **Figures 1** and **2**.

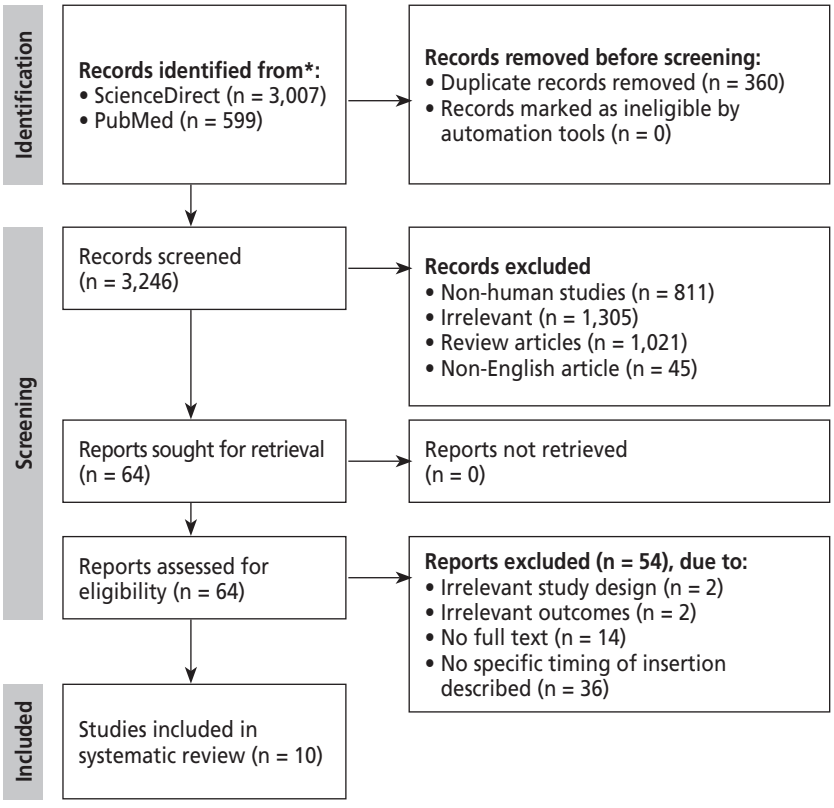
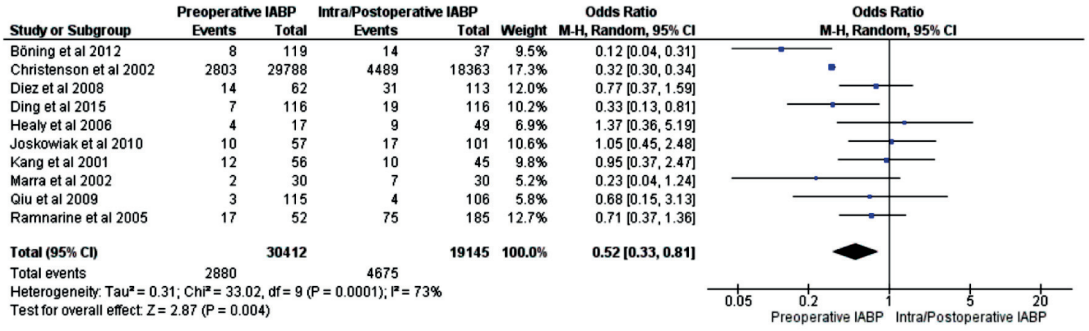
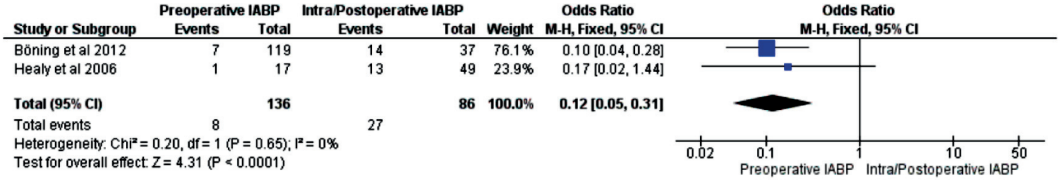


Fig. 1 – PRISMA 2020 flow diagram for included studies.
Identification of studies via databases and registers

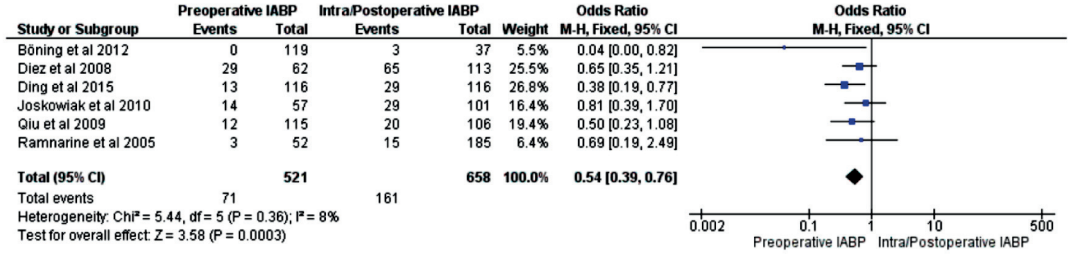
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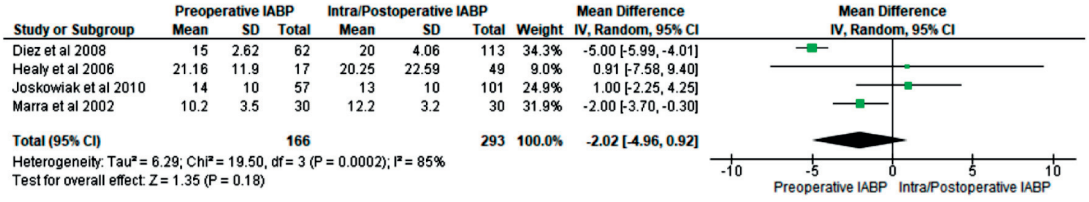
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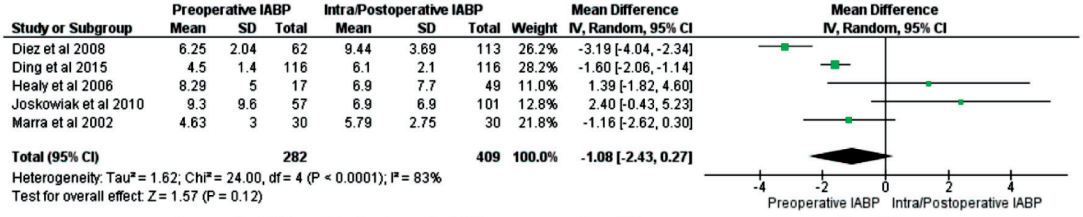
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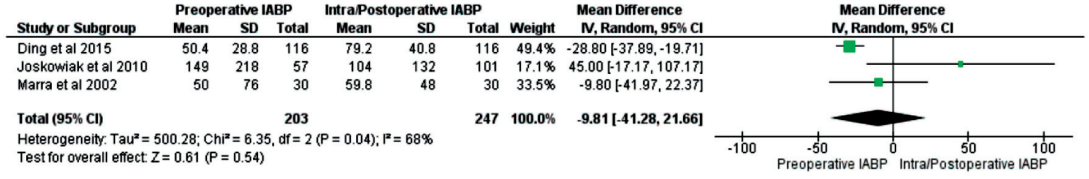
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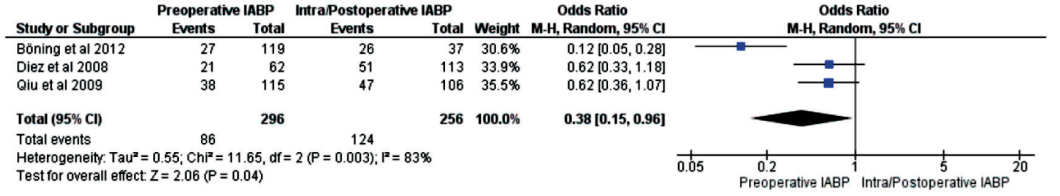
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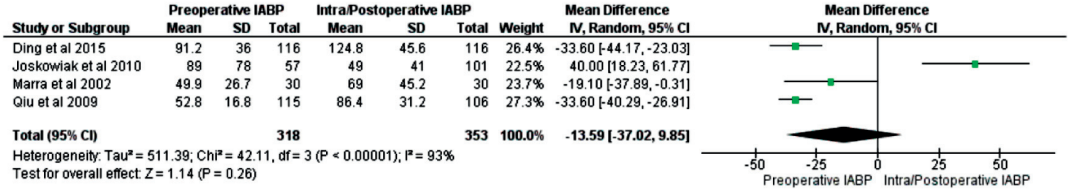


Fig. 2 – Forest plot of the meta-analysis. (A) Inhospital mortality. (B) 30-day mortality. (C) Major adverse cardiac events (MACE). (D) Length of hospital stay. (E) Length of ICU stay. (F) Duration of mechanical ventilation. (G) Prolonged of mechanical ventilation. (H) Duration of IABP support.

Study characteristics

A total of 10 studies met the inclusion criteria and were included in the final analysis. Nine studies were retrospective cohort designs,[14–19,21–23] while one study was a prospective randomized trial.[20] The studies were conducted across Europe, Asia, and Australia. Definitions of high-risk CABG varied among studies but commonly included reduced left ventricular ejection fraction (LVEF ≤30–40%),[19–21] elevated operative risk scores such as EuroSCORE,[16,18] or clinical instability and emergent presentation.[14,23] Preoperative IABP was generally inserted prophylactically in high-risk or hemodynamically unstable patients,[14,16,17,20,23] whereas intraoperative or postoperative IABP was typically initiated in response to failure to wean from cardiopulmonary bypass or development of postoperative low cardiac output syndrome.[18,19,22] Despite heterogeneity in study design and risk stratification, all studies directly compared outcomes between preoperative and delayed IABP insertion strategies.[14–23]

Baseline demographics and clinical characteristics

Most cohorts included high-risk CABG populations defined by reduced LVEF, hemodynamic instability, emergent status, or elevated operative risk scores.[16–19,22,23] The proportion of female patients ranged from 14% to 40% in preoperative IABP groups and from 22% to 37% in intraoperative/postoperative groups.[14,19,23] Mean age was generally comparable across intervention arms, ranging between 63 and 72 years.

Comorbidity burden was substantial across studies. Diabetes mellitus prevalence ranged from approximately 19% to 43% when reported, and hypertension was present in up to 90% of patients in certain cohorts. Prior cerebrovascular accident was reported in a minority of patients, generally below 20%. Left ventricular dysfunction was a defining feature in several studies, particularly in Marra et al.[20] and Qiu et al.,[21] both of which specifically enrolled patients with severe LVEF impairment. Joskowiak et al.[19] reported impaired LV function (EF <40%) in 68% of preoperative IABP patients. Left main disease and triple-vessel disease were common across multiple cohorts, particularly in Kang et al.[23] and Ramnarine et al.[22]

Overall, baseline characteristics were broadly comparable between preoperative and intraoperative/postoperative IABP groups within individual studies, without consistent systematic imbalance across cohorts.[14–23]

In-hospital mortality

All ten studies reported in-hospital mortality. Preoperative IABP insertion was associated with lower mortality in several cohorts, including Böning et al.[14] (6.7% vs 37.8%), Ding et al.[17] (6.0% vs 16.4%), Marra et al.[20] (6.7% vs 23.3%), Qiu et al.[21] (2.6% vs 3.8%), and Christenson et al.[15] (9.4% vs 24.4%). Comparable mortality rates were reported in Healy et al.[18] and Joskowiak et al.,[19] while Kang et al.[23] demonstrated similar outcomes between groups. Ramnarine et al.[22] reported higher mortality in patients requiring delayed IABP insertion.

Pooled meta-analysis (10 studies; n = 49,557) demonstrated significantly reduced in-hospital mortality with preoperative IABP (OR 0.52; 95% CI 0.33–0.81; $p = 0.004$; $I^2 = 73\%$).

30-day mortality

Thirty-day mortality was reported in selected studies. Healy et al.[18] demonstrated significantly lower 30-day mortality in the preoperative group (5.8% vs 26.5%). Meta-analysis confirmed significant reduction in 30-day mortality (OR 0.12; 95% CI 0.05–0.31; $p < 0.001$; $I^2 = 0\%$).

Major adverse cardiac events (MACE)

Reduced MACE rates with preoperative IABP were observed in Diez et al.[16] (46.8% vs 57.5%), Ding et al.[17] (11.2% vs 25.0%), Qiu et al.[21] (10.4% vs 18.9%), and Ramnarine et al.[22] (5.8% vs 8.1%). Meta-analysis confirmed significant reduction in MACE (OR 0.54; 95% CI 0.39–0.76; $p < 0.001$; $I^2 = 8\%$).

Length of hospital stay

Diez et al.[16] reported shorter hospitalization in the preoperative group (15 ± 2.6 vs 20 ± 4.1 days), whereas Healy et al.[18] reported comparable durations. Pooled analysis did not demonstrate statistical significance (MD –2.02 days; 95% CI –4.96 to 0.92; $p = 0.18$; $I^2 = 85\%$).

Length of ICU stay

Shorter ICU stay with preoperative IABP was reported in Diez et al.[16] and Marra et al.,[20] while Joskowiak et al.[19] demonstrated similar durations between groups. Meta-analysis showed no statistically significant difference (MD –1.08 days; 95% CI –4.23 to 2.07; $p = 0.12$; $I^2 = 83\%$).

Duration of mechanical ventilation

Ding et al.[17] and Marra et al.[20] reported shorter ventilation duration in the preoperative group, whereas Joskowiak et al.[19] observed longer duration in early IABP patients. Meta-analysis showed no significant difference (MD –9.81 hours; 95% CI –41.28 to 21.66; $p = 0.54$; $I^2 = 68\%$).

Prolonged mechanical ventilation

Lower prolonged ventilation rates were reported in Böning et al.,[14] Diez et al.,[16] and Qiu et al.[21] in the preoperative groups. Pooled analysis demonstrated significant reduction (OR 0.38; 95% CI 0.15–0.96; $p = 0.04$; $I^2 = 83\%$).

Duration of IABP support

Shorter IABP duration in preoperative groups was reported in Ding et al.,[17] Marra et al.,[20] and Qiu et al.[21] Meta-analysis did not show statistical significance (MD –13.59 hours; 95% CI –37.02 to 9.85; $p = 0.26$; $I^2 = 93\%$).

Discussion

This meta-analysis demonstrates that preoperative intra-aortic balloon pump (IABP) insertion in high-risk CABG patients is associated with significant reductions in in-hospital and 30-day mortality, as well as lower incidence of major adverse cardiac events and prolonged mechanical ventilation. These findings are consistent with several earlier observational studies[16,20,23] and align with prior meta-analyses suggesting benefit of prophylactic IABP in high-risk surgical populations.[9,10] However, unlike earlier analyses conducted in the pre-modern surgical era, the present study includes contemporary cohorts, thereby

Table 1 – Study characteristics

No	Author	Study type	Country	Sample (n)	Participant	Intervention	Control	Gender (female)	Mean Age	Comorbidity					Low EF	Left main disease	TVD
										Diabetes	Hypertension	CVA	Heart failure	Renal Failure			
1	Böning et al., 2012	Retrospective cohort	Germany	156	Patients undergoing coronary surgery with IABP support	Preoperative IABP = 119	Intraoperative IABP = 37	Pre-operative IABP: 37 (31.1%), intra-operative IABP: 10 (27%)	Pre-operative IABP: 70 (63–76), intraopera-tive IABP: 72 (64–78)	Pre-operative IABP: 39.5%, intraoperative IABP: 51.4%	N/A	N/A	N/A	N/A	<30% Pre-operative IABP: 30.3%, intraoperative IABP: 29.7%	N/A	Pre-operative IABP: 87.4%, intraoperative IABP: 91.9%
2	Christen-son et al., 2002	Retrospective cohort	Switzer-land	119	Patients undergoing cardiac surgery with IABP support	Preoperative IABP = 29788, Benchmark = 3721, STS = 26067	Intraoperative IABP = 18363, Benchmark = 3380, STS = 14983	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3	Diez et al., 2008	Retrospective cohort	Germany	175	Patients undergoing cardiac surgery with IABP support	Preoperative IABP = 62	Intra-postope-rative IABP = 113	Preoperative IABP = 21, intra-postope-rative IABP = 40	Preoperative IABP = 69 (62–74), intra--postoperative IABP = 67 (60–72)	N/A	N/A	N/A	Preoperative IABP = 51, intra-postope-rative IABP = 81	N/A	N/A	Preoperative IABP = 21, intra-postope-rative IABP = 15	Preoperative IABP = 67, intra-postope-rative IABP = 48
4	Ding et al., 2015	Cohort	China	232	High-risk patients (based on Euro- SCORE) undergoing off-pump coronary artery bypass grafting	Preoperative IABP = 116	Intra-postope-rative IABP = 113	Preoperative IABP = 21, intra-postope-rative IABP = 40	Preoperative IABP = 63.0 ± 8.2, intra-post-operative IABP = 64.1 ± 9.5	Preoperative IABP = 42, intra-postope-rative IABP = 45	Preoperative IABP = 92, intra-postope-rative IABP = 89	Preoperative IABP = 24, intra-postope-rative IABP = 18	Preoperative IABP = 59, intra-postope-rative IABP = 46	Preoperative IABP = 6, intra-postope-rative IABP = 4	Preoperative IABP = 37, intra-postope-rative IABP = 28	Preoperative IABP = 39, intra-postope-rative IABP = 28	Preoperative IABP = 112, intra-postope-rative IABP = 114
5	Healy et al., 2006	Cohort retrospective	Ireland	66	Patients undergoing CABG-related procedures from January 2000 to De-cember 2001 who required an IABP	Group 1A (low EuroSCORE/preo-perative IABP), group 1B (low EuroSCORE/postoperative IABP), group 2A (high EuroSCORE/preo-perative IABP), group 2B (high EuroSCORE/postoperative IABP), pre operative (1A + 2A): 17, post operative (1B + 2B): 49		Preopera-tive IABP: 4 (23,5%), postoperative IABP: 9 (22,5%)	Preoperative IABP: 64.35 ± 10, postoperative IABP: 66.9 ± 8,5	Preopera-tive IABP: 4 (23,5%),post-operative IABP: 8 (16,3%)	N/A	N/A	N/A	N/A	Preoperative IABP: 16 (94,12%), post-operative IABP: 38 (77,5%)	N/A	N/A
6	Joskowiak et al., 2010	Retrospective cohort	Germany	158	Patients with AMI (NSTEMI and STEMI) underwent emergency CABG	Preoperative IABP	Intraoperative IABP	Preoperative IABP = 8 (14,03%), postoperative IABP = 28 (27,7%)	Preoperative IABP = 65 ± 11, postoperative IABP = 68 ± 9	Preoperative IABP = 23 (43%), post-operative IABP = 39 (39%)	Preoperative IABP = 49 (86%), postoperative IABP = 91 (91%)	N/A	N/A	Preoperative IABP = 23 (40%), post-operative IABP = 23 (23%)	Impaired LV function (EF < 40%), preoperative IABP = 32 (68%), postoperative IABP = 39 (38%)	Left main stem stenosis > 70%, preoperative IABP = 27 (52%), postoperative IABP = 37 (37%)	Number of diseased vessels: preoperative IABP = 2.8 ± 0.4, postopera-tive IABP = 2.8 ± 0.4
7	Kang et al., 2001	Retrospective cohort	Australia	101	Patients having open heart surgery from January 1998 to October 1999	Group A (preoperative IABP for high-risk nonemergent cases), group B (preoperative IABP for emergent cases), and group C (intra/postoperative IABP); group A (35) + B (21) = 56; group C = 45		Group A + B = 7 + 4 = 11 (19.64%), group C: 16 (37.2%)	Preoperative – high risk (64.8), – low risk (63.6), intra/postope-rative (64.2)	Group A + B = 15 (26.79%), group C: 8 (18.6%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
8	Marra et al., 2002	Prospective randomised study	Italy	60	Coronary artery bypass graft (CABG) patients with low left vent-ricular ejection fraction (LVEF)	Preoperative IABP (just before induc-tion)	Intra-operative IABP	Preoperative IABP = 12 (40%), intraoperative IABP = 11 (36,6%)	Preoperative IABP = 63.8 ± 1.5, intraoperative IABP = 64.1 ± 2.3	Preoperative IABP = 12 (40), intraoperative IABP = 15 (50)	Preoperative IABP = 5 (16.6), intraoperative IABP = 3 (10)	N/A	Preoperative IABP = 13 (43.3), intraoperative IABP = 12 (40)	N/A	Preoperative IABP = 30 (100%), intraoperative IABP = 30 (100%)	N/A	N/A
9	Qiu et al., 2009	Cohort ob-servational	China	221	221	Preoperative IABP insertion	Post operative IABP insertion	Early IABP 42 (36,5%); post-operative IABP 32 (30,2%)	N/A	Early IABP 35 (30,4%); post-operative IABP 36 (34,0%)	Early IABP 70 (60,9%); post-operative IABP 79 (74,5%)	Early IABP 5 (4,3%); post-operative IABP 3 (2,8%)	Early IABP 35 (30,4%); post-operative IABP 36 (34,0%)	Early IABP 4 (3,5%); post-operative IABP 3 (2,8%)	N/A	Early IABP 20 (17,2%); post-operative IABP 21 (19,8%)	N/A
10	Ramnari-ne et al., 2005	Retrospecti-ve observa-tional	UK	237	237	(Group B: preoprative IABP in high risk patients, group C: preoperative IABP in stabile haemodyna-mics), preoperative IABP 52	(Group D: intraoperative IABP, group E: postoperative IABP), intraoperative IABP 185	Preoperative 12 (23,1%), intraoperative 56 (30,2%)	Preoperative 67,05, intrao-perative 68,05	Preoperative 10 (19,23%), intraoperative 41 (22,16%)	Preoperative 27 (51,92%), intraoperative 99 (53,51%)	Preoperative 9 (17,30%), intraoperative 25 (13,51%)	N/A	Preoperative 10 (19,23%), intraoperative 69 (14,22%)	Preoperative 18 (34,61%), intraoperative 49 (26,48%)	Preoperative 21 (34,61%), intraoperative 39 (21,08%)	Preoperative 33 (34,61%), intraoperative 143 (77,29%)

Table 2 – Clinical outcomes

No	Study Group 1		In-hospital mortality		30-day mortality		Major adverse cardiac events (MACE)		Length of hospital stay (d)		Length of ICU stay (d)		Duration of mechanical ventilation (h) (mean ± SD)		Prolonged mechanical ventilation (percentage)		Duration of IABP used (h)	
			Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1
1	Böning et al., 2012	Overall = 156	119	37	119	37	119	37	N/A	N/A	N/A	N/A	N/A	N/A	119	37	N/A	N/A
		Yes	8 (6.7%)	14 (37.8%)	7 (5.9%)	14 (37.8%)	0 (0%)	3 (8.3%)	N/A	N/A	N/A	N/A	N/A	N/A	27 (22.7%)	26 (72.2%)	N/A	N/A
		No	111 (93.3%)	23 (62.2%)	112 (94.1%)	23 (62.2%)	119 (100%)	34 (91.7%)	N/A	N/A	N/A	N/A	N/A	N/A	92 (77.3%)	11 (27.8%)	N/A	N/A
2	Christenson et al., 2002	Overall = 48151	29788	18363	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		Yes	2803 (9.4%)	4489 (24.4%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		No	26985 (90.6%)	13874 (75.6%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3	Diez et al., 2008	Overall = 175	62	113	N/A	N/A	62	113	62	113	62	113	N/A	N/A	62	113	N/A	N/A
		Yes	14 (22.6%)	31 (27.4%)	N/A	N/A	29 (46.77%)	65 (57.52%)	15 ± 2.62#	20 ± 4.06#	6.25 ± 2.04#	9.44 ± 3.69#	N/A	N/A	21 (33.87%)	51 (45.13%)	N/A	N/A
		No	48 (77.4%)	82 (72.6%)	N/A	N/A	33 (53.23%)	48 (42.48%					N/A	N/A	41 (66.13%)	62 (54.67%)	N/A	N/A
4	Ding et al., 2015	Overall = 232	116	116	N/A	N/A	116	116	N/A	N/A	116	116	116	116	N/A	N/A	116	116
		Yes	7 (6.0%)	19 (16.4%)	N/A	N/A	13 (11.2%)	29 (25.0%)	N/A	N/A	4.5 ± 1.4	6.1 ± 2.1	50.4 ± 28.8	79.2 ± 40.8	N/A	N/A	91.2 ± 36	124.8 ± 45.6
		No	109 (94,0%)	97 (83,6%)	N/A	N/A	103 (88.8%)	87 (75.0%)	N/A	N/A					N/A	N/A		
5	Healy et al., 2006	Overall = 66	17	49	17	49	N/A	N/A	17	49	17	49	N/A	N/A	N/A	N/A	N/A	N/A
		Yes	4 (23.5%)	9 (22.5%)	1 (5.8%)	13 (26.5%)	N/A	N/A	21.16 ± 11.9	20.25 ± 22.59	8.29 ± 5	6.9 ± 7.7	N/A	N/A	N/A	N/A	N/A	N/A
		No	13 (76.5%)	40 (77.5%)	16 (94.2%)	36 (73.5%)	N/A	N/A					N/A	N/A	N/A	N/A	N/A	N/A
6	Joskowiak et al., 2010	Overall = 158	57	101	N/A	N/A	57	101	57	101	57	101	57	101	N/A	N/A	57	101
		Yes	10 (17.6%)	17 (16.8%)	N/A	N/A	14 (25.0%)	29 (30.5%)	14 ± 10	13 ± 10	9.3 ± 9.6	6.9 ± 6.9	149 ± 218 (h)	104 ± 132 (h)	N/A	N/A	89 ± 78	49 ± 41
		No	47 (82,4%)	84 (83,2%)	N/A	N/A	43 (75.0%)	72 (69.5%)							N/A	N/A		
7	Kang et al., 2001	Overall = 101	56	45	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		Yes	12 (21.43%)	10 (22.2%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		No	44 (78.57%)	35 (77.78%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
8	Marra et al., 2002	Overall = 60	30	30	N/A	N/A	N/A	N/A	30	30	30	30	30	30	N/A	N/A	30	30
		Yes	2(6,67%)	7 (23,33%)	N/A	N/A	N/A	N/A	10.2 ± 3.5	12.2 ± 3.2	4.63±3	5.79 ± 2.75	50 ± 76 (h)	59.8 ± 48 (h)	N/A	N/A	49.9 ± 26.7	69 ± 45.2
		No	28 (93,3%)	23 (76,6%)	N/A	N/A	N/A	N/A							N/A	N/A		
9	Qiu et al., 2009	Overall = 221	115	106	N/A	N/A	115	106	N/A	N/A	N/A	N/A	N/A	N/A	115	106	115	106
		Yes	3 (2,6%)	4 (3,8%)	N/A	N/A	12 (10.4%)	20 (18.9%)	N/A	N/A	N/A	N/A	N/A	N/A	38 (33.0%)	47 (44.3%)	52.8 ± 16.8	86.4 ± 31.2
		No	112 (97,4%)	102 (96,2%)	N/A	N/A	103 (89.6%)	86 (81.1%)	N/A	N/A	N/A	N/A	N/A	N/A	77 (67,0%)	59 (55.7%)		
10	Ramnarine et al., 2005	Overall 237	52	185	N/A	N/A	52	185	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		Yes	17 (32,69%)	75 (40,54%)	N/A	N/A	3 (5.77%)	15 (8.10%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		No	35 (67,31%)	110 (59,46%)	N/A	N/A	49 (94.23%)	170 (91.90%)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

strengthening the external validity of the mortality signal in current practice.

The biological plausibility of early IABP support is supported by well-established hemodynamic principles. Counterpulsation augments diastolic coronary perfusion and reduces left ventricular afterload, thereby improving myocardial oxygen supply-demand balance.[5,6] In patients with severely impaired ventricular function, surgical stress and cardiopulmonary bypass may precipitate further myocardial injury and low cardiac output syndrome.[24] Early hemodynamic unloading before anesthetic induction may attenuate ischemia-reperfusion injury and reduce subendocardial hypoperfusion. This is particularly relevant in patients with severe left ventricular dysfunction, a population shown in the STICH and STICHES trials to derive long-term survival benefit from surgical revascularization,[3,25] but who remain at high perioperative risk.

Importantly, the timing of IABP insertion appears to be a critical determinant of outcome. Intraoperative or postoperative IABP deployment often reflects failure to wean from bypass or established hemodynamic collapse,[22] a scenario associated with worse prognosis independent of support strategy.[26] The IABP-SHOCK II trial demonstrated no mortality benefit of routine IABP use in acute myocardial infarction complicated by cardiogenic shock,[27] however, extrapolation of these findings to elective or urgent CABG populations is inappropriate. Cardiogenic shock represents a distinct pathophysiologic entity characterized by systemic inflammatory response and microvascular dysfunction,[28] whereas perioperative CABG patients experience controlled ischemia-reperfusion injury under cardioplegic protection. Thus, the absence of benefit in shock trials does not negate potential benefit in prophylactic surgical settings.

Although mortality and MACE outcomes demonstrated consistent benefit, resource-utilization outcomes such as ICU stay and hospital length of stay did not reach statistical significance and were characterized by substantial heterogeneity. Similar variability has been reported in prior surgical meta-analyses of mechanical circulatory support.[29] This heterogeneity likely reflects institutional differences in extubation protocols, enhanced recovery pathways, and criteria for IABP weaning rather than absence of clinical effect. Furthermore, improvements in myocardial protection, anesthetic management, and perioperative critical care over the past two decades,[1,2] may attenuate measurable differences in length-of-stay metrics despite persistent survival benefit.

The predominance of observational studies remains an important limitation and introduces the possibility of confounding by indication. However, consistent directionality of effect across geographically diverse cohorts[14–23] and the strong pooled reduction in 30-day mortality support the robustness of the findings. Moreover, contemporary revascularization guidelines emphasize individualized risk stratification and multidisciplinary decision-making in complex coronary disease.[1,30] Within this framework, selective prophylactic IABP use in patients with severe ventricular dysfunction, left main disease, or elevated operative risk scores may represent a rational adjunct to surgical strategy rather than routine application.

In summary, this analysis supports a proactive approach to mechanical circulatory support in carefully selected high-risk CABG patients. Preoperative IABP insertion appears to mitigate perioperative risk and improve early survival, whereas delayed insertion may reflect irreversible hemodynamic deterioration. Future multicenter randomized trials in the era of modern myocardial protection and enhanced recovery protocols are warranted to further refine patient selection and confirm causality.

Conclusion

In high-risk patients undergoing coronary artery bypass grafting, preoperative intra-aortic balloon pump insertion is associated with significantly reduced in-hospital and 30-day mortality, as well as lower incidence of major adverse cardiac events and prolonged mechanical ventilation compared with intraoperative or postoperative deployment. These findings support the concept that early hemodynamic stabilization before surgical stress and cardiopulmonary bypass may mitigate perioperative myocardial injury and improve short-term survival.

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Původní sdělení | Original research article

Impact of COVID-19 Pandemic on In-hospital and Long-term Outcomes of ST Elevation Myocardial Infarction

Azza Abdel Moniem Farrag[a], Ahmed Adel Mohamed Elamragy[a], Sameh Mohamed Helmy Elkaffas[a], Dalia Rifaat Elremisy[a], Wafaa Hamed Omar Khalifa[b]

[a] *Cardiology Department, Faculty of Medicine, Cairo University, Cairo, Egypt*
[b] *Cardiology Department, Student´s Hospital, Cairo University, Cairo, Egypt*

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SOUHRN

Kontext: Pandemie covidu-19 významně ovlivnila kardiovaskulární zdraví populace na celém světě. Cílem této studie bylo zjistit, jak pandemie covidu-19 ovlivnila výsledný stav – během hospitalizace i v dlouhodobém horizontu (1 roku) – pacientů po infarktu myokardu s elevacemi úseku ST (ST elevation myocardial infarction, STEMI), u nichž byla provedena primární perkutánní koronární intervence (PPCI).
Metody: Do této retrospektivní observační studie bylo zařazeno 317 pacientů po STEMI, léčených v období od 1. března 2019 do 28. února 2022 primární perkutánní koronární intervencí. Pacienti byli rozděleni do skupiny A (období před pandemií, n = 107), skupiny B1 (během pandemie, bez diagnózy covidu-19, n = 169) a skupiny B2 (během pandemie, s potvrzenou diagnózou covidu-19, n = 41). Mezi analyzované parametry patřily klinické charakteristiky, nemocniční komplikace po PCI, délka pobytu v nemocnici a výsledný stav po jednoletém sledováním (opětovný příjem pro bolest na hrudi a mortalita).
Výsledky: Nejčastější nemocniční komplikací po PCI bylo srdeční selhání, které se vyskytlo u statisticky významně většího počtu pacientů s diagnózou covid-19 (skupina B2) ve srovnání s pacienty hospitalizovanými před pandemií (48,8 % vs. 24,3 %; $p = 0,004$). U pacientů skupiny B2 bylo rovněž zaznamenán vyšší výskyt kardiogenního šoku (29,3 % vs. 6,5 %; $p < 0,001$), kontrastní látkou indukované nefropatie (22,0 % vs. 8,4 %; $p = 0,024$) a statisticky významně delší pobyt v nemocnici (9,27 ± 5,30 vs. 4,20 ± 3,26 dní; $p < 0,001$). Naopak pacienti bez infekce onemocněním covid-19 během pandemie zůstávali v nemocnici kratší dobu (3,14 ± 2,40 dne; $p = 0,004$). Po jednom roce sledování byl opětovný příjem do nemocnice pro bolest na hrudi častější před pandemií, přičemž jednoroční mortalita byla ve všech skupinách srovnatelná.
Závěr: U pacientů s diagnózou infekčního onemocnění covid-19, kteří prodělali STEMI a následně byli léčeni PPCI, bylo přítomno vyšší riziko nemocničních komplikací po PCI i delší hospitalizace, i když jednoroční mortalita zůstala srovnatelná s hodnotami před pandemií.

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Keywords:
Acute coronary syndrome
COVID-19
ST-elevation myocardial infarction

ABSTRACT

Background: The COVID-19 pandemic significantly impacted cardiovascular outcomes worldwide. This study evaluated the impact of the COVID-19 pandemic on in-hospital and long-term (1-year) outcomes in patients with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PPCI).
Methods: This retrospective observational study included 317 STEMI patients treated with PPCI between March 1, 2019, and February 28, 2022. Patients were categorized into group A (pre-pandemic, n = 107), group B1 (during pandemic, non-COVID-19, n = 169), and group B2 (during pandemic, confirmed COVID-19, n = 41). Clinical characteristics, in-hospital post-PCI complications, hospital stay duration, and 1-year follow-up outcomes (readmission for chest pain and mortality) were analyzed.
Results: Heart failure was the most common in-hospital post-PCI complication, occurring significantly more in COVID-19 patients (group B2) compared to pre-pandemic patients (48.8% vs. 24.3%, $p = 0.004$). Group B2 patients also experienced higher rates of cardiogenic shock (29.3% vs. 6.5%, $p < 0.001$), contrast-induced nephropathy (22.0% vs. 8.4%, $p = 0.024$), and significantly longer hospital stays (9.27 ± 5.30 vs. 4.20 ± 3.26 days, $p < 0.001$). Conversely, non-COVID-19 patients during the pandemic had shorter hospital stays (3.14 ± 2.40 days, $p = 0.004$). At the 1-year follow-up, hospital readmission for chest pain was more frequent before the pandemic, whereas 1-year mortality rates remained comparable across all groups.
Conclusion: STEMI patients with concomitant COVID-19 infection undergoing PPCI face higher risks of in-hospital post-PCI complications and prolonged hospitalization, though 1-year mortality rates remain comparable to pre-pandemic.

Address: Wafaa Hamed Omar Khalifa, Cardiology Department, Student's Hospital, Cairo University, Cairo, Egypt, e-mail: drkhalifa.wafaa@gmail.com
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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as coronavirus disease 2019 (COVID-19), is one of the most widely spread viruses in the recent era, affecting more than 10 million cases all over the globe (and numbers are increasing daily). It is one of the coronavirus's family along with the severe acute respiratory syndrome (SARS) virus and the influenza A virus H1N1 virus.[1] COVID-19 was announced as a worldwide pandemic by the WHO on January 30, 2020, and in February 2020, the Egyptian Ministry of Health announced the first case of COVID-19. By March 9, 2020, it had spread to more than 100 countries all over the globe.[2–4]

At the start of the pandemic, the main symptoms and effects of COVID-19 were related to the respiratory system. Still, shortly it was noticed and reported to affect the cardiovascular system seriously. This effect was associated with the pathological effect of the virus, the impact of quarantine and social distancing measures, and even the effect of anti-COVID-19 medications.[4] In addition to the burden of the COVID-19 infection, the presence of previous cardiovascular disorders is associated with a high risk of mortality.[5] An increase in cardiovascular incidents was noticed during the COVID-19 era compared to periods before the pandemic. COVID-19 patients were at higher risk for arrhythmias such as paroxysmal supraventricular tachycardia, atrial fibrillation, sinus bradycardia, and ventricular tachycardia. A prolonged QT interval was observed more in patients who received any experimental medication regimen against SARS-CoV-2.[6,7]

It was noticed that despite the risk of myocardial injury caused by COVID-19, many patients with acute coronary syndrome were reluctant to seek medical services due to the fear of catching the infection at the medical facilities, and a delay in acute coronary syndrome patients' presentation, referral, and transfer worldwide was reported.[8] COVID-19 affected the demographic and angiographic characteristics of STEMI patients, and a decreased number of presentations was noticed with a longer total ischemic time and more hospital-related major complications and long-term impact compared to pre-pandemic.[9]

Methods

Study population

This study retrospectively included all STEMI patients who underwent primary PCI and were either hospitalized or presented to the emergency department at Cairo University Hospital and a private hospital between March 1, 2019, and February 28, 2022, and had a complete medical record.

Inclusion criteria

This study included patients diagnosed with STEMI who presented within 12 hours of symptom onset. The STEMI diagnosis was based on the 2017 ESC guidelines for STEMI management.[10]

Exclusion criteria

1. Patients who presented after more than 12 hours from symptom onset.
2. Age less than 18 years old.
3. Pregnant ladies.
4. Patients who refused to sign a consent form for primary PCI.
5. Revascularization by acute thrombolysis or pharmaco--invasive strategy.
6. Patients who developed cardiac arrest, did not respond to CPR, and declared death before reaching the cath lab.

Methodology

The study retrospectively included patients diagnosed with STEMI who were treated with primary percutaneous coronary intervention between March 1, 2019, and February 28, 2022. This was a retrospective observational study, and data were collected anonymously. The investigators took all necessary precautions to ensure data privacy. STEMI diagnosis was based on the 2017 ESC guidelines for STEMI management. Patients exhibiting symptoms suggestive of COVID-19 were referred for a chest CT without contrast. Laboratory tests, including complete blood count, C-reactive protein (CRP), and serum ferritin, were conducted. COVID-19 was confirmed through reverse transcription-polymerase chain reaction (RT-PCR) assays or through clinical symptoms and CT chest findings consistent with COVID-19.

The study population was classified into two groups:

- Group A: STEMI patients who presented before the COVID-19 pandemic (from March 1, 2019 to February 29, 2020).
- Group B: STEMI patients who presented during the COVID-19 pandemic (from March 1, 2020 to February 28, 2022); this group will be divided into two subgroups:
  - Group B1: STEMI patients who presented during COVID-19 pandemic, and do not have a confirmed diagnosis of COVID-19.
  - Group B2: STEMI patients who presented during the COVID-19 pandemic and had a confirmed diagnosis of COVID-19.

Clinical and demographic data for all patients were gathered from the hospital database and medical records, including a full history of the current condition, the presenting symptoms and signs, history of comorbidities and risk factors. A standard 12-lead ECG at first medical contact, post-PCI, and follow-up during hospital stay. Additional laboratory tests (CRP, serum ferritin, and D-dimer) were done for patients with symptoms suspicious of COVID-19, and the diagnosis was confirmed with reverse transcription-polymerase chain reaction assays (PCR). Procedural observations reported for the access site, the culprit artery, the site of the lesion, Final Thrombolysis In Myocardial Infarction (TIMI) flow.[11]

Follow-up and documentation for in-hospital complications, including: dissection, cardiogenic shock, contrast-induced nephropathy, significant bleeding, access site hematoma, post-MI decompensated heart failure, development of arrhythmia, and the type of arrhythmia

that developed during the hospital stay, post-MI arrest, and in-hospital mortality. One-year follow-up for mortality due to cardiac causes and for rehospitalization due to chest pain was collected either by phone call to the patients or from the patients' hospital medical files.

Statistical analysis

All statistical studies were conducted using Statistical Package for Social Sciences software (SPSS 20.0 for Windows, SPSS Inc., Chicago, IL). The quantitative variables are expressed as mean ± standard deviation (SD). Non-normally distributed variables were expressed as median and interquartile range (IQR). Categorical variables were expressed in numbers and percentages. Comparisons between two groups were performed using the Student's t-test or Mann–Whitney U test for continuous variables, and the Chi-square or Fisher's exact test for categorical variables. A p-value <0.05 was considered statistically significant.

Results

This study enrolled 317 patients diagnosed with STEMI and were treated with primary percutaneous coronary intervention (PPCI). The study population was classified into three groups: **Group A** (107 patients, 33.8%), **group B1(**169 patients, 53.3%), and **group B2** (41 patients, 12.9%).

Comparison between group A (Before the COVID-19 pandemic) and group B1 (no confirmed diagnosis of COVID-19)

I. Risk profile and clinical presentation

A history of previous coronary heart disease was reported in 27 patients (25.2%) of group A and 46 (27.2%) of group B1 (p = 0.716). There was no significant difference in the risk profile and clinical presentation between both groups. **Table 1** shows a comparison of the risk profile and clinical presentation.

Table 1 – Comparison of the risk profile and clinical presentation

		Group A (before pandemic) (total n 107)		Group B1 (non-COVID-19) (total n 169)		p-value	Group B2 (COVID-19) (total n 41)		p-value
Age (years) (mean ± SD)#		55.36 ± 11.90		53.95 ± 12.38		0.348	55.02 ± 13.69		0.882
Gender (N, %)*	Male	95	88.8%	152	89.9%	0.760	33	80.5%	0.186
Smoking (N, %)*	Smoker	57	53.3%	106	62.7%	0.120	17	41.5%	0.199
	Ex-smoker	15	14.0%	20	11.8%	0.595	6	14.7	0.923
HTN (N, %)*		58	54.2%	92	54.4%	0.970	20	48.8%	0.554
DM (N, %)*		46	43.0%	72	42.6%	0.949	14	34.1%	0.327
Dyslipidemia (N, %)*		66	61.7%	109	64.5%	0.636	23	56.1%	0.535
PAD (N, %)*		12	11.2%	12	7.1%	0.237	2	4.9%	0.238
Previous CHD (N, %)*	STEMI	8	7.5%	8	4.7%	0.342	2	4.9%	0.727
	NSTEMI	8	7.5%	7	4.1%	0.234	1	2.4%	0.445
	CCD	10	9.3%	22	13.0%	0.353	4	9.8%	1.00
	UA	1	0.9%	5	3.0%	0.250	0	0.0%	1.00
	STEMI + CABG	0	0.0%	2	1.2%	0.374	0	0.0%	–
	NSTEMI + CABG	0	0.0%	2	1.2%	0.374	1	2.4%	0.277
CKD (N, %)*		8	7.5%	10	5.9%	0.609	4	9.8%	0.738
Presentation (N, %)*	Chest pain	100	93.5%	158	94.0%	0.843	33	80.5%	0.019
	SOB	5	4.7%	7	4.2%	0.841	3	7.3%	0.685
	Palpitation	0	0.0%	1	0.6%	0.611	1	2.4%	0.277
	Arrest	2	1.9%	1	0.6%	0.336	3	7.3%	0.130
	Syncope	0	0.0%	0	0.0%	–	1	2.4	0.277
	Vomiting	0	0.0%	1	0.6%	0.611	0	0.0%	–
Systolic BP (mmHg), (mean ± SD)*		132.80 ± 21.75		132.07 ± 22.42		0.792	122.55 ± 22.99		0.015
Diastolic BP (mmHg), (mean ± SD)*		78.64 ± 18.20		80.28 ± 17.20		0.456	72.84 ±15.58		0.083
HR (beat/min), (mean ± SD)*		84.70 ± 17.16		82.55 ± 15.64		0.288	75.47 ± 26.31		0.016

BP – blood pressure; CABG – coronary artery bypass graft; CCD – chronic coronary disease; CHD – coronary heart disease; CKD – chronic kidney disease; DM – diabetes mellitus; HR – heart rate; HTN – hypertension; NSTEMI – non-ST-elevation myocardial infarction; PAD – peripheral artery disease; SOB – shortness of breath; STEMI – ST-elevation myocardial infarction; UA – unstable angina.
* Data is presented by numbers (N) and percentages (%). # Data is presented by mean and standard deviation (SD).

Table 2 – Comparison of complications

	Group A (Before pandemic) (total n 107)		Group B1 (Non-COVID-19) (total n 169)		*p*-value	Group B2 (COVID-19) (total n 41)		*p*-value
	N	%*	N	%*		N	%*	
Dissection	1	0.9	1	0.6	0.626	2	4.9	0.186
Shock	7	6.5	11	6.5	0.991	12	29.3	< 0.001
CIN	9	8.4	10	5.9	0.425	9	22.0	0.024
Bleeding	3	2.8	6	3.6	0.513	2	4.9	0.617
Hematoma	13	12.1	18	10.7	0.701	13	31.7	0.005
Heart failure	26	24.3	30	17.8	0.188	20	48.8	0.004
Arrest	12	11.2	11	6.5	0.168	8	19.5	0.186
In-hospital mortality	4	3.7	3	1.8	0.264	5	12.2	0.116
Arrythmia								
VT	6	5.6	6	3.6	0.414	2	4.9	1.00
AF	4	3.7	4	2.4	0.376	3	7.3	0.396
VF	1	0.9	5	3.0	0.250	2	4.9	0.1863
SVT	3	2.8	0	0.0	0.057	0	00	0.561
CHB	0	0.0	1	0.6	0.612	2	4.9	0.075

AF – atrial fibrillation; CHB – complete heart block; CIN – contrast-induced nephropathy; VF – ventricular fibrillation; VT – ventricular tachycardia.
* Data is presented by numbers (N) and percentages (%).

II. Complications
Heart failure was the most common in-hospital post-PCI complication, with no significant difference in other complications between the two groups. **Table 2** presents a comparison of complications.

III. Hospital stay duration
Group B1 had a shorter hospital stay, with a mean duration of 3.14 ± 2.40 days compared to 4.20 ± 3.26 days in group A, $p = 0.004$, $p = 0.31$, $p = 0.024$).

IV. One-year follow-up
At the one-year follow-up, 8 patients from group A and 10 patients from group B1 were lost to follow-up. There was no significant difference in one-year readmission due to chest pain, with readmission rates of 47.5% in group A and 32.1% in group B1 ($p = 0.013$). Similarly, the one-year mortality rate was 12.1% in group A and 6.4% in group B1 ($p = 0.110$).

Comparison between Group A (before the COVID-19 pandemic) and group B2 (confirmed diagnosis of COVID-19)

I. Risk profile and clinical presentation
A history of previous coronary heart disease was reported in 27 patients (25.2%) in group A and 8 patients (19.5%) in group B2 ($p = 0.464$). Chest pain was a more common presentation in group A. Systolic blood pressure and heart rate were significantly lower in group B2. There were no significant differences in other risk factors or clinical presentation between groups A and B2. **Table 1** shows a comparison of the risk profile and clinical presentation.

II. Complications
Heart failure was the most common complication in both groups. Cardiogenic shock, contrast-induced nephropathy (CIN), puncture site hematoma, and heart failure were more frequent in group B2. **Table 2** presents a comparison of complications.

III. Hospital stay duration
Group B2 had a significantly longer hospital stay (9.27 ± 5.30 days) compared to group A (4.20 ± 3.26 days, $p < 0.001$).

IV. One-year follow-up
At the one-year follow-up, 8 patients from group A and 6 patients from group B2 were lost to follow-up. One-year readmission due to chest pain was higher in group A (47.5% versus 20.0%, $p = 0.004$), while the one-year mortality rate was comparable between groups A and B2 (12.1% versus 11.4%, $p = 0.591$).

Discussion

Coronavirus Disease 2019 (COVID-19) is one of the most widely spread viruses in recent history. During the pandemic, there was an increase in cardiovascular incidents compared to the pre-pandemic period. It became clear that the COVID-19 pandemic influenced the demographic and angiographic characteristics of STEMI patients. Our study compared STEMI patients before the pandemic with those during the pandemic, distinguishing between those with no confirmed COVID-19 diagnosis and those

with a confirmed diagnosis. This approach differs from most studies, which compared patients before and during the pandemic without considering the COVID-19 status.

Risk profile and clinical presentation

There was no significant difference in gender between the groups, with males being the predominant gender in all groups (88.8% before the pandemic, 89.9% in non-COVID-19 patients, p = 0.760, and 80.5% in COVID-19 patients, p = 0.186). Other studies comparing the pre-pandemic and pandemic eras align with our findings, such as Sherif Ayad et al.[12] (85.7% vs. 81.5%, p = 0.607), and Callum Little et al.[13] (78.0% vs. 80.0%, p = 0.510). However, John Coughlan et al. [14] reported a higher percentage of male patients before the pandemic (100% vs. 55.0%, p = 0.014). There was no significant difference in the prevalence of smoking (53.3% before the pandemic, 62.7% in non-COVID-19 patients, p = 0.120, and 41.5% in COVID-19 patients, p = 0.199). Other studies reported similar findings: Sherif Ayad et al.[12] (57.1% vs. 45.6%, p = 0.364), Chun Kwok et al.[15] (40.9% vs. 38.1%, p = 0.260). In contrast, Callum Little et al.[13] found higher smoking rates in patients before the pandemic (55.7% vs. 41.6%, p <0.001). Similarly, we found no significant difference in the rates of hypertension (54.2% before the pandemic, 54.4% in non-COVID-19 patients, p = 0.970, and 48.8% in COVID-19 patients, p = 0.554). These results are consistent with findings from other studies: Sherif Ayad et al.[12] (42.9% vs. 39.6%, p = 0.411), Chun Kwok et al.[15] (43.2% vs. 39.4%, p = 0.067). However, Mustafa Erol et al.[16] reported a higher prevalence of hypertension during the pandemic (38.4% vs. 45.6%, p = 0.013). Regarding diabetes, there was no significant difference in its prevalence (43.0% before the pandemic, 42.6% in non-COVID-19 patients, p = 0.949 and 34.1% in COVID-19 patients, p = 0.327). This finding is consistent with previous studies, such as Sherif Ayad et al.[12] (35.7% vs. 35.2%, p = 0.521), John Coughlan et al.[14] (0% vs. 22.0%, p = 0.142). However, Xuhe Gong et al.[17] reported a significantly higher prevalence of diabetes during the pandemic (21.3% vs. 35.5%, p = 0.014). The prevalence of dyslipidemia remained similar in all groups (61.7% before the pandemic, 64.5% in non-COVID-19 patients, p = 0.636 and 56.1% in COVID-19 patients, p = 0.535). This pattern is consistent with findings from several studies, including Sherif Ayad et al.[12] (50.0% vs. 45.2%, p = 0.501), Chun Kwok et al.[15] (34.9% vs. 32.8%, p = 0.290). Conversely, Mustafa Erol et al.[16] reported a significantly higher incidence of dyslipidemia among patients during the pandemic (9.4% vs. 22.3%, p <0.001). We found no significant difference in the prevalence of previous coronary heart disease (25.2% before the pandemic, 27.2% in non-COVID-19 patients, p = 0.716 and 19.5% in COVID-19 patients, p = 0.464). This observation aligns with the findings of Tuncay Kiris et al.[18] (12.0% vs. 13.0%, p = 0.865), and John Coughlan et al.[14] (21.0% vs. 22.0%, p = 0.990). Chest pain remained the most common presenting symptom both before and during the pandemic, with no significant difference between pre-pandemic and non-COVID-19 patients (93.5% vs. 94.0%, p = 0.843). However, when compared to COVID-19 patients, our study found a higher prevalence of chest pain among pre-pandemic patients (93.5% vs. 80.5%, p = 0.019). Similarly, Tuncay Kiris et al.[18] reported that chest pain was more frequently observed before the pandemic (75.0% vs. 68.0, p = 0.004). This difference may be attributed to the fact that COVID-19 patients were more likely to present with shortness of breath rather than chest pain. The mean age of patients remained similar (55.36 ± 11.90 years before the pandemic, 53.95 ± 12.36 years non-COVID-19 patients, p = 0.348 and 55.02 ± 13.69 years COVID-19 patients, p = 0.882). We found a slightly higher mean age without a statistically significant difference between groups, such as Sherif Ayad et al.[12] (58.9 ± 13.35 vs. 57.1 ± 12.60 years, p = 0.568), John Coughlan et al.[14] (59 ± 10 vs. 58 ± 17 years, p = 0.912). In contrast, Tuncay Kiris et al.[18] found a higher mean age among pre-pandemic patients than during the pandemic (61.9 ± 12.4 vs. 60.6 ± 12.4 years, p = 0.029). Variations in clinical characteristics between our study and others may be attributed to differences in study populations.

Complications

Our study demonstrated statistically significant differences in in-hospital post-PCI complications. Heart failure (HF) was the most common complication across all groups, with COVID-19 patients being more likely to develop HF compared to patients before the pandemic (24.3% before the pandemic, 17.8% in non-COVID-19 patients, p = 0.188 and 48.8% in COVID-19 patients, p = 0.004), cardiogenic shock (6.5% before the pandemic, 6.5% in non-COVID-19 patients, p = 0.991 and 29.3% in COVID-19 patients, p <0.001), and contrast-induced nephropathy (CIN) (8.4% in before the pandemic vs. 5.9% in non-COVID-19 patients, p = 0.425 and 22.0% in COVID-19 patients, p = 0.024). In contrast, no significant differences were found in other complications, including, major bleeding (2.8% before the pandemic, 3.6% in non-COVID-19 patients, p = 0.513 and in 4.9% in COVID-19 patients, p = 0.617), and in-hospital mortality (3.7% before the pandemic, 1.8% in non-COVID-19 patients, p = 0.264 and 12.2% in COVID-19 patients, p = 0.116). Chun Kwok et al.[15] found no significant differences in in-hospital mortality (4.8% vs. 3.5%, p = 0.120), major bleeding (0.2% vs. 0.4%, p = 0.190), cardiogenic shock (7.4% vs. 6.2%, p = 0.200), and renal failure requiring dialysis (0.2% vs. 0.2%, p = 0.640). Similarly, Callum Little et al.[13] reported comparable rates of in-hospital mortality (8.6% vs. 10.9%, p = 0.280) and cardiogenic shock (13.5% vs. 12.5%, p = 0.680). Tuncay Kiris et al.[18] also found no significant differences in in-hospital mortality (7.0% vs. 8.0%, p = 0.205) or shock rates (9% vs. 9%, p = 0.846) before and during the pandemic. In contrast, John Coughlan et al.[14] reported a numerically higher in-hospital mortality during the pandemic, which nearly reached statistical significance (22.0% vs. 0%, p = 0.060). Mustafa et al.[16] found a significant increase in heart failure or cardiogenic shock (4.2% vs. 11.1%, p = 0.001), while in-hospital mortality remained unchanged (5.3% vs. 4.7%, p = 0.642). Sherif Ayad et al.[12] observed a higher incidence of in-hospital mortality during the pandemic (7.4% vs. 4.6%, p = 0.036), though rates of heart failure, stroke, and bleeding were similar between groups. The higher risk of complications in STEMI patients with

COVID-19 could be attributed to the underlying pathology of COVID-19 and the side effects of its treatment protocols. Differences in complication rates between our study and others could be due to several contributing factors. In particular, our study included only patients who presented early, excluding those who arrived more than 12 hours after symptom onset. Additionally, variations in study populations, comorbidities, and ischemia time may have contributed to the differing results.

Hospital stay duration

Our study revealed that before the pandemic STEMI patients had a longer hospital stay duration than non-COVID-19 group (4.20 ± 3.26 vs. 3.14 ± 2.40 days, p = 0.004), this could be explained by the efforts to minimize hospital exposure for non-COVID-19 patients, while COVID-19 patients had a significantly longer hospitalization (4.20 ± 3.26 vs 9.27 ± 5.30 days, p <0.001), due to isolation requirements and a higher risk of complications. Similar findings were reported by Sherif Ayad et al.[12] (3.5 ± 2.3 vs. 6.85 ± 4.22 days, p = 0.002) and Callum Little et al.[13] (3 [2–4] vs. 3 [2–5] days, p <0.001), showing an increase in hospital stay during the pandemic. However, other studies found shorter hospital stays, such as Chun Kwok et al.[15] (2 [1–3] vs. 3 [2–4] days, p <0.001) and Xuhe Gong et al.[15] (9 [8–11] vs. 8 [6–10] days, p <0.001).

One-year follow-up

The readmission to the hospital for chest pain was more frequent before the pandemic (45.5% before the pandemic, 32.1% in non-COVID-19 patients, p = 0.013, and 20% in COVID-19 patients, p = 0.04). However, one-year mortality rates remained comparable across the groups (12.1% before the pandemic, 6.4% in non-COVID-19 patients, p = 0.110, and 11.4% in COVID-19 patients, p = 0.591). Only a limited number of studies have investigated the follow-up of STEMI patients during the pandemic, with even fewer examining long-term outcomes. Xuhe Gong et al.[17] conducted a 30-day follow-up and found no significant difference in mortality rates (1.5% vs. 3.6%, p = 0.274).

Conclusion

When comparing patients before the pandemic and non-COVID-19 patients our study found no significant differences in clinical characteristics and in-hospital post-PCI complications or in-hospital mortality. In non-COVID-19 patients, the mean hospital stay duration was notably shorter. Non-COVID-19 patients had a higher mean WMSI. A one-year follow-up revealed that hospital readmission for chest pain was more common before the pandemic, while one-year mortality rates were comparable between the groups. Comparing patients before the pandemic and COVID-19 patients, COVID-19 patients were more likely to develop post-PCI cardiogenic shock, contrast-induced nephropathy (CIN), hematoma, and heart failure, while other post-PCI complications and in-hospital mortality rates were similar. The mean hospital stay duration was significantly shorter for COVID-19 patients. A one-year follow-up revealed that hospital readmission for chest pain was more common before the pandemic, while one-year mortality rates were comparable between the two groups.

Limitations

Our study had some limitations inherent to its observational design. The sample size was relatively small, and the follow-up time was limited to the hospitalization period and up to one year after discharge. The long-term effects of the COVID-19 pandemic, such as newly diagnosed heart failure or even increased mortality, are yet to be determined. Additionally, some patients were lost during the follow-up period, highlighting the need for a more structured follow-up system.

Conflicts of interest

The authors declare no competing interests.

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Availability of data and materials

Available from the corresponding author upon request.

Ethical statement

This study was approved by the Cairo University Faculty of Medicine Research Ethics Committee (approval date 23-2-2023).

Informed consent

Not applicable.

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Původní sdělení | Original research article

Chronic Hypertension as a Risk Factor for Peripartum Cardiomyopathy (PPCM): Insights from a Case-Control Study in Indonesia

Witri Pratiwi[a,b], Yogi Puji Rachmawan[c], Asri C. Adisasmita[a], Sudarto Ronoatmodjo[a], Amiliana Mardiani Soesanto[d]

[a] *Department of Epidemiology, Faculty of Public Health, University of Indonesia, Depok, Indonesia*
[b] *Department of Community Medicine and Public Health, Faculty of Medicine, Universitas Swadaya Gunung Jati, Cirebon, Indonesia*
[c] *Department of Cardiovascular Medicine, Faculty of Medicine, Universitas Swadaya Gunung Jati, Cirebon, Indonesia*
[d] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Harapan Kita National Cardiovascular Centre, Jakarta, Indonesia*

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SOUHRN

Kontext: Peripartální kardiomyopatie (PPCM) je vzácná, ale závažná příčina mateřského srdečního selhání. Hypertenze představuje jeden z hlavních přispívajících faktorů vzniku PPCM, avšak důkazy z Indonésie jsou dosud omezené.
Cíl: Cílem této studie bylo prozkoumat souvislost mezi chronickou hypertenzí a vznikem PPCM ve dvou referenčních nemocnicích v Cirebonu (západní Jáva) v letech 2019–2024.
Metoda: Studie využila uspořádání případ–kontrola a zahrnovala 84 žen s diagnózou PPCM dle kritérií Evropské kardiologické společnosti (ESC) a 336 kontrol bez PPCM. Bylo provedeno párování podle nemocnice. K posouzení nezávislého rizika chronické hypertenze pro PPCM byla použita multivariační nepodmíněná logistická regresní analýza.
Výsledky: Chronická hypertenze vykazovala silnou souvislost s PPCM (cOR 22,2; 95% CI 6,21–79,31), která zůstala statisticky významná i po adjustaci na věk matky, obezitu před těhotenstvím a nemocnici (aOR 17,13; 95% CI 3,71–79,14). Chronická hypertenze je tedy nezávislým rizikovým faktorem pro rozvoj PPCM.
Závěr: Zjištění zdůrazňují význam kardiovaskulárního hodnocení rizik a optimální kontroly krevního tlaku u žen s chronickou hypertenzí s cílem snížit riziko PPCM a zlepšit mateřské výsledky.

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Keywords:
Chronic hypertension
Maternal health
Peripartum cardiomyopathy
Pregnancy

ABSTRACT

Background: Peripartum cardiomyopathy (PPCM) is a rare but serious cause of maternal heart failure. Hypertension is a major contributing factor of PPCM, but evidence from Indonesia remains limited.
Objective: This study examined the association between chronic hypertension and PPCM in two referral hospitals in Cirebon, West Java, from 2019 to 2024.
Method: A case-control design included 84 women diagnosed with PPCM according to the European Society of Cardiology (ESC) criteria and 336 controls without PPCM. Frequency matching based on hospital was conducted. Multivariable unconditional logistic regression was performed to assess the independent risk of chronic hypertension for PPCM.
Results: Chronic hypertension showed a strong association with PPCM (cOR 22.2; 95% CI 6.21–79.31), which remained significant after adjusting for maternal age, pre-pregnancy obesity and hospital (aOR 17,13; 95% CI 3,71–79,14). In conclusion, chronic hypertension is an independent risk factor for PPCM.
Conclusion: These findings highlight the importance of cardiovascular risk assessment and optimal blood pressure control in women with chronic hypertension to reduce PPCM risk and improve maternal outcomes.

Address: Witri Pratiwi, Department of Community Medicine and Public Health, Faculty of Medicine, Universitas Swadaya Gunung Jati, Cirebon, Indonesia, e-mail: we3.borneo@gmail.com
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Introduction

Peripartum cardiomyopathy (PPCM) is a rare but serious form of heart failure that occurs during late pregnancy or in the months following delivery. It is characterized by left ventricular systolic dysfunction without another identifiable cause of cardiomyopathy. Although its incidence varies globally, PPCM remains an important cause of maternal morbidity and mortality. The burden is particularly high in low- and middle-income countries, where delayed diagnosis and limited resources contribute to poor outcomes. Understanding risk factors associated with PPCM is essential to support early recognition, prevention, and timely management.[1,2]

Previous studies have identified several maternal and obstetric risk factors associated with PPCM, including advanced maternal age, multiparity, multiple gestation, anemia, and hypertensive disorders of pregnancy. Meta-analyses demonstrated strong associations between PPCM and pre-eclampsia or gestational hypertension.[3,4] However, research on the association between chronic hypertension and PPCM remains very limited, particularly in Indonesia. This highlights a significant knowledge gap, as chronic hypertension is increasingly common in women of reproductive age, mainly due to the rising prevalence of obesity and metabolic syndrome.[3,5–7]

Chronic hypertension refers to hypertension that existed before pregnancy or was diagnosed before 20 weeks of gestation. It also includes women who used antihypertensive medication prior to pregnancy or whose elevated blood pressure persists for more than 12 weeks after delivery, as defined by the American College of Obstetricians and Gynecologists.[8,9] It may predispose to PPCM through prolonged pressure overload, endothelial dysfunction, and maladaptive cardiac remodelling. Unlike gestational hypertension or pre-eclampsia, which develop acutely during pregnancy, chronic hypertension exerts continuous hemodynamic stress on the myocardium beginning before conception and persisting throughout gestation. While gestational hypertension and pre-eclampsia have been extensively investigated as risk factors for PPCM, the contribution of chronic hypertension remains insufficiently explored.[4,10]

Research on PPCM in Indonesia remains limited, primarily based on single-center retrospective studies or isolated case reports. PPCM presents a major maternal health concern, particularly with the increasing burden of cardiovascular disease–related maternal mortality.[11,12] To address this gap, we conducted a case-control study in two tertiary hospitals in Cirebon, Indonesia. This study aimed to investigate the association between chronic hypertension and PPCM.

Materials and methods

Study design and setting

This was a hospital-based case-control study that was conducted at two tertiary hospitals in Cirebon, West Java, Indonesia. Both hospitals were the primary referral centers for maternal and cardiovascular cases in the region, receiving patients from primary health centers and secondary hospitals within Cirebon City and Cirebon Regency, as well as from surrounding districts. The first study site was Waled District General Hospital (RSUD Waled), which serves as the main referral hospital in Cirebon Regency and provides advanced maternal, obstetric, and cardiology services. The second site, Gunung Jati Regional General Hospital (RSD Gunung Jati) is the principal referral hospital in Cirebon City, accommodating a large volume of high-risk obstetric patients and offering comprehensive cardiovascular care. These hospitals collectively provide healthcare services to a wide catchment area and serve as the primary centers for the management of maternal complications and cardiovascular emergencies in the Cirebon region.

Study population and eligibility criteria

The study included women who delivered or were hospitalized during pregnancy or within five months postpartum at the participating hospitals between January 2019 and December 2024. Cases included all women diagnosed with PPCM according to the European Society of Cardiology (ESC) criteria: (1) development of heart failure toward the end of pregnancy or within five months postpartum, (2) left ventricular ejection fraction (LVEF) <45%, and (3) absence of another identifiable cause of heart failure.[13] Women who delivered or were hospitalized but did not meet the diagnostic criteria for PPCM were eligible as controls. **Frequency matching was performed based on hospital.** A case-to-control ratio of 1 : 4 was applied to increase statistical power and improve the precision of effect estimates. Patients with incomplete medical records were excluded.

Data collection

Data were collected retrospectively from paper-based medical records at the participating hospitals. In this study, PPCM data at RSUD Waled were only available for 2023 and 2024, as cardiovascular services were initiated in 2023. Data from RSD Gunung Jati were collected over a longer period, from 2019 to 2024. Information collected included maternal age, place of residence, parity, twin pregnancy, pre-pregnancy obesity, type 2 diabetes mellitus (T2DM), and chronic hypertension. Chronic hypertension was defined as a documented diagnosis of hypertension prior to pregnancy or before 20 weeks of gestation, or documented use of antihypertensive medication before pregnancy, in accordance with ACOG criteria.[8,9] The diagnosis was based on information recorded in the patients' medical records by the treating physicians. In this study, the severity of chronic hypertension was not classified. Blood pressure levels recorded in the medical records may vary over time and may be influenced by ongoing antihypertensive treatment and clinical conditions, which could lead to misclassification of hypertension severity. Therefore, chronic hypertension was analyzed as a binary variable based on documented diagnosis.

The hospitals did not yet use standardized computerized medical record systems. Therefore, all information was manually extracted from patients' paper charts. Data were abstracted using a standardized data collection form to ensure consistency and completeness across hos-

pitals. To ensure data accuracy, all extracted data were independently verified by a research assistant and the principal investigator before analysis.

Statistical analysis

Categorical variables were summarized as frequencies with percentages. Comparisons between cases and controls were performed using the chi-square test or Fisher's exact test, as appropriate. Bivariable analyses were conducted using unconditional logistic regression to examine the crude OR and 95% confidence intervals (CI) between each independent variable and PPCM. The independent association between chronic hypertension and PPCM was examined using multivariable unconditional logistic regression. The model was adjusted for the matching variable (hospital) to mitigate potential negative confounding effects that arise from matched design, as well as for covariates including maternal age and pre-pregnancy obesity. Results were reported as aOR and 95% CI. All analyses were conducted using Stata version 17.0 (StataCorp, College Station, TX, USA).

Results

In this study, a total of 84 women with PPCM were included, consist of 56 cases from RSD Gunung Jati and 28 cases from RSUD Waled. The selection of study participants is illustrated in **Figure 1**.

Baseline characteristics of the study sample are showed in **Table 1**. Among the 84 women diagnosed with PPCM, the majority were aged 20–35 years (60.71%), followed by those older than 35 years (35.71%) and younger than 20 years (3.57%). Most PPCM cases resided in Cirebon Regency (77.38%). Approximately 70.24% of PPCM cases were multiparous, and twin pregnancies occurred in 2 cases (2.38%). Regarding nutritional status, 17.86% of patients were overweight, 13.10% had class I obesity, and 8.33% had class II obesity. Type 2 DM was present in 4 cases (4.76%), and chronic hypertension was noted in 14 PPCM cases (16.67%). Among patients with chronic hypertension, no cases of secondary hypertension were documented in the medical records. All patients with chronic hypertension (n = 17) received methyldopa. Two patients received methyldopa as monotherapy, while nine received methyldopa in combination with nifedipine and six received methyldopa in combination with amlodipine. Given the small number of patients and overlapping treatment regimens, antihypertensive medication use was presented descriptively and was not included in further analyses.

Statistically significant differences between cases and controls were observed in maternal age distribution (p = 0.012), pre-pregnancy obesity (p = 0.003), T2DM (p = 0.002), and chronic hypertension ($p \leq 0.001$). Place of residence, parity, and twin pregnancy did not differ significantly between cases and controls.

In bivariable analysis, several factors were significantly associated with PPCM, as presented in **Table 2**. Chronic hypertension showed the strongest association, with an cOR of 22.2 (95% CI 6.21–79.31). Women with pre-pregnancy obesity (class I–II) also had higher odds of developing PPCM compared to those with underweight to overweight (cOR 3.00; 95% CI 1.57–5.74). Maternal age >35 years was associated with an increased risk of PPCM (cOR 2.15; 95% CI 1.28–3.61). While twin pregnancy and multiparity were not significantly associated with PPCM.

The results of the multivariable analysis are presented in **Table 3**. After adjusting for maternal age, pre-pregnancy obesity, and hospital, chronic hypertension remained strongly associated with PPCM (aOR 17.13; 95% CI 3.71–79.14).

Discussion

This case-control study identified chronic hypertension as a strong independent risk factor for PPCM, even after ad-

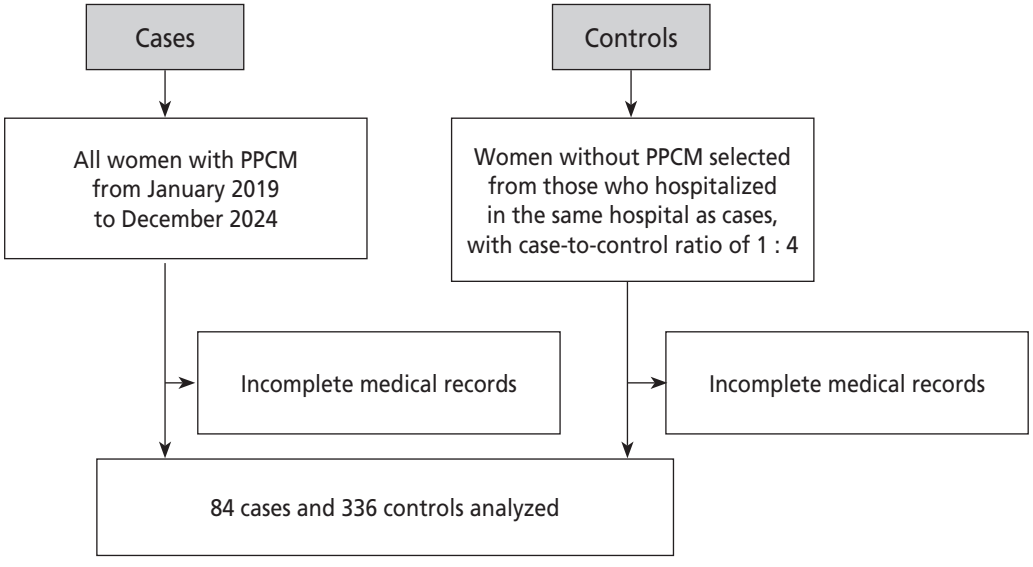


Fig. 1 – Sample selection process.

Table 1 – Baseline characteristics of study sample

Characteristics	Total (n = 420)	PPCM (n = 84)	Controls (n = 336)	*p*-value
Maternal age				**0.012**
<20 years	23 (5.48)	3 (3.57)	20 (5.95)	
20–35 years	298 (70.95)	51 (60.71)	247 (73.51)	
>35 years	99 (23.57)	30 (35.71)	69 (20.54)	
Place of residence				**0.103**
Cirebon City	48 (11.43)	11 (13.10)	37 (11.01)	
Cirebon Regency	299 (71.19)	65 (77.38)	234 (69.64)	
Outside Cirebon	73 (17.38)	8 (9.52)	65 (19.35)	
Parity				**0.792**
Primiparity	130 (30.95)	25 (29.76)	105 (31.25)	
Multiparity	290 (69.05)	59 (70.24)	231 (68.75)	
Twin pregnancy				**0.345**
No	414 (98.57)	82 (97.62)	332 (98.81)	
Yes	6 (1.43)	2 (2.38)	4 (1.19)	
Pre-pregnancy obesity				**0.003**
Underweight & normal	288 (68.57)	51 (60.71)	237 (70.54)	
Overweight	86 (20.48)	15 (17.86)	71 (21.13)	
Obesity class I	33 (7.86)	11 (13.10)	22 (6.55)	
Obesity class II	13 (3.10)	7 (8.33)	6 (1.79)	
T2DM				**0.002**
No	416 (99.05)	80 (95.24)	336 (100)	
Yes	4 (0.95)	4 (4.76)	0 (0)	
Chronic hypertension				**<0.001**
No	403 (95.95)	70 (83.33)	33 (99.11)	
Yes	17 (4.05)	14 (16.67)	3 (0.89)	
Antihypertensive medication among patients with chronic hypertension				
Methyldopa	2 (11.8)			
Methyldopa + nifedipine	9 (52.9)			
Methyldopa + amlodipine	6 (35.3)			

T2DM – type 2 diabetes mellitus.

Table 2 – Bivariable analysis (cOR) of risk factors for PPCM

Characteristics	PPCM (n = 84)	Controls (n = 336)	cOR (95% CI)	*p*-value
Maternal age				**0.004**
≤35 years	54 (64.29)	267 (79.46)	Reff.	
>35 years	30 (35.71)	69 (20.54)	2.15 (1.28–3.61)	
Parity				**0.792**
Primiparity	25 (29.76)	105 (31.25)	Reff.	
Multiparity	59 (70.24)	231 (68.75)	1.07 (0.64–1.81)	
Twin pregnancy				**0.420**
No	82 (97.62)	332 (98.81)	Reff.	
Yes	2 (2.38)	4 (1.19)	2.02 (0.36–11.24)	
Pre-pregnancy obesity				**0.001**

Pokračování na další straně

Table 2 – Bivariable analysis (cOR) of risk factors for PPCM

Characteristics	PPCM (n = 84)	Controls (n = 336)	cOR (95% CI)	*p*-value
Underweight–overweight	66 (78.57)	308 (91.67)	Reff.	
Obesity class I–II	18 (21.43)	28 (8.33)	3.00 (1.57–5.74)	
Chronic hypertension				**<0.001**
No	70 (83.33)	33 (99.11)	Reff.	
Yes	14 (16.67)	3 (0.89)	22.20 (6.21–79.31)	

Table 3 – Multivariable unconditional logistic regression (aOR) for PPCM

Characteristics	Adjusted OR	95% CI (lower–upper)	*p*-value
Chronic hypertension	17.13	3.71–79.14	<0.001
Maternal age	1.26	0.68–2.32	0.458
Pre-pregnancy obesity	2.22	2.06–4.63	0.002

Results were adjusted for matching variable (hospital).

justing for maternal age and pre-pregnancy obesity (aOR 17.13; 95% CI 3.71–79.14). Our findings are consistent with recent meta-analyses demonstrating that hypertensive disorders, particularly chronic hypertension, significantly increase the risk of PPCM by amplifying hemodynamic and vascular stress during pregnancy (pooled OR 4.73; 95% CI 3.33–6.73).[14] Chronic hypertension induces persistent pressure overload and endothelial dysfunction, leading to left ventricular remodelling and impaired myocardial recovery. These maladaptive alterations may manifest clinically when further stressed by marked plasma volume expansion of late pregnancy and the hemodynamic shifts of the postpartum period.[15,16]

The pathophysiological link between chronic hypertension and PPCM may also involve systemic inflammation, oxidative stress, and altered angiogenic signalling. Chronic hypertension induces microvascular damage and myocardial fibrosis, impairing myocardial contractility and limiting cardiac reserve.[17] Advanced maternal age further exacerbates these processes due to vascular stiffening, higher prevalence of comorbidities, and diminished myocardial adaptation to pregnancy-related volume overload. Similarly, obesity and diabetes mellitus remain biologically plausible contributors through mechanisms of metabolic dysregulation and increased cardiovascular strain.[18–20]

The coexistence of multiple comorbidities may exert a synergistic effect in predisposing women to PPCM. Previous studies suggest that the combination of chronic hypertension, obesity, and multiparity imposes an additive burden on the cardiovascular system by increasing myocardial workload, metabolic demand, and oxidative stress during pregnancy. This cumulative strain can compromise myocardial adaptation and impair recovery in the peripartum period.[4,21]

Meta-analysis showed that pre-pregnancy obesity was significantly associated with an increased risk of PPCM compared to normal-weight women (pooled OR 1.79; 95% CI 1.16–2.76). Subgroup analysis showed that women with pre-pregnancy obesity class I had a higher risk of PPCM (pooled OR 1.58; 95% CI 1.20–2.07), while those with class II and III obesity had an even greater risk (pooled OR 2.65; 95% CI 2.04–3.45) compared to normal-weight women.[22] Additionally, the meta-analysis demonstrated that multiparity was a significant risk factor for PPCM (pooled OR 1.79; 95% CI 1.21–2.67).[4]

Increasing parity and higher pre-pregnancy BMI are associated with progressive metabolic dysregulation, including insulin resistance, lipid abnormalities, and an imbalance between reactive oxygen species production and antioxidant defense. Repeated pregnancies may exacerbate physiological insulin resistance, leading to endothelial injury and maladaptive cardiac remodelling.[21,23,24] These mechanisms together may explain why women with coexisting chronic hypertension, obesity, or multiparity have a markedly higher susceptibility to PPCM. Although multiparity and twin pregnancy were not significantly associated with PPCM in the bivariable analysis of the present study, pre-pregnancy obesity remained significantly associated (cOR 3; 95%CI 1.57–5.74). The lack of significant association for multiparity or twin pregnancy in this study may be due to the limited sample size. However, these factors should not be disregarded, as they remain biologically plausible contributors to PPCM risk.

These findings highlight the need for an integrated approach to maternal cardiovascular health. Screening for chronic hypertension, obesity, and metabolic disorders before and during pregnancy should be prioritized to identify women at elevated risk for PPCM. Early blood pressure control, optimization of metabolic status, and patient education on cardiovascular symptoms may help prevent disease onset or enable earlier detection. In resource-limited settings, targeted echocardiographic surveillance and multidisciplinary collaboration between obstetricians and cardiologists could further improve maternal outcomes.

To the best of our knowledge, this is the first study in Indonesia to specifically evaluate the association between chronic hypertension and peripartum cardiomyopathy PPCM. The study collected PPCM data from referral

hospitals in the Cirebon region, Indonesia over a six-year period, providing a comprehensive overview of patient characteristics and risk factors within a real-world clinical setting. By employing a case-control design and standardized diagnostic criteria, this study strengthens the evidence on the role of chronic hypertension as an independent risk factor for PPCM in a low- and middle-income country context. The use of multivariable unconditional logistic regression further enhances the internal validity of the findings.

This study has several limitations. The retrospective design relies on medical record data, which may be incomplete or subject to documentation bias. However, the number of missing records was small for both cases and controls, suggesting that potential selection bias affecting internal validity is likely minimal. The relatively small sample size may limit the statistical power, particularly for subgroup analyses. Additionally, as this was a hospital-based study, the results may not be fully generalizable to the broader population of pregnant women in the community. Furthermore, the onset and duration of chronic hypertension were difficult to determine, as many patients were first identified as having hypertension at their initial antenatal visit before 20 weeks of gestation. Consequently, information on the onset and duration of chronic hypertension prior to pregnancy was not consistently available in the medical records. In addition, whether hypertension was controlled or uncontrolled could not be reliably assessed, as repeated blood pressure measurements over time were not consistently available for all patients.

Conclusions

This study demonstrates that chronic hypertension is a strong and independent risk factor for PPCM in Indonesian women. The findings emphasize the need for early cardiovascular risk assessment and optimal management of blood pressure before and during pregnancy to prevent PPCM. Integrating cardiac evaluation into antenatal care, particularly for women with a history of hypertension may help reduce the burden of PPCM and improve maternal outcomes in resource-limited settings. Screening for chronic hypertension should also be conducted at the primary healthcare level (Puskesmas), with timely referral to hospitals equipped with the capacity and facilities to assess the risk of PPCM. This enables more intensive patient monitoring and earlier recognition of PPCM, **thereby** preventing maternal complications and mortality. Future research should investigate maternal and long-term cardiovascular outcomes among PPCM patients with a history of chronic hypertension, particularly in low- and middle-income countries.

Author contributions

Conceptualization: W.P.; methodology: W.P., Y.P.R., A.C.A, S.R. and A.M.S; validation: W.P. and Y.P.R.; formal analysis: W.P., A.C.A, S.R. and A.M.S; investigation: W.P. and Y.P.R.; resources:: W.P. and Y.P.R.; data curation: W.P.; writing:: original draft preparation, W.P., Y.P.R., A.C.A, S.R. and A.M.S; writing: review and editing, W.P., Y.P.R., A.C.A, S.R. and A.M.S.; visualization: W.P.; supervision: A.C.A, S.R. and A.M.S.; project administration: W.P.; funding acquisition: W.P. and Y.P.R. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare no conflicts of interest.

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Ethical statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of RSD Gunung Jati Cirebon City No. 057/LAIKETIK/KEP-PKRSGJ/IX/2024 on 30 September 2024.

Informed consent

Patient consent was waived due to the retrospective nature of the study and the use of anonymized medical record data. All data were handled in accordance with ethical standards to ensure patient confidentiality. Written informed consent for publication was not required as no identifiable patient information is included in this article.

Data availability statement

Data is contained within the article or supplementary material.

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Differences in Outcomes Between Major Amputation and Wound Debridement on Inflammatory Response and Length of Stay in Type 2 Diabetic Foot Ulcer Patients Treated at Airlangga University Hospital: A Retrospective Study

Aloysius Denzel Joshua Reviano[a], Danang Himawan Limanto[b], Hermawan Susanto[c], Satriyo Dwi Suryantoro[c]

[a] *Medical Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[b] *Department of Thoracic Cardiovascular Surgery, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Academic Hospital, Surabaya, Indonesia*
[c] *Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Academic Hospital, Surabaya, Indonesia*

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Klíčová slova:
Débridement rány
Diabetes mellitus 2. typu
Syndrom diabetické nohy
Vysoká amputace

SOUHRN

Kontext: Podle Mezinárodní diabetologické federace (International Diabetes Federation, IDF) dosahovala v roce 2021 prevalence diabetes mellitus (DM) v Indonésii 10,8 % (toto onemocnění tam bylo diagnostikováno přibližně u 19,4 milionu osob). Pokud se týče nejčastější komplikace, tedy syndromu diabetické nohy (diabetic foot ulcer, DFU), existuje u diabetiků 15–34% riziko vzniku tohoto postižení s recidivou ve výši 40–60 %. V časném stadiu DFU je třeba odstranit detritus z rány, ale se stupňující se bolestí a imobilitou nakonec vyvstává nutnost amputace. Význam této studie spočívá ve srovnání předoperačních a pooperačních počtů leukocytů, poměru neutrofily/lymfocyty (neutrophil-lymphocyte ratio, NLR) a délky hospitalizace (length of stay, LOS) při odstraňování detritu z rány versus vysoká amputace, stejně jako účinek odstranění detritu na DFU zamezující nutnosti amputace.
Metody: V tomto článku popisujeme observační kohortní retrospektivní studii, v níž byla pro vyhledání potřebné zdravotnické dokumentace uložené ve fakultní nemocnici Airlangga University ve městě Surabaja a zahrnující období od ledna do června 2024 použita metoda totálního výběru. Zkoumanou populací byli dospělí pacienti ve věku nad 18 let s diagnózou DM 2. typu a s DFU stupně 0–5 ve Wagnerově klasifikaci, u nichž bylo provedeno odstranění detritu nebo vysoká amputace. Mezi hodnocené proměnné patřily předoperační a pooperační hodnoty leukocytů, diferenciální rozpočet leukocytů, předoperační a pooperační hodnoty NLR, předoperační a pooperační LOS a celková LOS. Uvedené proměnné jsme srovnali u dvou skupin pacientů, jedné s odstraněním detritu z rány a druhé s vysokou amputací. Údaje byly analyzovány s použitím softwaru SPSS 27 a Microsoft Excel, verze 16.102.2.
Výsledky: Mezi oběma skupinami jsme nalezli statisticky významný rozdíl v předoperačním počtu leukocytů a diferenciálním rozpočtu leukocytů ($p < 0,05$); rozdíly mezi ostatními proměnnými nebyly statisticky významné ($p > 0,05$). Skupina s odstraněním detritu z rány vykazovala nižší předoperační počty leukocytů a menší pokles počtu leukocytů než skupina s vysokou amputací, což ukazuje na méně intenzivní zánětlivou odpověď u pacientů s odstraněním detritu z rány ve srovnání s pacienty s vysokou amputací. I když pooperační hodnoty nejsou statisticky významné, rozdíl předoperačních a pooperačních hodnot statisticky významný byl, což ukazuje na větší pokles počtu leukocytů po vysoké amputaci a odráží potlačení zánětu.
Závěr: Odstranění detritu z rány je spojeno s nižšími předoperačními počty leukocytů a s menším rozdílem mezi jejich předoperačními a pooperačními počty. K bližšímu poznání zánětlivých procesů u pacientů s DFU se doporučuje zkoumat i ostatní proměnné.

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Keywords:
Diabetic foot ulcer
Major amputation
Type 2 diabetes mellitus
Wound debridement

ABSTRACT

Background: According to the International Diabetes Federation (IDF) in 2021, Indonesia had a diabetes mellitus (DM) prevalence of 10.8% out of the total population, approximately 19.4 million individuals. The most common complication, diabetic foot ulcer (DFU), has a 15–34% risk of developing in diabetic patients and

Address: dr. Danang Himawan Limanto, Department of Thoracic Cardiovascular Surgery, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, e-mail: danang.himawan@fk.unair.ac.id
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a 40–60% recurrence rate. The early stage of DFU requires wound debridement, but as pain and immobility worsen, the need for amputation ultimately rises. The importance of this study is to compare preoperative and postoperative level of leukocyte, neutrophil-lymphocyte ratio (NLR), and length of stay (LOS) between wound debridement and major amputation, as well to evaluate wound debridement's healing factor on DFU to avoid amputation.

Methods: This is an observational cohort retrospective study. A total sampling method was used to retrieve medical records from Airlangga University Hospital, Surabaya, with the study period of January–June 2024. The population was adult patients above 18 years old and diagnosed with type 2 DM with DFU in Wagner scale of 0–5 that had received wound debridement or major amputation. The research variables were preoperative leukocyte, postoperative leukocytes, leukocyte difference, preoperative NLR, postoperative NLR, preoperative LOS, postoperative LOS, and total LOS. We compared those variables between two groups, which are wound debridement and major amputation. Data were analyzed using SPSS 27 and Microsoft Excel version 16.102.2.

Results: We found that there is a significant difference between the two groups in terms of preoperative leukocyte and leukocyte difference (p <0.05), while other variables were found not significant (p >0.05). Wound debridement groups had lower preoperative leukocytes and a smaller leukocyte decrease compared to those undergoing major amputation. This represents lower inflammation response in patients receiving wound debridement compared to major amputation. Although postoperative leukocytes aren't significant, the leukocyte difference between preoperative and postoperative was significant. This marks a greater reduction in leukocytes following major amputation, reflecting inflammation suppression.

Conclusion: Wound debridement has lower preoperative leukocyte and leukocyte difference. Further studies on other variables are recommended to describe inflammatory processes in patients with DFU.

Introduction

Diabetes mellitus (DM) is characterized by either a deficiency of insulin (type 1 DM) or insulin dysfunction (type 2 DM). According to the International Diabetes Federation in 2021, Indonesia has a DM prevalence of 10.8% of the total population, approximately 19.4 million individuals.[8] This finding is supported by the Indonesian Ministry of Health, reporting 19.5 million people with DM in 2024, with an increased prediction of 28.5 million by 2045.[7] In terms of cost, it was reported that the direct medical cost for DM care amounted to USD 576 million, with 56% represented by hospital inpatient care.[6]

Type 2 diabetes mellitus (T2DM) is responsible for 90–95% of all DM cases globally and is characterized by insulin resistance in pancreatic cells. One of the most adverse chronic complications of T2DM is diabetic foot ulcer (DFU), which is classified as a type of peripheral artery disease (PAD). DFU can lead necrotic tissue in the affected limb. According to recent studies, patients with T2DM have a 15–34% lifetime risk of developing DFU and a 40–60% recurrence rate.[4,12] DFU is also a risk factor to nontraumatic lower extremity amputations (LEA) in diabetic patients, which is responsible for 85% of total cases. DFU consists of pain and immobility, which can ultimately reduce quality of life. Mortality rates associated with DFU are approximately 11% annually and increased to 22% among patients who underwent LEA.

Because of the urgency in terms of high cost inpatient care and increasing postoperative amputation mortality, this study is crafted to evaluate the alternative intervention to DFU treatment. This retrospective study aims to assess the effect of wound debridement therapy on DFU healing, specifically analyzing reductions in leukocyte counts and length of hospital stays (LOS) among patients treated at Airlangga University Hospital, Surabaya, Indonesia. The goal of this study is to provide insights in DFU healing from wound debridement as a form of prevention to amputation.

Methods

This study is an observational cohort retrospective study. Samples were taken from medical records of the Airlangga University Hospital, Surabaya, Indonesia from January-June 2024 period. This research conducted total sampling methods. The inclusion criteria were adult patients above 18 years old and diagnosed with T2DM with DFU in Wagner scale of 0–5 that had wound debridement or major amputation interventions. This research excludes data of patients besides T2DM, mortality during treatment, and incomplete medical records. Dependent variables such as, preoperative leukocyte, postoperative leukocytes, leukocyte difference, preoperative NLR, postoperative NLR, preoperative LOS, postoperative LOS, and total LOS are being analyzed and grouped based on the independent variables, which are wound debridement and major amputation. Data were analyzed with SPSS 27 and Microsoft Excel version 16.102.2.

Results

Data analysis of patient's characteristics have proven that there are 34 samples with frequencies almost equal between 16 male (47%) and 18 female (53%) (**Table 1**). This indicates that in this research, DFU isn't necessarily bound to genders, because of the relatively equal frequencies between male and females. Most of the sample, which is 30 patients (88%) are from the age range of 18–65 years old, meanwhile there are only four patients (12%) that are >65 years old (**Table 1**). There are 30 patients (88%) that don't have hypertension (**Table 1**). Most of the DFU samples occurred in the left side of the limb in 19 patients (56%), right side in 13 patients (38%), and bilateral in two patients (6%) (**Table 1**). These findings proved that DFU most likely occurred unilaterally. Meanwhile, findings in terms of Wagner scale mostly occurred in scale of 2–4. Whereas level 2 in two patients (6%), Wagner 3

in 15 patients (44%), and Wagner 4 in 17 patients (15%). Lastly, patients receiving wound debridement occurred in 25 patients (74%) and major amputation in nine patients (26%) (**Table 1**).

Based on total descriptive analysis of DFU patients, data showed the mean and standard deviation of preoperative leukocyte were 18.25 ± 8.8 (**Table 2**), which decreased in postoperative to 15.51 ± 6.94 (**Table 2**), with a mean leukocyte difference of 2.66 ± 6 (**Table 2**). The preoperative neutrophil-lymphocyte ratio (NLR) has 15.55 ± 16.05 (**Table 2**), while postoperative NLR was 13 ± 13.28 (**Table 2**). The results of preoperative and postoperative LOS, respectively, were 2.94 ± 1.75 days and 3.76 ± 3.08 days (**Table 2**). Meanwhile, the total LOS is 6.71 ± 4.17 days (**Table 2**). The data from **Table 2** provide a general overview of inflammatory response before and after intervention, as well as the overall LOS.

Based on analysis of 25 samples from the wound debridement group, it was found that preoperative leukocyte was 15.17 ± 6.15, postoperative leukocyte was 14.52 ± 6.57, and leukocyte difference was 1.15 ± 4.63 (**Table 3**). This indicates decrease in leukocytes preoperative to postoperative measurements within the wound debridement group, although high standard deviation is present in this variable, which suggests high heterogeneity among patients. Meanwhile, preoperative and postoperative NLR was 14.04 ± 15.82 and 11.07 ± 7.96, respectively (**Table 3**). This finding suggests a potential reduction in NLR following wound debridement. Preoperative, postoperative, and total LOS were 2.72 ± 1.56 days, 3.88 ± 3.33

Table 1 – Sample characteristics

Characteristics	Frequency	Percentage
Gender		
Male	16	47%
Female	18	53%
Age		
18–65 years	30	88%
>65 years	4	12%
Hypertension history		
Yes	4	12%
No	30	88%
Ulcer location		
Left	19	56%
Right	13	38%
Bilateral	2	6%
Wagner classification		
1	0	0%
2	2	6%
3	15	44%
4	17	50%
5	0	0%
Intervention		
Debridement	25	74%
Amputation	9	26%

Table 2 – Total descriptive inflammation markers

Characteristics	Mean ± SD (n = 34)
Preoperative leukocyte	18.25 ± 8.8
Postoperative leukocyte	15.51 ± 6.94
Leukocyte difference	2.66 ± 6
Preoperative NLR	15.55 ± 16.05
Postoperative NLR	13 ± 13.28
Preoperative LOS	2.94 ± 1.75
Postoperative LOS	3.76 ± 3.08
Total LOS	6.71 ± 4.17

Table 3 – Patient's characteristics with debridement

Characteristics	Mean ± SD (n = 25)
Preoperative leukocyte	15.17 ± 6.15
Postoperative leukocyte	14.52 ± 6.57
Leukocyte difference	1.15 ± 4.63
Preoperative NLR	14.04 ± 15.82
Postoperative NLR	11.07 ± 7.96
Preoperative LOS	2.72 ± 1.56
Postoperative LOS	3.88 ± 3.33
Total LOS	6.6 ± 4.54

Table 4 – Patient's characteristics with major amputation

Characteristics	Mean ± SD (n = 9)
Preoperative leukocyte	25.3 ± 11.39
Postoperative leukocyte	18.28 ± 7.6
Leukocyte difference	6.84 ± 7.57
Preoperative NLR	19.75 ± 16.86
Postoperative NLR	18.34 ± 22.23
Preoperative LOS	3.56 ± 2.18
Postoperative LOS	
Total LOS	7 ± 3.12

Table 5 – Comparison of mean values between wound debridement and major amputation

Characteristics	*p*-value
Preoperative leukocyte	0.018
Postoperative leukocyte	0.166
Leukocyte difference	0.012
Preoperative NLR	0.301
Postoperative NLR	0.922
Preoperative LOS	0.224
Postoperative LOS	0.827
Total LOS	0.324

days, and 6.6 ± 4.54 days, respectively. This indicates longer LOS postoperatively compared to preoperative LOS in the wound debridement group.

Based on analysis of nine samples from the major amputation group, it was found that preoperative leukocyte was 25.3 ± 11.39, postoperative leukocyte was 18.28 ± 7.6, and leukocyte difference was 6.84 ± 7.57 (**Table 4**). This indicates prominent decrease in leukocytes preoperative to postoperative measurements within the major amputation group, which suggests positive inflammatory response reduction. Meanwhile, preoperative and postoperative NLR was 19.75 ± 16.86 and 18.34 ± 22.23, respectively (**Table 3**). This finding suggests a potential reduction in NLR following wound debridement, although high standard deviations are present, which indicate variability in inflammatory response. Preoperative, postoperative, and total LOS were 3.56 ± 2.18 days, 3.44 ± 2.4 days, and 7 ± 3.12 days, respectively. This indicates relatively balanced LOS in both preoperative and postoperative in the major amputation group.

After analyzing 34 samples, it was found that few variables are significant (p <0.05), which are leukocyte preoperative with p-value of 0.018 and leukocyte difference with 0.012 in (**Table 5**). These proved that there are significant differences in both variables between wound debridement and major amputation. Meanwhile, other variables weren't found to have any significant difference in p-value between the two groups.

Discussion

Preoperative leukocytes function as an indicator of the severity of inflammatory response in patients with DFU. Based on (**Table 5**) a significant difference was found in preoperative leukocytes between patients who receive wound debridement and major amputation, with a p--value of 0.018. The analysis showed that reduction from preoperative to postoperative leukocyte in the wound debridement group only has minimal reduction. Another study also supports this finding, where the preoperative and postoperative leukocytes are 13.902 g/dL and 13.804 g/dL, respectively, among DFU patients undergoing debridement.[9] The previous study was aligned with this research, which also indicates a relative small difference in preoperative and postoperative leukocytes.

The significant difference between preoperative leukocytes between the two groups suggests a distinct inflammatory response in patients undergoing wound debridement and major amputation prior to the procedure. Additional findings support this research, which identified elevated leukocyte as a predictor of prolonged wound healing duration.[2] Another findings also mentioned, that the presence of wound infection can delay the healing process.[2] Significant differences of leukocyte prior to procedure are important for surgeons to pick the most optimal option to treat wounds in DFU patients. Another study supports this research, by reporting that preoperative leukocyte tends to be higher in patients who receive amputation.[5] Therefore, it can be summarized that lower preoperative leukocytes are associated with wound debridement as intervention to treat DFU, whereas higher preoperative leukocytes may lead surgeons to consider major amputation as more suitable.

Postoperative leukocytes reflect the inflammatory response reduction following intervention either wound debridement or major amputation. Conversely, the difference between preoperative and postoperative leukocytes represents the effectiveness of intervention in reducing inflammation. Based on data that were analyzed in **Table 5**, the difference between the two groups in terms of postoperative leukocyte was not significant (p = 0.166). However, the reduction of leukocyte from preoperative to postoperative between wound debridement and major amputation was significant (p = 0.012). The mean postoperative leukocytes for wound debridement and major amputation were 14.52 (**Table 3**) and 18.28 (**Table 4**), respectively, while the mean of leukocyte differences were 1.15 (**Table 3**) and 6.82 (**Table 4**). This analysis indicates although postoperative leukocytes did not differ between the two groups, the significance in reduction did.

NLR represents neutrophils as mediators of acute inflammation and lymphocytes which serve in adaptive immune response. Another study stated that NLR is an indicator of chronic inflammatory response.[11] Neutrophil reflects ongoing inflammatory response, while reduction in lymphocytes is a characteristic of T2DM. Additionally, increase in neutrophil and lymphocyte reduction is a key characteristic of T2DM.[3] Recent study also suggests that NLR in T2DM patients that had amputation is equivalent as NLR on chronic wound infection.[10] Based on data from (**Table 5**), there were no significant differences in preoperative and postoperative NLR between the two groups, with p-values of 0.301 and 0.922, respectively. However, each group reported a consistent reduction trend from preoperative to postoperative NLR. In the wound debridement group, the mean NLR decreased from 14.04 to 11.07 (**Table 3**), meanwhile in the major amputation group, it decreased from 19.75 to 18.34 (**Table 4**) These findings suggest a general reduction trend in inflammatory postintervention. On the other hand, the absence of significant difference indicates that NLR may not be an effective parameter for predicting the severity of infection in DFU patients.

LOS reflects the duration of recovery and potential cost of hospitalization. From **Table 5**, it was found that the comparison between preoperative, postoperative, and total LOS between the two groups was not statistically significant, with p-values of 0.224, 0.827, and 0.324, respectively. This indicates no significant difference in duration of stay in hospital between patients who underwent wound debridement and major amputation. Mean of preoperative and postoperative LOS in wound debridement group were 2.72 and 3.88 days, respectively (**Table 3**), whereas for the major amputation group were 3.55 and 3.44 days (**Table 4**). This aligns with another study, which suggests mean LOS of 8.13, 8.86, and 9.8 days for patients undergoing mild, moderate, and severe debridement treatment, respectively across 75 DFU cases.[1] Shorter LOS in this research may be attributed to different clinical pathways and postoperative management protocols. Since there are no significant differences in preoperative, postoperative, and total LOS, this suggests

that both wound debridement and major amputation have the same effectiveness in managing inflammatory responses, as reflected from hospitalization duration.

Conclusion

After analyzing medical records of samples with DFU, there are several conclusions that can be drawn. Firstly, there are differences in preoperative leukocytes that may serve as potential considerations for surgeons in determining the approach for DFU treatment. Although postoperative leukocytes were relatively similar in both groups, differences in leukocyte reduction are significant between patients who receive wound debridement and major amputation. Preoperative and postoperative NLR showed no significant difference between both groups, which suggests that NLR may not be effective to assess severity of infection. Preoperative, postoperative. and total LOS did not show any difference between both groups, indicating wound debridement and major amputation are equally effective in managing DFU in terms of hospitalization duration. Additional research is required to assess other inflammatory markers such as, HbA_{1c}, C-reactive protein, procalcitonin, and other mediators to determine effectiveness of wound debridement and major amputation.

Conflict of interest
The authors declare no conflict of interest for this article.

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Přehledový článek | Review article

Novinky a nové přístupy v léčbě srdeční dyssynchronie

(Innovations and new approaches in cardiac resynchronization therapy)

Jan Řeháček, Petr Ošťádal, Jakub Honěk

Kardiologická klinika, 2. lékařská fakulta Univerzity Karlovy a Fakultní nemocnice Motol a Homolka, pracoviště Motol, Praha Česká republika

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Stimulace převodního systému

Keywords:
Cardiac dyssynchrony
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Conduction system pacing
Heart failure
Left bundle branch area pacing

SOUHRN

V článku jsou shrnuty klíčové směry a novinky v srdeční resynchronizační léčbě s předpokládaným největším dopadem na klinickou praxi. Úvodem je pojednáno o patofyziologii srdeční dyssynchronie a jsou shrnuty diagnostické metody a postupy (včetně moderních metod jako ultra-vysokofrekvenční EKG či nové metody vyhodnocování ultrasonografie). V další části popisujeme nové postupy v rámci implantace elektrod včetně stimulace Hisova svazku a oblasti levého raménka Tawarova. Tyto nové přístupy mají za cíl snížit procento pacientů, u kterých se nedostaví efekt resynchronizační léčby.

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ABSTRACT

The article summarizes the key directions and innovations in cardiac resynchronization therapy with the greatest anticipated impact on clinical practice. The introduction discusses the pathophysiology of cardiac dyssynchrony and reviews diagnostic methods and workflows (including modern techniques such as ultra-high-frequency ECG and new approaches to ultrasound assessment). In subsequent sections, we also describe new techniques for lead implantation including His bundle pacing and left bundle branch area pacing. These approaches aim to reduce the proportion of patients who do not respond to resynchronization therapy.

Úvod

Srdeční selhání představuje zásadní zátěž pro zdravotnický systém, s prevalencí odhadovanou na 1–2 % dospělé populace v Evropě a Spojených státech amerických, ovšem stoupající na více než 10 % u osob starších 70 let. V České republice srdečním selháním trpí přibližně 250–300 tisíc pacientů a incidence i prevalence nadále narůstají. I přes dosavadní pokroky a nové léky zůstává prognóza nepříznivá – pětileté přežití po stanovení diagnózy se pohybuje okolo 50 %, což je srovnatelné s některými onkologickými chorobami.

Jedním z klíčových patofyziologických mechanismů zhoršujících prognózu je srdeční dyssynchronie, nejčastěji v důsledku blokády levého Tawarova raménka (LBBB). Dyssynchronie vede k poklesu systolické funkce, remodelaci levé komory a dalšímu zhoršování symptomů.

Srdeční resynchronizační terapie (cardiac resynchronization therapy, CRT) je jednou z nefarmakologických možností terapie a je standardní léčebnou metodou u vybraných pacientů se srdečním selháním a těžkou systolickou dysfunkcí levé komory (heart failure with reduced ejection fraction, HFrEF) a širokým komplexem QRS.[1–4] Od prvních velkých randomizovaných studií CARE-HF a COMPANION, které prokázaly pokles mortality a morbidity, je CRT pevně zakotvena v klinických doporučeních.[5,6] Ty jsou shrnuty v **tabulce 1**.

Navzdory významnému pokroku však zůstává přibližně 30 % pacientů s CRT tzv. non-respondéry, tedy bez klinického či echokardiografického zlepšení.[2,5,7–17] To vedlo k vývoji nových metod stimulace, sofistikovaných postupů při zavádění elektrod a k rozvoji alternativních strategií, jako je selektivní stimulace převodního systému (conduction

Adresa pro korespondenci: MUDr. Jan Řeháček, Kardiologická klinika, 2. lékařská fakulta Univerzity Karlovy a Fakultní nemocnice Motol a Homolka, pracoviště Motol, V Úvalu 84/1, 150 00 Praha 5, Česká republika, e-mail: jan.rehacek@fnmotol.cz
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Tabulka 1 – Přehled indikací CRT (ESC, 2021)

Třída doporučení	Indikace
I	EF ≤ 35 %, sinusový rytmus, LBBB, QRS ≥ 150 ms, NYHA II–IV
IIa	EF ≤ 35 %, QRS 130–149 ms s LBBB; EF ≤ 35 % s fibrilací síní, pokud lze zajistit vysoké procento stimulace
IIb	EF ≤ 35 %, QRS ≥ 150 ms bez LBBB; EF ≤ 35 %, QRS 130–149 ms bez LBBB s mechanickou dyssynchronií

CRT – srdeční resynchronizační léčba; EF – ejekční frakce; ESC – Evropská kardiologická společnost; LBBB – blokáda levého Tawarova raménka; NYHA – New York Heart Association.

system pacing, CSP), multipoint pacing či algoritmy pro automatickou optimalizaci CRT.[16,18,19]

Cílem této přehledové práce je shrnout současné poznatky o patofyziologii dyssynchronie, standardních i nových přístupech v léčbě, včetně výsledků recentních studií, a nastínit budoucí směry v léčbě pacientů se srdeční dyssynchronií.

Patofyziologie srdeční dyssynchronie

Srdeční dyssynchronie je komplexní fenomén zhoršující průběh srdečního selhání, který se projevuje jak na elektrické, tak na mechanické úrovni. Jde o poruchu načasování a koordinace kontrakce jednotlivých srdečních oddílů vycházející z chybného vedení vzruchu a neefektivní kontrakci komor s regionální dyskinezí. Nejčastější příčinou je LBBB, která způsobuje opožděnou depolarizaci a kontrakci zejména bazálního inferolaterálního segmentu levé komory, v důsledku čehož dochází k paradoxnímu pohybu septa a k maladaptivní remodelaci levé komory.[7,14,20] Patofyziologicky obdobná je dyssynchronie pravé komory spojená s blokádou pravého raménka Tawarova (RBBB).[21]

Elektrická dyssynchronie

Elektrická dyssynchronie je porucha časování aktivace komor daná poruchou vedení vzruchu, a dochází tak ke zpoždění depolarizace v různých částech myokardu.[10,20,22] Rozlišujeme několik typů dyssynchronie: interventrikulární, intraventrikulární a atrioventrikulární.[8,20,22,23] Interventrikulární dyssynchronie je charakterizována vzájemným opožděním aktivace komor, měřitelným na povrchovém EKG. Intraventrikulární dyssynchronie se týká nekoordinované aktivace jednotlivých segmentů levé komory, často přítomné u LBBB.[8,23] Atrioventrikulární (AV) dyssynchronie vzniká při poruše koordinace kontrakce síní a komor.[8,22–24]

Ne vždy platí, že široký komplex QRS na EKG odpovídá skutečné mechanické dyssynchronii. Tento jev, označovaný jako elektrická pseudodyssynchronie, vzniká v situacích, kdy porucha šíření vzruchu vede k prodloužení či atypické morfologii komplexu QRS, avšak mechanická kontrakce komor zůstává relativně synchronní.[14,22,23,25,26] Typickým příkladem jsou nespecifické intraventrikulární poruchy vedení (IVCD) nebo hemibloky, kdy aktivace levé komory není významně opožděna.[8] K pseudodyssynchronii mohou dále přispět i farmakologické vlivy (antiarytmika zpomalující vedení), metabolické a iontové poruchy (např. hyperkalemie) či artefakty EKG záznamu. V klinické praxi je proto nutné hodnotit nejen šířku, ale i morfologii komplexu QRS a doplnit posouzení mechanické synchronie pomocí zobrazovacích nebo pokročilých elektrofyziologických metod (např. echokardiografie se strain analýzou, QRS area nebo ultra-high-frequency EKG). Rozlišení pravé a pseudodyssynchronie je zásadní pro správnou indikaci CRT, protože samotné rozšíření QRS bez typického obrazu LBBB nepředpovídá jednoznačný klinický benefit.[14,22,26]

Mechanická dyssynchronie

Mechanická dyssynchronie představuje bezprostřední funkční důsledek dyssynchronie elektrické. Dochází k paradoxní časné kontrakci septa („septal flash“) a opožděné aktivaci laterální stěny, což se manifestuje jako kývavý pohyb hrotu levé komory („apical rocking“).[10,13,20,27,28] Tyto jevy nejsou pouze echokardiografickým fenoménem, ale odrážejí významnou neefektivitu kontrakce.[27,29] Septum v časné fázi systoly vykonává neefektivní paradoxní pohyb, který nepřispívá k ejekci. Opožděná kontrakce laterální stěny může naopak nastat až po uzávěru aortální chlopně, tedy mimo systolické okno. Výsledkem je ztráta synchronie mezi jednotlivými segmenty, pokles systolické funkce a vzestup enddiastolických tlaků; mechanická dyssynchronie dále narušuje koordinaci uzávěru mitrální chlopně, což vede k funkční mitrální regurgitaci a dalšímu objemovému zatížení levé komory.[20,27,30] Tím vzniká patologický cyklus dilatace, zvýšené náplně, progrese remodelace a zhoršování srdečního selhání.[29,31] Dyssynchronie levé komory se přenáší i na komoru pravou prostřednictvím septa a perikardu. Paradoxní septální pohyb může vést k omezenému plnění pravé komory a k nárůstu tlaků v plicnici. Tento jev, označovaný jako ventrikulární interdependence, ukazuje, že se nejedná pouze o izolovaný problém levé komory.[20,32]

Obecně tedy platí, že mechanická složka dyssynchronie je pro klinický stav pacienta rozhodující, protože přímo ovlivňuje tepový objem, diastolické plnění a vznik sekundární mitrální regurgitace, přispívá ke zhoršení pravostranného srdečního selhání a akceleruje progresi symptomů. Proto se v současnosti více zdůrazňuje její hodnocení v predikci odpovědi na CRT.[27,29,31,33]

Elektromechanická dyssynchronie

Elektromechanická dyssynchronie označuje nesoulad mezi okamžikem elektrické aktivace a mechanické kontrakce. Tento fenomén je zvláště patrný u pacientů s rozsáhlou fibrotickou přestavbou – elektrický impuls dorazí včas, ale svalový stah je opožděný nebo oslabený.[6,20]

Diagnostické metody včetně novinek

Diagnostika zaměřující se výlučně na elektrické nebo na mechanické parametry dyssynchronie vede k chybnému výběru pacientů – v současnosti se proto uplatňuje přístup multiparametrický.[13,28,34] Příkladem zastaralého přístupu jsou programy založené výhradně na echokardiografických markerech, které nepřinesly terapeutický posun.[7,9,25,29,33] Negativní výsledky studií PROSPECT a EchoCRT upozornily na variabilitu metodiky, nízkou reprodukovatelnost i fakt, že u úzkého QRS nemá CRT významný přínos.[26,34,35] Spolehlivější výběr pacientů, kteří budou z léčby profitovat, tedy přináší přístupy zakládající se na kombinaci jasné elektrické dyssynchronie (zejména LBBB), anatomicko-mechanických známek jizvení a pozdní aktivaci. V praxi to znamená začínat EKG, pokračovat zobrazovacími metodami a v některých indikovaných případech i cílenou implantací elektrod podle skutečného průběhu aktivace a přítomnosti jizev.

EKG a elektrická dyssynchronie

Základními EKG parametry jsou šíře a morfologie komplexu QRS.[20,36] U nemocných se srdečním selháním při sinusovém rytmu a ejekční frakci (EF) ≤ 35 % je optimální indikace k CRT reprezentována LBBB se širokým QRS (obvykle ≥ 150 ms).[20,24] Přesnější diagnostická kritéria přinesla upravená Straussova definice (2011), která klade důraz na přesnou identifikaci LBBB a je v současnosti široce přijímána.[24,37] Kromě šířky QRS pracuje i s typickými morfologickými znaky v laterálních svodech a absencí R v pravostranných svodech.[29]

U QRS 130–149 ms s LBBB je pravděpodobnost odpovědi nižší než u QRS ≥ 150 ms, ale stále klinicky smysluplná – zejména pokud další metody (viz níže) hovoří pro pozdní aktivaci laterální stěny a nízký stupeň jizvení v cílové oblasti implantace.[11,35,38–40] Pro selekci těchto pacientů je vhodné doplnění pokročilé elektrografie (UHF-ECG, QRS area) a zobrazovacích metod prokazujících mechanickou dyssynchronii (septal flash, apical rocking).

U non-LBBB morfologie (RBBB, nespecifická IVCD) šance na odpověď klesá a EKG by mělo být také doplněno minimálně echokardiografickým nebo vyšetřením magnetickou rezonancí (MR).[24,41]

QRS area a vektorkardiografie (VCG)

Na úrovni EKG se ukazuje, že šíře QRS není dostatečným prediktorem účinnosti CRT; novější přístupy hodnotí QRS area jako přesnější ukazatel elektrické dyssynchronie. Studie autorů Eerenberg et al. (2024) prokázala, že určení parametru QRS area může zlepšit stratifikaci pacientů, kteří budou mít užitek ze zavedení levokomorové elektrody.[5,6,14,42] Integrální ukazatel QRS area (odvozený z vektorkardiografie nebo zrekonstruovaný z 12svodového záznamu) lépe vystihuje rozsah elektrické dyssynchronie a v řadě studií překonává prostou šířku QRS v predikci reverzní remodelace i klinické odpovědi na CRT. V praxi se QRS area uplatní při výběru pacienta (hraniční šíře QRS či non-LBBB morfologie) a také při plánování místa implantace levostranné elektrody – vyšší QRS area s přetrvávajícími známkami dyssynchronie po implantaci může signalizovat suboptimální umístění nebo potřebu reprogramace.[10,14,24,42–45]

Ultra-high-frequency EKG (UHF EKG)

UHF je relativně nová technologie, která je v současnosti zaváděna do klinické praxe. UHF-EKG rozšiřuje klasické 12svodové EKG do vyšších frekvenčních pásem, a tím dokáže rozlišit jemné rozdíly v časování lokálních aktivací ve stěnách komor. Zachycuje první část depolarizace, a to jen v oblasti přímo snímané daným EKG svodem. Prokazuje se, že UHF-EKG detekuje intraventrikulární zpoždění, které standardní EKG nerozliší a které koreluje s hemodynamickým efektem akutní stimulace a i s dlouhodobou reverzní remodelací. Díky tomu může selektovat pacienty s relativně úzkým komplexem QRS, kteří budou přesto z resynchronizační terapie profitovat. Praktická přidaná hodnota je největší u non-LBBB a hraniční šíře QRS, kde může UHF-EKG zpřesnit, zda jde o skutečnou dyssynchronii, nebo pouze pseudodyssynchronii.[17,19,46,47]

Echokardiografie

Echokardiografie byla dlouho považována za hlavní nástroj detekce mechanické dyssynchronie. Jednoduché morfologické fenomény septal flash a apical rocking jsou snadno reprodukovatelné a dobře detekovatelné markery, které mají solidní prediktivní hodnotu pro odpověď na CRT u LBBB.[5,7,8,13,28,29,34,35] Studie PROSPECT (2008) však ukázala, že jednotlivé echokardiografické parametry, jako např. inter- a intraventrikulární zpoždění nebo tkáňový doppler, mají nízkou reprodukovatelnost a omezenou prediktivní hodnotu.[8] Negativní výsledky studií RETHINQ (2007) a EchoCRT (2013) dále potvrdily, že samotné echokardiografické známky bez přítomnosti širokého QRS nejsou dostačující pro indikaci CRT.[25,26,34] Novější metody, jako je speckle tracking echokardiografie, strain analýza a analýza myokardiální práce, přinášejí přesnější zhodnocení mechanické dyssynchronie.[5,7–9,23,48,49] Kombinace těchto metod umožňuje kvantifikovat regionální zpoždění místo dříve využívaných jednoduchých časových rozdílů. Dnes bývají preferovány pokročilejší metriky, jako jsou čas k vrcholové deformaci v definovaných segmentech, mechanická disperze, regionální „encircling" (označení lokální oblasti) z mapy pozdní aktivace. 3D echokardiografie přidává exaktnější pohled na objemy levé komory (ESV – endsystolický objem, EDV – enddiastolický objem) a přesněji kvantifikuje reverzní remodelaci, což je vhodné zejména pro střednědobé hodnocení účinku terapie.[7,8,23,29] Tkáňový doppler (tissue doppler imaging, TDI) v rukou zkušeného echokardiografisty má stále své místo v diagnostice, ačkoli samostatné hraniční hodnoty se dnes pro samotný výběr pacientů nedoporučují.[5,34] Vhodným využitím je optimalizace a kontrola naprogramovaného spouštění stimulace jednotlivých elektrod.[50,51]

Kardio-MR a CT

Kontrastní MR s pozdním sycením gadoliniem (late gadolinium enhancement, LGE) má význam v rozpoznání a určení rozsahu jizvy. Uplatnění nachází zejména u jizev laterální stěny levé komory – rozsáhlá jizva v cílové oblasti implantace je prediktorem špatné mechanické odpovědi při klasické biventrikulární CRT (BiV-CRT) a MR může pomoci s vytipováním pozice elektrody tak, aby stimulace zasáhla pozdně aktivované a viabilní myokardiální segmenty.[7] Významným faktorem ovlivňujícím

odpověď na CRT se zdá být jizva v oblasti septa.[7,29] Jako alternativu k MR lze použít vyšetření jednofotonovou emisní výpočetní tomografií (SPECT).[8] CT koronárního sinu a jeho přítoků včetně variant, stenóz a vzdálenosti n. phrenicus může být užitečné při plánování přístupu, zkracuje dobu implantace a snižuje riziko suboptimální polohy elektrody, a to zejména u pacientů s anatomickými odchylkami, typicky u pacientů s vrozenými srdečními vadami.[8,21,52–55]

Cílení pomocí elektro-anatomického mapování

Cílené mapování a nalezení oblasti pozdní aktivace, např. měření času od začátku QRS do lokálního ventrikulárního signálu na elektrodě LK (QLV) nebo využití 3D elektro-anatomického mapování prokázalo, že resynchronizace této oblasti myokardu zvyšuje šanci na odpověď, zlepšuje stimulační parametry a snižuje podíl non-respondérů.[5,41,48,56] V randomizovaných a prospektivních studiích se ukázalo, že mapovací systémy mají klinický význam zejména u pacientů s non-LBBB, jizvou anebo po selhání původní resynchronizační terapie.[41,45,56]

Multiparametrický výběr a plánování

Prediktivní hodnota jednotlivých parametrů je omezená a izolované ukazatele mají nízkou reprodukovatelnost i predikční schopnost. Proto je třeba najít jednoduchý postup kombinující jak klinické, tak laboratorní a zobrazovací vyšetření.[7] Nejprve je vhodné pomocí EKG potvrdit LBBB podle přísnějších kritérií a kvantifikovat elektrickou dyssynchronii (QRS area/VCG, případně UHF-EKG u hraničních případů).[24,42,47] Dalším krokem by mělo být echokardiografické zhodnocení fenotypu (septal flash/apical rocking) a ozřejmení případné konzistentní pozdní aktivace. Pomocí MR pak můžeme zmapovat jizvu, abychom se vyhnuli stimulaci jizevnaté tkáně, eventuálně odhalit anatomické odchylky a následně naplánovat výkon.[7,8] V případě non-LBBB morfologie nebo anatomických poměrů znemožňujících optimální stimulaci je metodou volby fyziologická stimulace (LBBAP/HBP).[57] Tato posloupnost je v praxi proveditelná, využívá silné stránky jednotlivých metod, a umožňuje tak lépe identifikovat pacienty, kteří můžou z CRT skutečně profitovat (**tabulka 2**).

Standardní resynchronizační terapie

Biventrikulární stimulace představuje standardní metodu srdeční resynchronizační terapie u pacientů splňujících indikační kritéria. Principem je současná stimulace pravé a levé komory (prostřednictvím elektrody v povodí koronárního sinu). Tento přístup a jeho benefity byly ověřeny v řadě velkých randomizovaných klinických studií, které položily základy dnešní praxe. Klíčová randomizovaná studie CARE-HF prokázala, že CRT u pacientů se symptomatickým srdečním selháním a LBBB významně snižuje mortalitu a morbiditu oproti optimální farmakoterapii.[3,6,58,59] Podobně studie COMPANION (Bristow et al., 2004) ukázala redukci rizika úmrtí a hospitalizací při přidání CRT k farmakologické léčbě.[3,16,60] Tyto výsledky potvrdily CRT jako metodu schopnou zásadně měnit prognózu nemocných.

Rozšíření indikací přinesly studie jako MADIT-CRT (Moss et al., 2009), RAFT (Tang et al., 2010) nebo REVERSE (2008), které ukázaly přínos CRT (snížení cílového ukazatele složeného z úmrtí a hospitalizací pro srdeční selhání) i u pacientů s mírnější symptomatikou (NYHA II) a širším QRS.[31,33,40,59,61,62] CRT se tak stala nejen léčbou poslední linie, ale i metodou schopnou zbrzdit progresi remodelace a zlepšit klinický stav v časnějších fázích onemocnění.[33,34,40,61,63]

Naopak studie RETHINQ a EchoCRT ukázaly, že u pacientů s úzkým QRS (< 130 ms) či bez průkazu jasné mechanické dyssynchronie není CRT přínosem, a může být dokonce škodlivá – studie byly předčasně ukončeny pro vyšší mortalitu u pacientů s CRT.[25,26] Tyto výsledky vedly k zásadnímu vymezení indikačních kritérií, která dnes zdůrazňují přítomnost blokády levého Tawarova raménka a šíři QRS ≥ 150 ms jako nejsilnější prediktory odpovědi na CRT.[5,6,24,32,39] CRT je také preferována u pacientů s HFrEF a indikací k trvalé stimulaci pro AV blokádu. Tito pacienti mají očekávané vysoké procento stimulace a jsou ve vyšším riziku stimulací indukované kardiomyopatie.[3–5,13,46] BLOCK-HF a následné práce podporují časné zvažování CRT nebo CSP, abychom minimalizovali riziko iatrogenní dyssynchronie.[46]

Přes jednoznačný přínos konvenční CRT zůstává její účinnost omezená. Přibližně 30–40 % pacientů nere-

Tabulka 2 – Multiparametrický výběr a plánování

Kroky	Způsob
Kombinovat základní informace	Klinika + laboratorní + zobrazovací metody
Potvrdit elektrickou dyssynchronii	Dvanáctisvodové EKG s přísnými kritérii LBBB; kvantifikace QRS area/VCG; u hraničních případů UHF-EKG
Zhodnotit mechanickou dyssynchronii	Echokardiografický fenotyp: **septal flash** / **apical rocking**; ověřit konzistentní pozdní aktivaci
Zmapovat jizvu a anatomii u rizikových pacientů	**MR**: lokalizace/rozsah jizvy, anatomické odchylky
Zvolit stimulační strategii	Typické LBBB → cílená BiV/LBBAP; **non-LBBB**/nevýhodná anatomie → **CSP (LBBAP/HBP)**
Implantace a následná optimalizace nastavení	Implantace dle plánu; kontrola QRS/echokardiografie/klinika; úprava programování dle nálezu

BiV – biventrikulární; CSP – stimulace převodního systému; HBP – His bundle pacing; LBBAP – left bundle branch area pacing; LBBB – blokáda levého Tawarova raménka; MR – magnetická rezonance; VCG – vektorkardiografie.

aguje na terapii, a to i přes splnění indikačních kritérií.[3,15,18,29,30,40,59] K příčinám patří nepříznivá anatomie koronárního sinu, jizvy v oblasti stimulace, suboptimální poloha levostranné elektrody, komorbidity nebo přítomnost fibrilace síní.[48,55,64,65] Technickými komplikacemi jsou obtíže při zavádění elektrody, její dislokace, stimulace bránice či vysoké prahové hodnoty. Periprocedurální komplikace (infekce v ráně, iatrogenní pneumotorax a žilní trombózy) představují další rizika, která je nutné při implantaci zohlednit.[12,15,26,40,46]

Nové přístupy v resynchronizační terapii

Stimulace levé komory (LV-only pacing)

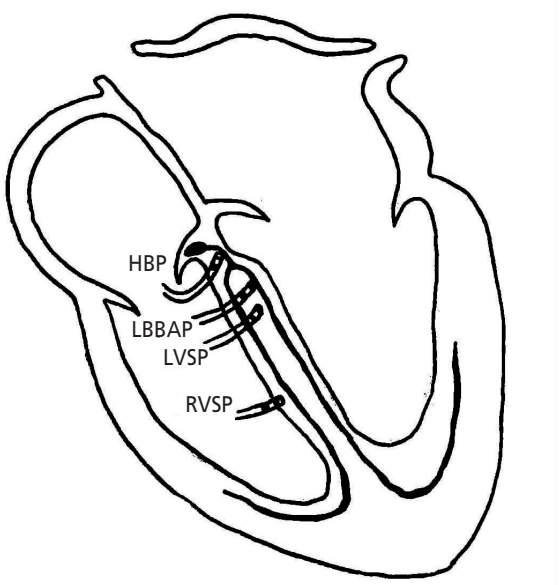
Stimulace levé komory ve fúzi s nativním převodem (LV-only pacing, LVO) představuje alternativní strategii k tradiční BiV. Principem je dosažení resynchronizace pomocí současné stimulace pozdně aktivovaných částí levé komory a zachování fyziologické aktivace pravé komory nativním převodním systémem. Dochází tak k částečné korekci dyssynchronie a k zachování elektrické i mechanické integrity kontrakce pravé komory. Tato metoda je teoreticky vhodná zejména u pacientů s intaktním atrioventrikulárním (AV) vedením, s izolovanou blokádou levého Tawarova raménka a relativně zachovanou funkcí pravé komory. První klinické studie ukázaly, že LV-only pacing může vést ke zlepšení ejekční frakce levé komory (EF LK), klinických symptomů i parametrů remodelace srovnatelnému s BiV.[66] Významnou výhodou LVO je i nižší spotřeba energie přístroje, což může prodloužit životnost baterie a snížit počet reintervencí. Na druhou stranu tato metoda vyžaduje velmi pečlivý výběr pacientů a precizní nastavení AV intervalů, aby nedocházelo ke ztrátě synchronie nebo k abnormální aktivaci. Limitací je také menší množství dat z velkých multicentrických studií; dosud publikované práce zahrnují spíše menší soubory pacientů a kratší doby sledování.[57] V současných doporučeních Evropské kardiologické společnosti (ESC) ani HRS není LV-only pacing standardní volbou první linie. Je však ke zvážení v individuálních případech, zejména u pacientů s neuspokojivou odpovědí na biventrikulární stimulaci, nebo u těch, kde je dosažení resynchronizace cestou LVO technicky jednodušší a bezpečnější. Do budoucna může LV-only pacing hrát větší roli v kombinaci s pokročilými algoritmy automatické optimalizace AV synchronie.[50,67,68]

Stimulace převodního systému

Fyziologická stimulace převodního systému (conduction system pacing, CSP) se etablovala jako nadějná alternativa BiV-CRT.[2,11,18,19,39,46,57,69,70] Cílem je dosažení co nejfyziologičtější aktivace komor, a tím zajištění optimální elektrické i mechanické synchronie.[2,36] Hlavními metodami CSP jsou HBP, LVSP a LBBAP, která je z těchto metod nejpoužívanější.[1,71] Rozdíly v pozici elektrody ukazuje **obrázek 1**.

His bundle pacing (HBP)

His bundle pacing využívá implantaci elektrody přímo do oblasti Hisova svazku, tedy místa, kde se převodní systém fyziologicky dělí na Tawarova raménka.[19,46,70,72,73] Výhodou je zcela fyziologická aktivace obou komor s prokazatelným zlepšením hemodynamických parametrů a reverzní remodelace u vybraných pacientů.[2,71] Randomizované i observační studie ukázaly významné zlepšení EF LK, zmírnění symptomů a snížení počtu hospitalizací pro srdeční selhání.[19,70,72–74] Limitací však zůstává technická náročnost, relativně nízká úspěšnost implantace (70–85 %), vysoké stimulační prahy a vyšší riziko dislokace elektrody.[19,46,72,73] Přesto se tato metoda uplatňuje zejména u pacientů s AV blokádou a zachovaným distálním vedením nebo jako součást hybridních přístupů (HOT-CRT).[70,75]

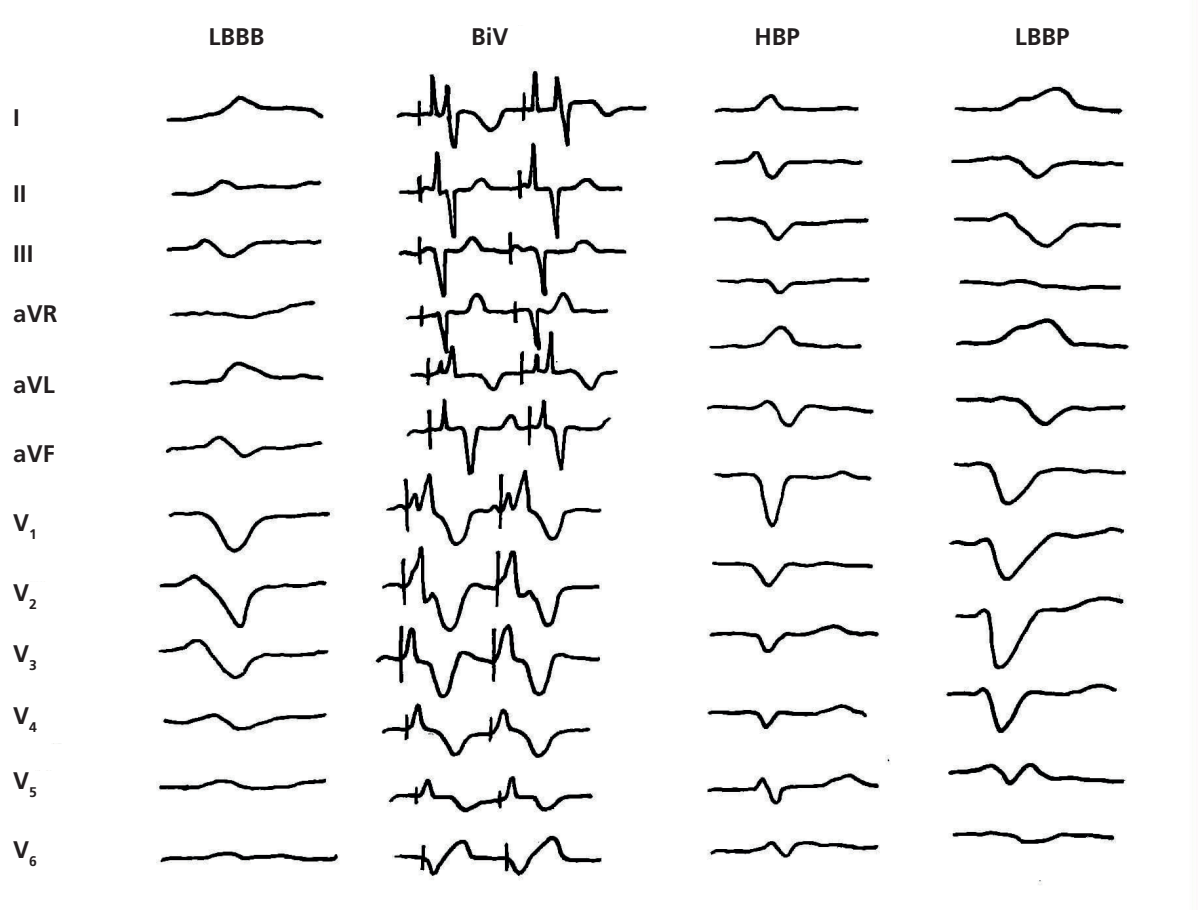


Obr. 1 – Pozice stimulačních elektrod u CSP
HBP – His bundle pacing; LBBAP – left bundle branch area pacing; LVSP – left ventricular septal pacing; RVSP – right ventricular septal pacing.

Left bundle branch area pacing (LBBAP)

LBBAP představuje v současnosti nejdynamičtěji se rozvíjející metodu CSP. Elektroda je zaváděna transvenózně přes interventrikulární septum až do oblasti levého Tawarova raménka. Implantace se provádí cíleným šroubováním elektrody z oblasti septa PK směrem k levé komoře do subendokardiální oblasti.[11,18,19,46,59,76,77] Kritéria úspěšné implantace zahrnují charakteristickou změnu morfologie QRS – přechod k vzoru RBBB, qR v aVL, r' ve V_1 (podrobněji **obr. 2**), měření stimulačně-ventrikulárního intervalu (stimulus–LV interval < 80 ms), selektivní zachycení LBB s viditelnou Hisovou–Purkyňovou aktivací na intrakardiálních záznamech a ev. doplňkově UHF-ECG pro detailní mapování průběhu depolarizace.[17,19,46,47,78,79] Speciální pozornost si zaslouží využití LBBAP u ischemické kardiomyopatie, kde výsledky ukazují zlepšení mechanické synchronie i navzdory jizvám.[11,65,78] U RBBB a nespecifické IVCD je výběr pacientů vhodných pro BiV obtížnější, často se jedná o pacienty s vrozenými srdečními vadami a po operacích.[41,52,54] Nejlepších výsledků v této subpopulaci dosahuje LBBAP v centrech, kde je metoda již etablována.[17,36,54]

Úspěšnost implantace se ve velkých sériích pohybuje nad 90 %.[17,32,46,80,81] S implantací LBBAP se objevuje i pojem deep septal pacing (DSP). Je to typ stimulace, který nejčastěji vznikne při nedostatečně hluboko zavedené elektrodě nebo její suboptimální pozici. Často udávaná procenta



Obr. 2 – Morfologie EKG
BiV – biventrikulární; HBP – His bundle pacing; LBBAP – left bundle branch area pacing; LBBB – blokáda levého Tawarova raménka.

úspěšnosti implantace LBBAP jsou dohromady a „pravého" LBBAP se dosahuje v cca 60 % implantací.[17] LBBAP vykazuje nízké stimulační prahy (< 1 V u většiny pacientů), stabilní parametry při dlouhodobém sledování a nižší výskyt dislokací než HBP. Randomizovaná studie LBBP-RESYNC prokázala, že LBBAP vede k větší redukci ESV LK, zlepšení mechanické synchronie a markantnějšímu zlepšení EF než BiV-CRT u pacientů s typickým LBBB.[2,11,16,59,69,75–78,82] Na rozdíl od BiV stimulace není nutné hledat vhodnou větev koronárního sinu; další výhodu představují nižší energetické nároky, a tím i menší počet potenciálních reintervencí. Mezinárodní registry potvrzují konzistentní výsledky s průměrným nárůstem EF o 10–15 % a snížením hospitalizací pro srdeční selhání o 30–40 %.[11,16,42,59,69,75,82] Dlouhodobá data (3–5 let) ukazují stabilní stimulační parametry bez významného nárůstu počtu komplikací.[11,72,76,76,82] Nevýhodami jsou menší počet velkých multicentrických randomizovaných studií, nedostatečná standardizace diagnostických kritérií (selektivní vs. neselektivní zachycení LBB), možné prodloužení aktivačního času pravé komory a pro tuto metodu specifické komplikace jako zvýšené riziko perforace septa či poškození koronární arterie s incidencí udávanou do 3 %.[2,5,59,69,71,82]

Left ventricular septal pacing (LVSP)

LVSP je koncepčně blízký LBBAP, elektroda je zavedena do interventrikulárního septa tak, aby stimulovala levokomorovou svalovinu blízko systému Tawarových ramének.[19,70,79] Výsledkem je aktivace myokardu fyziologičtější cestou než při klasickém biventrikulárním pacingu. Experimentální a časné klinické studie (např. Rijks et al., 2022) ukázaly, že LVSP zajišťuje kratší dobu od stimulu k aktivaci levé komory a také příznivější vektor křivky QRS než BiV.[43,79,83] Výhodou oproti LBBAP je jednodušší, méně hluboké zavedení, menší riziko perforace a lepší možnost přestavby na klasickou BiV CRT. Nevýhodou je zatím omezený počet klinických studií s absencí studií randomizovaných a ne zcela jasná dlouhodobá stabilita prahů.[40,70,75]

Left bundle branch optimized CRT (LOT-CRT)

LOT-CRT kombinuje výhody LBBAP a klasické stimulace LK z koronárního sinu.[32,76,81,82,84] Typicky je elektroda umístěna v oblasti levého Tawarova raménka a současně se ponechává elektroda LK, čímž vzniká možnost duální stimulace. Cílem je dosáhnout lepší synchronie u non-respondérů klasické CRT, pacientů s rozsáhlými jizvami nebo s atypickou aktivací LK. Z klinických dat vyplývá vyšší míra reverzní remodelace a výraznější zlepšení EF oproti samotnému BiV pacingu.[75,84] Některé menší studie ukazují potenciál i u pacientů, u kterých nebylo dosaženo optimální LBBAP (např. DSP či QRS přes 171 ms) nebo kteří na ni nereagují.[32,75,81] LOT-CRT se tedy jeví jako slibná cesta pro obtížně léčitelné pacienty.

His optimized CRT (HOT-CRT)

HOT-CRT představuje kombinovaný přístup, kdy se elektroda umisťuje jako HBP s doplněním laterální elektrody LK. Cílem je využití fyziologické aktivace přes Hisův–Purkyňův systém a současně zlepšení synchronie stimulací laterální stěny LK. HOT-CRT vede k významnému zkrácení QRS a zlepšení EF ve srovnání s konvenční BiV stimulací u obtížně léčitelných pacientů.[70,75] Uplatnění najde především u pacientů, u nichž samotný HBP nestačí k dosažení kompletní korekce dyssynchronie.[72,73]

Multipoint pacing (MPP)

MPP rozšiřuje konvenční BiV stimulaci – levá komora je stimulována současně nebo téměř současně ze dvou a více míst na jedné multikontaktní elektrodě v koronárním sinu.[15] Cílem je aktivace většího objemu myokardu, zkrácení doby elektrické aktivace a dosažení homogennější depolarizace. Hlavní skupinou pacientů profitující z této metody jsou ti s jizvou v oblasti LK. Klinické studie, zejména MORE-CRT MPP trial (2019), ukázaly, že tato strategie může podpořit reverzní remodelaci a zlepšit funkční stav u pacientů, kteří nereagují na standardní CRT.[23,75] Na druhou stranu je metoda zatížena vyšší spotřebou energie, což může vést ke zkrácení životnosti baterie, a výsledky v různých studiích jsou nejednotné.[15] V současnosti je proto MPP považován spíše za záchrannou strategii pro non-respondéry než za univerzální metodu první volby.

Nové technologie a strategie v CRT

Umělá inteligence (AI) a prediktivní modely

Rozvoj umělé inteligence umožňuje integrovat data z EKG, echokardiografie, laboratorních parametrů a klinického stavu pacienta, díky čemuž můžeme přesněji předpovídat odpověď na CRT. Některé práce ukazují, že multiparametrické modely založené na AI dokážou snížit podíl non-respondérů až o třetinu.[10,22,50] Umělá inteligence má potenciál i v optimalizaci programování AV/VV intervalů, kde by mohla nahradit manuální echokardiografické metody.[15,50,51,67] Přetrvává ale nutnost vytvořit rozsáhlé a validované databáze a zajistit transparentnost algoritmů. Navzdory snaze o její implementaci zatím chybějí dlouhodobé důkazy její prospěšnosti při rutinním nasazení.[51]

3D mapování a cílené umístění elektrod

Využitím echokardiografického navádění elektrody při (re)implantaci můžeme dosáhnout dodatečného klinického přínosu.[5,41,45,56,62,63] Pokročilé zobrazovací modality (3D echokardiografie, MR, speckle-tracking echokardiografie) umožňují předem lokalizovat optimální místo implantace LK elektrody.[8,23,48,49,56,62] Implantace elektrody do nejvíce opožděného segmentu zlepšuje klinické výsledky a reverzní remodelaci.[15,23,41,45,48,55,56,62,63] K přesnějšímu určení elektrické dyssynchronie a vedení implantace můžeme také využít parametru QRS area a UHF EKG.[10,42,45,47] Tyto parametry mají vyšší prediktivní hodnotu než samotná šířka QRS a umožní také odhalit nejvíce opožděný segment.[8,10,22]

Nové generace přístrojů a senzory

Vývoj CRT přístrojů směřuje k postupné miniaturizaci. Inovace jako multipoint pacing či použití nových kvadripolárních elektrod zlepšily dosah stimulace v určitých oblastech LK. Algoritmy typu Adaptive CRT automaticky přizpůsobují AV a VV intervaly aktuálním potřebám pacienta, čímž zvyšují efektivitu terapie a snižují riziko hospitalizací.[67,68] Novinkou jsou také hemodynamické monitory, které pomáhají hodnotit úspěšnost terapie, a mohou tak předejít dekompenzacím srdečního selhání.[30,31,44,85,86]

Strategie u non-respondérů

Navzdory významnému klinickému přínosu metody zůstává přibližně 30 % pacientů po implantaci CRT tzv. non-respondéry, tedy bez výrazného zlepšení symptomů, EF LK, reverzní modelace nebo prognózy.[2,5,7,8,10,13,15,17,28] Identifikace těchto pacientů a terapeutický přístup k nim představuje zásadní výzvu současné praxe. Selhání terapie u této skupiny má multifaktoriální příčiny – od nesprávné indikace a suboptimální implantace elektrod např. v místě jizvy přes komorbidity až po nevhodné nastavení přístroje.[7,41,45,55,62,63] Patofyziologicky může jít o situace, kdy elektrická resynchronizace nevede k mechanické nebo kdy přítomná jizva znemožňuje účinnou aktivaci myokardu.[29] Mezi nejčastější prediktory špatné či chybějící odpovědi patří neúplná blokáda levého Tawarova raménka, přítomnost rozsáhlé jizvy v posterolaterální oblasti levé komory, perzistující fibrilace síní, suboptimální polohování elektrod a také špatná adherence k léčbě srdečního selhání.[31,63,64] Prvním krokem bývá optimalizace programování přístroje. Jednou z možností je úprava AV a VV intervalů s využitím echokardiografie nebo pokročilých algoritmů automatické adaptace.[23,50,51,55,68] Druhou možností je změna typu stimulace – např. pacienti s anodovou bipolární LBBAP typicky dosahují menšího zlepšení systolické funkce LK než pacienti s unipolární LBBAP.[15,32] Pokud tato opatření nevedou ke zlepšení, přistupuje se k pokročilejším strategiím – např. hybridní stimulaci kombinující klasickou BiV s CSP.[17] Koncept LOT-CRT nebo kombinace BiV a LBBAP prokazují nadějné výsledky zejména u pacientů s rozsáhlou jizvou nebo atypickou anatomií, kde konvenční elektroda LK není schopna zajistit dostatečnou resynchronizaci.[46,84] Zásadní význam má rovněž reimplantace levokomorové elektrody.[45,53] Studie ENHANCE-CRT (2018) ukázala, že u non-respondérů může echokardiograficky nebo elektroanatomicky naváděné umístění elektrody vést k významnému zlepšení klinických parametrů a reverzní remodelace.[5,13,23,29,41,48] Tento postup je technicky náročný, ale v centrech s dostatečnými zkušenostmi stále častěji využívaný.

U fibrilace síní (zejména s rychlou odpovědí komor) mechanické známky dyssynchronie ztrácejí výpovědní hodnotu. K zajištění vysokého procenta stimulace a stabilního resynchronizačního efektu je důležitá úspěšná rate/rhytm control léčba fibrilace síní. Obnovením a udržením sinusového rytmu nebo ablací AV junkce (vedoucí ke 100% stimulovanému rytmu) dosáhneme významného snížení mortality a hospitalizací pro srdeční selhání ve srovnání s farmakologickou kontrolou frekvence.[5,39,64,74,87]

V souhrnu lze říci, že u non-respondérů by měla být vždy provedena komplexní revize stimulační strategie – od optimalizace nastavení přes reimplantaci elektrod až po využití inovativních kombinovaných invazivních postupů. Tato personalizovaná strategie může vést k významné redukci podílu non-respondérů a je doporučena zejména

Tabulka 3 – Algoritmus přístupu k non-respondérům, ověření správnosti indikace a přítomnosti skutečné elektrické a mechanické dyssynchronie
1. Optimalizace programování přístroje včetně využití automatických algoritmů.
2. Revize polohy LK elektrody – pokud je nevhodná, zvážit repozici.
3. U pacientů s fibrilací síní zvážení ablace AVJ k dosažení 100% stimulace nebo izolace plicních žil.
4. U vysoce symptomatických nemocných, kde výše uvedené kroky selhávají, zvážení alternativních přístupů (HOT-CRT, LOT-CRT, LBBAP).

AVJ – atrioventrikulární junkce; HOT-CRT – His optimized CRT; LBBAP – left bundle branch area pacing; LK – levokomorový; LOT--CRT – left bundle branch optimized CRT (LOT-CRT).

u pacientů se složitou klinickou situací, kde selhává konvenční přístup. Toto je shrnuto v **tabulce 3**.

Závěr

Resynchronizační terapie prochází rychlým vývojem od prostého hodnocení šířky QRS a klasické BiV k pokročilejším a složitějším strategiím léčby a diagnostiky. Dnešní diagnostické metody využívají specializovanější nástroje kvantifikace elektrické a mechanické dyssynchronie v kombinaci s EKG a zobrazovacími metodami. V terapii se uplatňuje elektrogramem řízená implantace elektrod, CSP a nové možnosti programování přístrojů. Tyto moderní metody možná sníží podíl non-respondérů a zlepší klinické výsledky CRT.

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1. Repatha (evolokumab), Souhrn údajů o přípravku. 2. Mach F, et al. Eur Heart J. 2020;41(1):111-188. 3. Sabatine MS, et al. N Engl J Med. 2017;376(18):1713-1722.
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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 140 mg evolokumabu 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. U dospělých s prokázaným aterosklerotickým kardiovaskulárním onemocněním nebo s vysokým rizikem jeho rozvoje 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 pediatričtí pacienti (ve věku 10 let a starší). 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 aferéze mohou zahájit léčbu dávkou 420 mg 1x za 2 týdny, aby toto schéma odpovídalo cyklu aferézy. **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. **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 kojené novorozence/kojence 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 nasopharyngitis (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 uchovávání:** 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:** 21. srpna 2026.
Před předepsáním přípravku se, prosím, seznamte s úplným zněním Souhrnu údajů o přípravku. Výdej léčivého přípravku je vázán na lékařský předpis. Přípravek je hrazen z prostředků veřejného zdravotního pojištění u pacientů s heterozygotní familiární hypercholesterolemií nebo u pacientů s nefamiliární hypercholesterolemií či smíšenou dyslipidemií ve velmi vysokém kardiovaskulárním riziku s manifestním kardiovaskulárním onemocněním.
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Přehledový článek | Review article

Beyond the Classic Genes: Rare Variants, Phenocopies, and Polygenic Architecture in Familial Hypercholesterolemia

Kristina Zubieliene[a], Simona Berontaite[b], Diana Zaliaduonyte[b], Ieva Aleknaite[c], Vytautas Zabiela[b]

[a] *Kaunas Hospital of the Lithuanian University of Health Sciences, Kaunas, Lithuania*
[b] *Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania*
[c] *Lithuanian University of Health Sciences, Kaunas, Lithuania*

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SOUHRN

Familiární hypercholesterolemie (FH) je častá dědičná porucha metabolismu lipidů, pro niž jsou charakteristické výrazně zvýšené hodnoty cholesterolu lipoproteinů o nízké hustotě (low-density lipoprotein cholesterol, LDL-C) a zvýšené riziko předčasného rozvoje aterosklerotické kardiovaskulární nemoci. Familiární hypercholesterolemie se tradičně považuje za monogenní poruchu způsobenou patogenními variantami v klasických genech *LDLR*, *APOB* nebo PCSK9, které naruší dráhu receptorů pro LDL a odstraňování částic LDL v játrech. U značného procenta pacientů splňujících klinická diagnostická kritéria FH však patogenní varianty uvedených genů nejsou přítomny, což ukazuje na složitější genetickou architekturu. Pokrok zaznamenaný v poslední době v oblasti sekvenování nové generace (next-generation sequencing, NGS) a stanovení polygenního rizika rozšířil poznání genetiky FH. U pacientů bez mutací mohou být zvýšené hodnoty LDL-C důsledkem polygenní hypercholesterolemie, kdy kumulativní účinek několika častých variant přispívá k výslednému fenotypu. Kromě toho může několik vzácných genů vytvořit FH-like fenotyp nebo působit jako fenokopie. Do této skupiny patří *LIPA*, *ABCG5/ABCG8*, *APOE* a *LDLRAP*1, které ovlivňují metabolismus lipidů prostřednictvím různých molekulárních mechanismů. Úloha *STAP1* je i nadále sporná, přičemž současné důkazy napovídají, že pravděpodobně nepředstavuje kauzální gen pro FH. Tento přehled shrnuje podíl vzácných variant, fenokopií a polygenní architektury na klinických projevech FH. Rozšíření panelů pro genetické testování a stanovení skóre polygenního rizika může zvýšit diagnostickou přesnost a zajistit individualizovanější léčbu pacientů s těžkou hypercholesterolemií a péči o ně.

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ABSTRACT

Familial hypercholesterolemia (FH) is a common inherited lipid disorder characterized by markedly elevated low-density lipoprotein cholesterol (LDL-C) levels and an increased risk of premature atherosclerotic cardiovascular disease. Traditionally, FH has been considered a monogenic disorder caused by pathogenic variants in the classical genes *LDLR*, *APOB*, or *PCSK9*, which disrupt the LDL receptor pathway and impair hepatic clearance of LDL particles. However, a substantial proportion of patients fulfilling clinical diagnostic criteria for FH do not carry pathogenic variants in these genes, indicating a more complex genetic architecture. Recent advances in next-generation sequencing (NGS) and polygenic risk assessment have broadened the understanding of FH genetics. In mutation-negative patients, elevated LDL-C levels may result from polygenic hypercholesterolemia, where the cumulative effect of multiple common variants contributes to the phenotype. In addition, several rare genes may cause FH-like phenotypes or act as phenocopies. These include *LIPA*, *ABCG5/ABCG8*, *APOE*, and *LDLRAP1*, which affect lipid metabolism through distinct molecular mechanisms. The role of STAP1 remains controversial, with current evidence suggesting it is unlikely to represent a causal FH gene. This review summarizes the contribution of rare variants, phenocopies, and polygenic architecture to the clinical presentation of FH. Expanding genetic testing panels and integrating polygenic risk scores may improve diagnostic accuracy and facilitate more personalized management of patients with severe hypercholesterolemia.

Address: Simona Berontaite, Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania
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Familial hypercholesterolemia (FH) is a genetically inherited disorder characterized by markedly elevated low-density lipoprotein cholesterol (LDL-C) levels and a high risk of premature atherosclerotic cardiovascular disease. FH is a primary disorder of lipoprotein metabolism caused by defects in the LDL receptor pathway, leading to impaired hepatic clearance of LDL particles and progressive cholesterol accumulation within the arterial wall.

The pathogenesis of FH centers on the LDL receptor-mediated endocytic pathway. Under normal conditions, LDL particles bind to the LDL receptor (LDLR) via apolipoprotein B-100, are internalized with the help of adaptor proteins, and degraded in lysosomes, releasing cholesterol for cellular use. Proprotein convertase subtilisin/kexin type 9 (PCSK9) regulates this process by promoting LDLR degradation. Pathogenic variants disrupting LDLR, APOB, or PCSK9 reduce LDL clearance and result in persistently elevated plasma LDL-C, accelerated atherosclerosis, and early coronary artery disease.[1]

Traditionally, FH has been considered a monogenic disorder, in which a pathogenic variant in a single gene disrupts the LDL receptor pathway. The majority of genetically confirmed cases are caused by variants in the classical FH genes *LDLR*, *APOB*, and *PCSK9*, which together account for approximately 60–80% of molecularly diagnosed FH patients.[2,3] However, a substantial proportion of individuals who meet the clinical criteria for FH do not carry pathogenic variants in these genes. In such cases, elevated LDL-C levels may result from a polygenic architecture, in which the cumulative effect of multiple common LDL-C – raising variants contributes to the phenotype. These variants individually exert modest effects but may collectively increase LDL-C concentrations, particularly when combined with environmental factors such as diet, obesity, or metabolic conditions.[2,3] This model is often referred to as polygenic hypercholesterolemia and may explain a considerable proportion of mutation – negative FH cases.

Another important diagnostic category includes phenocopies, which are genetic disorders that mimic the clinical presentation of FH but arise from different molecular mechanisms. Examples include conditions caused by pathogenic variants in genes such as *LIPA*, *ABCG5/ABCG8*, or *LDLRAP1*. These disorders may present with markedly elevated LDL-C levels, tendon xanthomas, and premature atherosclerosis, making them clinically indistinguishable from FH without genetic testing.[2,4,5] Identifying such phenocopies is clinically important because their underlying pathophysiology and optimal management strategies may differ from those of classical FH.

In patients who fulfil clinical diagnostic criteria for FH but lack pathogenic variants in the major FH genes, polygenic risk scores (PRS) have emerged as a useful tool for assessing the cumulative contribution of multiple LDL-C – associated genetic variants. PRS can help differentiate polygenic hypercholesterolemia from monogenic FH and improve diagnostic interpretation in mutation-negative individuals.[3] The integration of expanded next-generation sequencing (NGS) panels and polygenic risk assessment therefore represents an important step toward more precise molecular diagnosis.

Taken together, these findings indicate that FH should be viewed as a genetically heterogeneous condition, encompassing monogenic disease, polygenic hypercholesterolemia, and phenocopies. In this manuscript, we review several less common genes that may contribute to FH – like phenotypes or modify LDL-C levels, including *STAP1, LIPA, ABCG5/ABCG8, APOE,* and *LDLRAP1*.

STAP1 (Signal Transducing Adaptor Family Member 1)

The association between *STAP1* and FH remains controversial, with conflicting findings across published studies. In 2014, Fouchier et al. identified *STAP1* as a potential fourth autosomal dominant hypercholesterolemia (ADH) gene in patients lacking mutations in LDLR, APOB, and PCSK9.[6] Four missense variants (p. Glu97Asp, p. Leu69Ser, p. Ile71Thr, p. Asp207Asn) were identified in patients with hypercholesterolemia. Variant carriers exhibited elevated total and LDL cholesterol, although levels were generally lower than in carriers of classical FH mutations. However, subsequent studies did not confirm cosegregation between STAP1 variants and hypercholesterolemia. Lamiquiz–Moneo et al. found no consistent association between genotype and LDL-C levels in seven families with predicted pathogenic STAP1 variants.[7] Some carriers had normal LDL-C, while some non-carriers displayed hypercholesterolemia. Mohebi et al. similarly reported a known *STAP1* variant (p. D207N) that did not segregate with the phenotype.[8] Due to the lack of robust evidence, several authors have recommended excluding *STAP1* from FH diagnostic panels. Early observations suggested a possible role in mild FH, but larger studies and family-based analyses do not support *STAP1* as a causative FH gene. Current evidence suggests that *STAP1* is unlikely to represent a causal FH gene and may instead act as a genetic modifier influencing lipid levels.

LIPA (Lysosomal Acid Lipase A)

LIPA is not a primary FH gene but plays an important role as an FH phenocopy. Biallelic pathogenic mutations in *LIPA* cause cholesteryl ester storage disease (CESD), a rare autosomal recessive disorder characterised by elevated LDL-C, hepatomegaly, abnormal liver function, progressive atherosclerosis, and early cardiovascular disease. CESD may closely resemble heterozygous FH, leading to potential misdiagnosis.[4,5] Several studies, including the Portuguese FH Study, have reported that a subset of FH-negative patients (those without LDLR, APOB, or PCSK9 mutations) carry *LIPA* variants, underscoring its relevance as a phenocopy gene.[2,4] As a result, *LIPA* is routinely included in expanded NGS panels for FH.[2,5] Although *LIPA* mutations account for only a small proportion of FH – negative cases (approximately 1–2% in some cohorts), identifying CESD is clinically important because management differs from classic FH. Thus, LIPA contributes to enhanced diagnostic precision and avoids misclassification.

ABCG5 and ABCG8 (ATP-binding cassette transporters)

ABCG5 and *ABCG8* encode sterol transporters involved in the absorption and excretion of plant sterols and cholesterol. Biallelic mutations in either gene cause sitosterolemia, an autosomal recessive disorder presenting with very high LDL-C, elevated plant sterols (e. g., sitosterol, campesterol), tendon xanthomas, and premature coronary artery disease.[9,10] Even heterozygous carriers may show modest LDL-C elevation. Several studies have reported that 1.5–2.4% of FH cohorts carry pathogenic variants in *ABCG5* or *ABCG8*.[4,10] These variants may appear alone or alongside classical FH mutations, resulting in oligogenic FH, where combined variants worsen the lipid profile.[9] Because clinical criteria alone may misclassify sitosterolemia as FH (especially in children), *ABCG5/ABCG8* are now standard components of expanded NGS panels. Distinguishing FH from sitosterolemia is essential because statins are often less effective in sitosterolemia, whereas dietary modification and ezetimibe have greater impact.[2,5]

APOE (Apolipoprotein E)

APOE plays a key role in the clearance of triglyceride-rich lipoproteins (VLDL, IDL, remnants) via interactions with LDLR and related receptors. It has three common isoforms: *ApoE2* – reduced receptor binding, associated with type III hyperlipoproteinemia, *ApoE3* – neutral, *ApoE4* – associated with higher LDL-C and increased cardiovascular risk.[11] Rare *APOE* variants can cause autosomal dominant hypercholesterolemia. The p. Leu167del variant accounts for ~3% of LDLR/APOB/PCSK9-negative ADH cases and causes LDLR downregulation by altering VLDL structure.[12] Common *APOE* isoforms, while not causal for FH, may modify the FH phenotype. For example, *APOE4* is associated with a modest LDL-C increase, while *APOE2* is linked to lower LDL-C but predisposes homozygotes to type III hyperlipoproteinemia under certain metabolic conditions.[11] *APOE* variants account for ~1–3% of mutation-negative FH cases.[5,12] Including *APOE* in NGS panels therefore improves diagnostic yield in patients with an FH phenotype but no mutations in the major FH genes.

LDLRAP1 (Low-Density Lipoprotein Receptor Adaptor Protein 1)

LDLRAP1 is essential for receptor-mediated endocytosis of LDL particles. Mutations in this gene cause autosomal recessive hypercholesterolemia (ARH), a condition that clinically resembles homozygous FH but differs in inheritance and molecular pathophysiology.[13,14] *LDLRAP1* encodes an adaptor protein required for internalising the LDL–LDLR complex via clathrin-coated pits. Mutations disrupt this process, impairing LDL clearance and leading to markedly elevated LDL-C, early atherosclerosis, and tendon xanthomas. ARH typically presents in childhood or adolescence and should be suspected in severe FH cases without mutations in LDLR, APOB, or PCSK9, particularly in families with parental consanguinity or multiple affected siblings.[3,13] Although rare globally, LDLRAP1 variants are identified in some mutation – negative FH patients through expanded NGS panels.[2,5] For this reason, *LDLRAP1* is included among rare genes associated with FH-like phenotypes.

Conclusion

FH is increasingly recognized as a genetically heterogeneous disorder rather than a purely monogenic condition. Although pathogenic variants in *LDLR, APOB,* and *PCSK9* account for most molecularly confirmed cases, many patients with a clinical FH phenotype remain mutation-negative. In these individuals, elevated LDL-C levels may result from polygenic hypercholesterolemia, oligogenic interactions, or genetic phenocopies. Rare genes such as *STAP1, LIPA, ABCG5/ABCG8, APOE,* and *LDLRAP1* may contribute to FH-like phenotypes through different mechanisms affecting lipid metabolism. Advances in NGS and polygenic risk assessment improve diagnostic accuracy and support more personalized management of patients with severe hypercholesterolemia.

Conflict of interest
None.

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Ethical statement
The work was written in accordance with the Declaration of Helsinki.

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

Zkrácená informace o přípravku LEQVIO 284 mg injekční roztok v předplněné injekční stříkačce • **Složení:** Jedna předplněná injekční stříkačka obsahuje sodnou sůl inklisiranu odpovídající 284 mg inklisiranu v 1,5 ml roztoku. **Indikace:** Přípravek Leqvio je indikován u dospělých s primární hypercholesterolemií (heterozygotní familiární a nefamiliární) nebo smíšenou dyslipidemií jako doplněk k dietním opatřením, a u pediatrických pacientů ve věku 12 let a starších s heterozygotní familiární hypercholesterolemií (HeFH): v kombinaci se statinem nebo statinem v kombinaci s jinými přípravky snižujícími hladinu lipidů u pacientů, u kterých nelze dosáhnout cílových hodnot pro LDL-C při maximální tolerované dávce statinu, nebo samostatně nebo v kombinaci s jinými přípravky snižujícími hladinu lipidů u pacientů s nesnášenlivostí statinu nebo u pacientů, u nichž je statin kontraindikován. **Dávkování:** Doporučená dávka u dospělých a pediatrických pacientů ve věku 12 let a starších je 284 mg inklisiranu podávaná jako jednorázová subkutánní injekce: na začátku léčby, znovu po 3 měsících a poté každých 6 měsíců. Pokud je plánovaná dávka opožděna o méně než 3 měsíce, má být inklisiran podán a dávkování má pokračovat podle pacientova původního schématu. Pokud je plánovaná dávka opožděna o více než 3 měsíce, má být zahájen nový dávkovací režim – má být podána počáteční dávka inklisiranu, další po 3 měsících a poté každých 6 měsíců. Inklisiran lze podávat okamžitě po poslední dávce monoklonální protilátky inhibující PCSK9. Pro udržení snížení lipoproteinového cholesterolu s nízkou hustotou (LDL-C) se doporučuje, aby byl inklisiran podán do 2 týdnů po poslední dávce monoklonální protilátky inhibující PCSK9. **Kontraindikace:** Hypersenzitivita na léčivou látku nebo na kteroukoli pomocnou látku. **Zvláštní upozornění/varování:** Účinek hemodialýzy na farmakokinetiku inklisiranu nebyl studován. Vzhledem k tomu, že inklisiran je vylučován ledvinami, nemá se hemodialýza provádět po dobu nejméně 72 hodin od podání inklisiranu. **Interakce:** Inklisiran není substrátem pro běžné transportéry léčiv, a přestože nebyly provedeny studie in vitro, nepředpokládá se, že bude substrátem pro cytochrom P450. Inklisiran není inhibitorem nebo induktorem enzymů cytochromu P450 nebo běžných transportérů léčiv. Proto se neočekává, že by inklisiran měl klinicky významné interakce s jinými léčivými přípravky. Na základě omezených dostupných údajů nejsou očekávány klinicky významné interakce s atorvastatinem, rosuvastatinem nebo jinými statiny. **Těhotenství a kojení:** Údaje o podávání inklisiranu těhotným ženám jsou omezené nebo nejsou k dispozici. Podávání inklisiranu v těhotenství se z preventivních důvodů nedoporučuje. Není známo, zda se inklisiran/metabolity vylučují do lidského mateřského mléka. Riziko pro kojené novorozence/děti nelze vyloučit. **Nežádoucí účinky:** Časté: Reakce v místě vpichu. **Podmínky uchovávání:** Chraňte před mrazem. **Dostupné lékové formy/velikosti balení:** Předplněná injekční stříkačka s ochranným pouzdrem jehly 1,5 ml roztoku v předplněné injekční stříkačce (sklo třídy I) s pístovou zátkou (brombutyl, fluorotekem potažená pryž) s jehlou, pevným krytem jehly a s ochranným pouzdrem jehly. Velikost balení jedna předplněná injekční stříkačka s ochranným pouzdrem jehly. **Poznámka:** Dříve než lék předepíšete, přečtěte si pečlivě úplnou informaci o přípravku. **Reg. č.:** EU/1/20/1494/002 **Datum registrace:** 9.12.2020 **Datum poslední revize textu SPC:** 03.08.2026 **Držitel rozhodnutí o registraci:** Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, Dublin 4, Irsko. *Výdej přípravku je vázán na lékařský předpis, přípravek je hrazen z prostředků veřejného zdravotního pojištění.*

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Přehledový článek | Review article

Machine Learning-Based Prediction of Long-Term Survival and Failure to Rescue after Coronary Artery Bypass Grafting: A Systematic Review

Merlinda Dwintasari[a,b], Danang Himawan Limanto[a,b], Chikita Nur Rachmi[b], Oky Revianto Sediono Pribadi[b], Yan Efrata Sembiring[a,b]

[a] *Departement of Thoracic, Cardiac, and Vascular Surgery, Faculty of Medicine, Airlangga University, Surabaya, Indonesia*
[b] *Departement of Thoracic, Cardiac, and Vascular Surgery, Dr. Soetomo General Teaching Hospital, Surabaya, Indonesia*

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Strojové učení
Umělá inteligence

SOUHRN

Úvod: Koronární bypass (coronary artery bypass grafting, CABG) nadále představuje zlatý standard chirurgické revaskularizace u komplexní ischemické choroby srdeční. I když došlo k podstatnému zlepšení v oblasti krátkodobé mortality, dlouhodobého přežívání a neúspěšných pokusů o záchranu pacienta se závažnými komplikacemi (failure to rescue, FTR), stále představují významné téma klinické praxe. Tradiční modely rizika používající regresní analýzu mohou nedostatečně zachycovat složité nelineární interakce mezi perioperačními proměnnými. Tento přehled je syntézou současných důkazů týkajících se rozhodujících faktorů přežívání a úlohy strojového učení (machine learning, ML) v predikování výsledného stavu po CABG.
Metody: S cílem vyhledat studie publikované v období mezi lednem 2015 a lednem 2024 byla s použitím kritérií PRISMA provedena systematická rešerše databází PubMed a ScienceDirect. Za vhodné pro daný účel byly považovány studie zahrnující dospělé pacienty s izolovaným koronárním bypassem (coronary artery bypass grafting, CABG), v nichž byly uvedeny hodnoty přežívání nebo neúspěšný pokus o záchranu pacienta se závažnými komplikacemi (FTR); ve studiích přitom musely být k predikci použity tradiční statistické modely nebo modely využívající strojové učení. Byly zvoleny relevantní parametry spolehlivosti modelu a klíčové proměnné predikce a byla provedena kvalitativní syntéza získaných hodnot.
Výsledky: Z celkového počtu 3 701 vyhledaných záznamů splňovalo kritéria pro zařazení do naší studie 26 studií a ty byly použity v kvalitativní syntéze. Jednoleté přežívání po CABG se pohybovalo v rozmezí 87–94 %, přičemž u pětiletého přežívání to bylo 67–88 % a v případě desetiletého přežívání byla hodnota 52–75 %. Celková incidence neúspěšných pokusů o záchranu pacienta se závažnými komplikacemi (FTR) dosáhla přibližně 2–3 %, přičemž mortalita byla výrazně vyšší po závažných komplikacích jako selhání ledvin (~25 %) a cévní mozková příhoda (~13 %). Mezi prediktory nepříznivého výsledku pravidelně patřily pokročilý věk, snížená ejekční frakce levé komory, diabetes mellitus, dysfunkce ledvin a cerebrovaskulární onemocnění. Modely s použitím strojového učení – zvláště souborové algoritmy v kombinaci s technikami intepretovatelnosti SHAP – prokázaly vyšší predikční přesnost a diskriminační spolehlivost ve srovnání s tradičními postupy využívajícími regresní analýzu.
Závěr: Délka dlouhodobého přežití po CABG se značně liší a závisí na velkém počtu klinických faktorů. Stratifikace rizika s použitím strojového učení zvyšuje přesnost predikce a umožňuje její interpretovatelnou individualizaci. Začlenění validovaných nástrojů umělé inteligence do jednotlivých kroků při provádění CABG může zvýšit perioperační rozhodování a snížit počty neúspěšných pokusů o záchranu pacienta při závažných komplikacích (FTR).

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ABSTRACT

Introduction: Coronary artery bypass grafting (CABG) remains the gold standard for surgical revascularization in complex coronary artery disease. Although short-term mortality has improved substantially, long-term survival and failure to rescue (FTR) after major complications remain clinically relevant. Traditional regression-based risk models may insufficiently capture complex nonlinear interactions among perioperative variables. This review synthesizes contemporary evidence regarding determinants of survival and the role of machine learning (ML) in outcome prediction after CABG.

Address: Yan Efrata Sembiring, Department of Thoracic and Cardiovascular Surgery, Faculty of Medicine, Airlangga University, Surabaya, Indonesia, Jl. Mayjend Prof. Dr. Moestopo No. 6-8, Surabaya, East Jawa 60285, Indonesia, e-mail: yan-e-s@fk.unair.ac.id
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Methods: A PRISMA-guided systematic search of PubMed and ScienceDirect was conducted for studies published between January 2015 and January 2024. Eligible studies included adult patients undergoing isolated coronary artery bypass grafting (CABG) that reported survival outcomes or failure-to-rescue (FTR) using statistical or machine learning-based predictive models. Relevant model performance metrics and key predictive variables were extracted and qualitatively synthesized.

Results: From 3,701 identified records, 26 studies met the inclusion criteria and were included in the qualitative synthesis. One-year survival after CABG ranged from 87–94%, while 5-year survival ranged from 67–88% and 10-year survival from 52–75%. The overall incidence of failure to rescue (FTR) was approximately 2–3%, with markedly higher mortality observed following major complications such as renal failure (~25%) and stroke (~13%). Consistent predictors of adverse outcomes included advanced age, reduced left ventricular ejection fraction, diabetes mellitus, renal dysfunction, and cerebrovascular disease. Machine learning models—particularly ensemble algorithms combined with SHAP interpretability techniques—demonstrated improved predictive accuracy and discriminatory performance compared with traditional regression-based approaches.

Conclusion: Long-term survival after CABG remains heterogeneous and influenced by multifactorial clinical determinants. Machine learning-based risk stratification provides improved predictive accuracy and interpretable individualized assessment. Integration of validated artificial intelligence tools into CABG workflows may enhance perioperative decision-making and reduce failure-to-rescue rates.

Introduction

Coronary artery bypass grafting (CABG) remains the cornerstone of surgical revascularization for patients with complex coronary artery disease (CAD), particularly those with multivessel disease, diabetes mellitus, or left main stenosis.[1] Despite continuous advances in percutaneous coronary intervention, CABG continues to provide durable survival benefit and long-term symptomatic improvement across diverse patient populations.[1]

However, the contemporary cardiac surgical landscape is characterized by increasing patient complexity, aging populations, and a growing emphasis on precision medicine. These changes necessitate a transformation in the way CABG is planned, delivered, and evaluated.[1] Although operative mortality has decreased substantially, postoperative morbidity and variability in long-term survival outcomes remain major clinical challenges.

Failure to rescue (FTR), defined as mortality following major postoperative complications such as stroke, renal failure, reoperation, or prolonged ventilation, has emerged as an important quality metric in cardiac surgery.[2] Identifying high-risk patients in the preoperative period may enable targeted optimization and resource allocation. Traditional statistical models have contributed to risk assessment; however, their predictive capacity may be limited by assumptions of linearity and difficulty capturing complex interactions among clinical variables.[2]

Long-term survival following CABG is influenced by multiple interrelated factors. A recent systematic review identified 43 determinants associated with survival after on-pump CABG, with age, left ventricular ejection fraction, diabetes mellitus, history of cerebrovascular disease, and renal function consistently reported as major predictors.[3] These findings highlight the multifactorial nature of post-CABG outcomes and underscore the need for robust, data-driven predictive tools.

Artificial intelligence (AI) and machine learning (ML) techniques have recently demonstrated substantial potential in cardiovascular outcome prediction. Interpretable ML models, such as random forest algorithms combined with SHapley Additive exPlanations (SHAP), have been successfully applied to identify and quantify preoperative risk factors associated with FTR after CABG, showing strong discriminatory performance.[2] Furthermore, systematic evidence indicates that ML-based approaches improve survival prediction accuracy and facilitate individualized risk stratification in CABG populations.[3]

Beyond predictive analytics, the future of CABG is shaped by technological and procedural innovations, including robotic-assisted surgery, hybrid coronary revascularization strategies, digital health integration, and enhanced recovery protocols.[1] These developments reflect a broader paradigm shift toward innovation, individualization, and integration in surgical revascularization.

In this evolving context, integrating machine learning-based risk prediction with contemporary surgical innovation may represent a critical step toward improving survival, reducing complications, and advancing patient-centered care in CABG.

Materials and methods

Search strategy and data sources

A structured literature review was conducted to synthesize current evidence regarding predictive factors of survival and postoperative adverse outcomes in patients undergoing coronary artery bypass grafting (CABG), as well as the application of artificial intelligence (AI) and machine learning (ML) methods in outcome prediction.

Electronic databases including PubMed, Scopus, Web of Science, and IEEE Xplore were systematically searched for studies published between January 2015 and January 2024. The search strategy combined controlled vocabulary (MeSH terms) and free-text keywords related to "coronary artery bypass grafting", "machine learning", "artificial intelligence", "risk prediction", "survival", and "failure to rescue". Boolean operators (AND/OR) were applied to optimize retrieval.

In addition to published literature, registry-based data sources frequently cited in the included studies—such as the Society of Thoracic Surgeons (STS) Adult Cardiac

Surgery Database and institutional cardiac surgery registries—were considered as primary data frameworks for AI-based risk modeling.

The review process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological transparency and reproducibility.

Eligibility criteria

Studies were included if they met the following criteria: (1) Investigated adult patients undergoing isolated CABG. (2) Evaluated survival outcomes, postoperative mortality, or failure to rescue (FTR). (3) Applied statistical modeling or machine learning techniques for risk prediction. (4) Reported identifiable clinical predictors associated with survival or adverse postoperative outcomes. (5) Published in English in peer-reviewed journals.

Studies were excluded if they: (1) Included mixed surgical populations without separate CABG analysis. (2) Focused solely on off-pump versus on-pump comparison without predictive modeling. (3) Were case reports, editorials, conference abstracts, or narrative reviews without original data. (4) Included pediatric populations.

Study selection

All retrieved records were exported into reference management software, and duplicate entries were removed. Two independent reviewers screened titles and abstracts for relevance according to predefined eligibility criteria. Full texts of potentially eligible studies were subsequently assessed.

Disagreements between reviewers were resolved through discussion and consensus. Where necessary, a third reviewer was consulted to reach final agreement. The final set of included studies comprised clinical outcome analyses, AI-based predictive modeling studies, and systematic evidence regarding survival determinants after CABG.

Quality assessment

The methodological quality and risk of bias of the included studies were independently assessed by two reviewers.

For observational and predictive modeling studies, methodological rigor was evaluated based on: Clarity of study population definition. Adequacy of outcome definition (e.g., survival, FTR). Completeness of variable

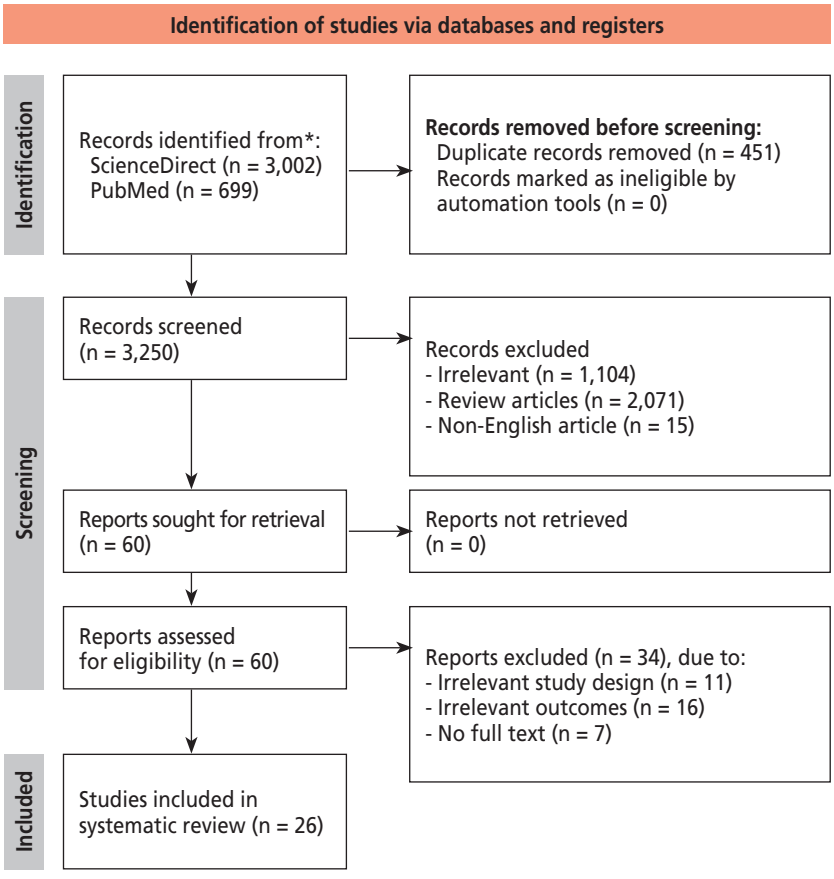


Fig. 1 – PRISMA 2020 flow diagram for included studies.[30]
* Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
** If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

selection and preprocessing. Validation strategy (internal and/or external validation). Model performance metrics (e.g., AUC, F1-score, calibration indices). For systematic review components, the Cochrane Collaboration Risk of Bias framework was adapted to assess data collection methods, outcome measurement, statistical reporting, and reproducibility. Studies were categorized as low, moderate, or high risk of bias based on these domains.

Outcome measures

The primary outcome measures included: (1) **Overall survival**, defined as short-term (30-day), mid-term (1–5 years), or long-term (>5 years) survival following CABG. (2) **Failure to rescue (FTR)**, defined as 30-day or in-hospital mortality occurring after major postoperative complications such as stroke, renal failure, reoperation, or prolonged mechanical ventilation. (3) **Model performance metrics**, including area under the receiver operating characteristic curve (AUC), precision-recall curve, F1-score, calibration indices, and interpretability measures (e.g., SHAP values). Secondary outcomes included identification of key predictive factors such as age, left ventricular ejection fraction, diabetes mellitus, renal function, cerebrovascular disease, hematologic parameters, and biochemical markers.

Results

Study selection

The study selection process was conducted in accordance with the PRISMA 2020 guidelines. The initial literature search identified 3,701 records, including 3,002 articles from ScienceDirect and 699 articles from PubMed. After removal of 451 duplicate records, a total of 3,250 records remained for title and abstract screening. During the screening phase, 3,190 records were excluded, including 1,104 irrelevant articles, 2,071 review articles, and 15 non-English publications.

Subsequently, 60 full-text reports were assessed for eligibility, and all reports were successfully retrieved. After full-text evaluation, 34 studies were excluded for the following reasons: irrelevant study design (n = 11), irrelevant outcomes (n = 16), and lack of accessible full text (n = 7). Ultimately, 26 studies met the predefined inclusion criteria and were included in the final qualitative synthesis. The study selection process is summarized in **Figure 1**.

Study characteristics

A total of 26 studies met the eligibility criteria and were included in the qualitative synthesis. Sample sizes among the included studies ranged from 269 to 347,977 patients. Most studies employed retrospective observational designs, frequently using large registry datasets such as the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database or national cardiac surgery registries. These datasets enabled the evaluation of survival outcomes and predictive factors associated with postoperative mortality and failure-to-rescue in patients undergoing CABG.

Reported survival outcomes varied: 1-year survival frequently exceeded 85–90%, whereas 5-year survival ranged between approximately 70% and 90%, depending on comorbidity burden and cohort characteristics.

The included studies were published between 2015 and 2025 and originated predominantly from North America and Europe, followed by Asia and the Middle East.

Methodologically, survival analysis was the most common analytical framework, particularly for long-term outcomes (1-, 5-, and 10-year survival). Machine learning approaches were increasingly used in more recent studies, particularly for risk stratification and complication prediction.

Across studies, survival rates following CABG demonstrated consistent short-term outcomes but variable long-term results:

- 1-year survival: approximately 87–94%,
- 5-year survival: approximately 67–88%,
- 10-year survival: approximately 52–75%.

Failure to rescue rates were reported at approximately 2–3% overall but were substantially higher among patients experiencing major postoperative complications.

Baseline demographics and clinical characteristics

Across the aggregated datasets, patients undergoing isolated CABG were predominantly male (approximately 70–75%) with a mean age ranging from 60 to 65 years.

Common comorbidities included:

- hypertension (>90%),
- prior myocardial infarction (~50%),
- diabetes mellitus (~45–55%),
- chronic lung disease (~25%),
- peripheral arterial disease (~13–22%),
- cerebrovascular disease (~20–25%),

In AI-based predictive modeling of FTR involving nearly 10,000 patients, the overall FTR rate was 2.5%. Mortality following specific complications was markedly higher, including:

- renal failure (~25%),
- stroke (~13%),
- reoperation (~11%),
- prolonged ventilation (~12%).

Feature selection algorithms identified 12 key preoperative predictors associated with FTR, including age, albumin level, bilirubin level, body mass index, creatinine level, ejection fraction, hematocrit, hemoglobin, hemoglobin A1c, MELD score, platelet count, and white blood cell count.

Discussion

The present review synthesizes contemporary evidence regarding long-term survival, failure to rescue (FTR), and

Table 1 – Study characteristics

Ref	Author (year)	Country	Design	Sample	Main focus	Key survival findings	LoE
4	Salmasi, 2023	UK	Retrospective	1,957	Ethnic outcomes	10-yr survival 83–86%	III
5	Jonsson, 2022	Sweden	Prospective	36,898	Stroke impact	Stroke ↓ survival (49% vs 81%)	II
6	Jegaden, 2022	UAE	Retrospective	1,432	Arterial graft strategy	Multi-arterial graft ↑ long-term survival	III
7	Hendriks, 2022	Netherlands	Retrospective	5,672	Hypothermia during CPB	Mild hypothermia best 5-yr survival	III
8	Omer, 2022	USA	Retrospective	61,477	LVEF & rescue	LVEF <35%, ↓ long-term survival	III
9	Han, 2021	USA	Retrospective	7,652	Surgeon experience	Higher experience, ↑ 5-yr survival	III
10	Sattartabar, 2021	Iran	Retrospective	24,328	Age & sex	Female & elderly ↓ survival	III
11	Parker, 2020	Lebanon	Prospective	1,560	Biomarkers	6-yr survival 86%	II
12	Zarei, 2020	Iran	Prospective	404	Vitamin D	Deficiency, ↓ survival	II
13	Gallo, 2020	USA	Retrospective	2,713	Redo CABG	5-yr survival 85–90%	III
14	Robich, 2019	USA	Retrospective	6,415	Glycemic control	Higher HbA_{1c}, ↓ survival	III
15	Wang, 2019	China	Retrospective	1,144	Renal dysfunction	eGFR <60, ↓ survival	III
16	Karim, 2018	Australia	Retrospective	46,573	Long-term registry outcomes	3-yr survival 93–98%	III
17	Luthra, 2018	UK	Retrospective	598	Third arterial conduit	Multi-arterial, ↑ long-term survival	III
18	Cheng, 2018	China	Prospective	600	Ventricular arrhythmia	Lower survival with VT/VF	II
19	Beller, 2018	USA	Retrospective	1,272	Troponin levels	Elevated troponin, ↓ survival	III
20	Malaisrie, 2018	USA	Retrospective	347,977	Pre-op AF	AF associated with, ↓ 5-yr survival	III
21	Benedetto, 2017	UK	Retrospective	12,244	Obesity & radial graft	Obesity modifies survival benefit	III
22	Luthra, 2017	UK	Retrospective	1,226	Second arterial conduit	Improved 10-yr survival	III
23	Najafi 2016	Iran	Prospective	566	Opium use	Lower 5-yr survival in users	II
24	Efird 2016	USA	Retrospective	4,801	COPD	COPD, ↓ 5-yr survival	III
25	Pang 2016	Singapore	Retrospective	5,720	Diabetes	20-yr survival lower in diabetics	III
26	Farhadi 2016	Iran	Retrospective	269	Severe LV dysfunction	Early mortality higher in low EF	III
27	Singh 2015	USA	Retrospective	1,141	Octogenarians	30-day survival 94%	III
28	Mortazavi 2016	USA	Retrospective	10,000+	Machine learning mortality prediction	ML models improved prediction accuracy vs logistic regression	III
29	Lee 2021	USA	Retrospective	10,000+	ML risk prediction using STS database	XGBoost model AUC ~0.85 for mortality prediction	III

Table 2 – Clinical determinants of long-term survival after CABG

Risk category	Identified predictors	Studies reporting association
Demographic	Advanced age, female sex	4, 10, 27
Cardiac function	Reduced LVEF (<35%), ventricular arrhythmia	8, 18
Renal function	Mild–moderate renal dysfunction	15
Metabolic	Diabetes mellitus, HbA_{1c} elevation	14, 35
Pulmonary	COPD	24

Table 2 – Clinical determinants of long-term survival after CABG

Risk category	Identified predictors	Studies reporting association
Neurological	Perioperative stroke	5, 29
Rhythm disorders	Preoperative atrial fibrillation	20
Biomarkers	Elevated troponin, galectin-3	11, 19
Graft strategy	Multi-arterial grafting improves survival	6, 17, 22
Surgeon/center factors	Surgeon experience	9

Table 3 – Methodological approaches used in survival analysis

Analytical method	Application	Frequency in included studies
Cox proportional hazard	Long-term mortality modeling	Most common
Logistic regression	Short-term mortality	Frequent
Kaplan–Meier	Survival estimation	Nearly universal
Propensity matching	Confounding adjustment	Several studies
Machine learning	Risk clustering/prediction	Limited but emerging

Table 4 – Reported survival rates across time horizons

Follow-up duration	Survival range
30-day	94–99%
1 year	82–97%
5 years	67–90%
10 years	52–86%
20 years	35–53%

Table 5 – Special populations and survival impact

Subgroup	Key finding
Stroke patients	Markedly reduced long-term survival
Severe LV dysfunction	Lower rescue rates and survival
Obese vs non-obese	Survival difference varies by conduit
COPD	Worse 5-year survival
Redo CABG	Acceptable survival but higher risk
South-Asian ethnicity	Comparable long-term outcomes

Table 6 – Determinants of long-term survival after CABG categorized by clinical domain

Clinical domain	Predictor variable	Supporting references
Demographic factors	Advanced age	4, 5, 6, 7, 16, 23, 25, 27
	Female sex	25, 28
	Body mass index (BMI)	7, 23
Cardiac functional status	Reduced left ventricular ejection fraction	4, 6, 8, 9, 16, 22, 23, 25, 26, 28
	Congestive heart failure	16
	NYHA functional class	22
	Previous myocardial infarction	22, 25, 29
	Left main coronary disease	17
	Extracardiac arteriopathy	17
Arrhythmia-related variables	Preoperative atrial fibrillation	20
	Ventricular tachycardia	18
	Ventricular fibrillation	18
	General arrhythmia history	16
Vascular & cerebrovascular disease	Peripheral vascular disease	5, 16
	Cerebrovascular disease / stroke	5, 16, 23
Metabolic & endocrine factors	Diabetes mellitus	6, 10, 16, 23
	Preoperative glycemic control (HbA_{1c})	14
	Hypercholesterolemia	16
	Serum vitamin D level (25[OH]D)	12

Table 6 – Determinants of long-term survival after CABG categorized by clinical domain

Clinical domain	Predictor variable	Supporting references
	Serum telomerase activity	12
	Galectin-3 concentration	11
Renal function	Impaired renal function / elevated creatinine	4, 7, 15, 16
Pulmonary conditions	Chronic obstructive pulmonary disease (COPD)	24
	Respiratory disease	16, 22
	Prolonged postoperative ventilation (PLOS)	24
Surgical & technical variables	Multi-arterial grafting	6, 21, 22
	Radial artery as second conduit	21
	Complete revascularization	6
	Left internal thoracic artery use	27
	Surgeon experience	9
	Prior cardiac surgery	5
	Intraoperative mild hypothermia	7
	CPB temperature (32–33 °C)	7
Risk stratification tools	EuroSCORE	17, 22
Clinical severity indicators	Critical preoperative status	5
	Preoperative angina requiring IV nitrates	5
	Complications during hospitalization	8
Lifestyle factors	Smoking	16
	Opium consumption	23
Treatment strategy	Type of medical intervention	26

Table 7 – Risk factors stratified by clinical outcome after CABG

Risk factor	Long-term survival	Early mortality	Failure-to-rescue (FTR)	Key references
Advanced age	✓ Strong predictor	✓	✓	4–7, 16, 28
Female sex	✓	–	–	25
Low ejection fraction	✓ Strong	✓ Strong	✓	6, 8, 25, 28
Prior myocardial infarction	✓	✓	–	22, 25
Left main disease	✓	✓	–	17
NYHA class III–IV	✓	✓	–	22
Diabetes mellitus	✓	✓	✓	6, 10, 23
Hypertension	✓	–	–	10, 16
Peripheral arterial disease	✓	✓	–	5, 16
Cerebrovascular disease	✓	✓	✓	5, 16, 23
COPD / chronic lung disease	✓	✓	–	22, 24
Renal dysfunction / creatinine	✓ Strong	✓ Strong	✓ Strong	7, 15, 28
Liver dysfunction / MELD score	✓	✓	✓	28
Low albumin	✓	✓	✓ Strong	28
Elevated bilirubin	✓	✓	✓	28
Anemia (low hemoglobin/hematocrit)	✓	✓	✓	28
Elevated HbA_{1c}	✓	✓	✓	14, 28
High inflammatory markers (WBC)	✓	✓	✓	28
Postoperative stroke	–	✓	✓ Very strong	28
Postoperative renal failure	–	✓	✓ Highest FTR rate	28
Reoperation	–	✓	✓	28

Table 7 – Risk factors stratified by clinical outcome after CABG

Risk factor	Long-term survival	Early mortality	Failure-to-rescue (FTR)	Key references
Prolonged ventilation	–	✓	✓	28
Complete revascularization	✓ Protective	✓	–	6
Multiarterial grafting	✓ Protective	–	–	27, 28
Radial artery use	✓	–	–	21
Surgeon experience	✓	✓	–	9
EuroSCORE / STS risk score	✓	✓	✓	17, 22, 29
AI-based risk prediction models	✓	✓	✓ Enhanced discrimination	28, 29

the evolving role of machine learning–based predictive modeling in patients undergoing coronary artery bypass grafting (CABG). Overall, the findings demonstrate that CABG continues to provide favorable survival outcomes, although substantial variability persists across patient populations. Reported one-year survival rates frequently exceed 85–90%, whereas five-year and ten-year survival range approximately between 67–90% and 52–86%, respectively.[4–7,16] These findings indicate that while short-term outcomes after CABG remain consistently strong, long-term prognosis is influenced by a complex interaction of patient characteristics, perioperative management, and surgical strategy.[4–7,16] Several observational studies and registry analyses have demonstrated that long-term outcomes following CABG are strongly associated with demographic and clinical factors, emphasizing the importance of comprehensive preoperative risk assessment and patient selection.[4–7,16]

Across the included studies, several predictors of adverse survival outcomes were repeatedly identified. Advanced age remains one of the most consistent determinants of mortality following CABG, reflecting the increased burden of comorbid conditions and reduced physiologic reserve among elderly patients.[4–7,23,25,27] Similarly, reduced left ventricular ejection fraction (LVEF), diabetes mellitus, renal dysfunction, and chronic pulmonary disease have consistently been associated with worse long-term outcomes after CABG.[8,10,14,15,24,25] These factors likely represent the systemic nature of coronary artery disease and the cumulative impact of cardiovascular risk factors on postoperative recovery and long-term survival.[8,10,14,15,24,25] In particular, impaired renal function and severe ventricular dysfunction have been shown to substantially increase perioperative vulnerability and long-term mortality risk.[8,15,24] Additionally, perioperative complications such as stroke and ventricular arrhythmias have been reported to significantly worsen long-term survival following CABG, highlighting the importance of early detection and effective postoperative management of complications.[5,18]

Beyond patient-related factors, surgical technique and procedural strategy also appear to influence long-term outcomes. Several studies have demonstrated that multiarterial grafting strategies and the use of additional arterial conduits are associated with improved long-term survival compared with single arterial grafting approaches, likely due to superior graft patency and more complete myocardial revascularization.[6,17,22] Surgeon experience and institutional expertise have also been shown to influence outcomes, suggesting that procedural volume and surgical proficiency remain important determinants of CABG success.[9] In addition to surgical factors, emerging evidence suggests that several biochemical and inflammatory biomarkers may contribute to prognostic assessment. Biomarkers such as galectin-3, vitamin D deficiency, and elevated troponin levels have been explored as potential predictors of adverse outcomes after CABG, reflecting underlying inflammatory, metabolic, and myocardial injury processes that may influence long-term survival.[11,12,19]

Another important concept highlighted in this review is failure to rescue (FTR), which refers to mortality following major postoperative complications. Although the overall incidence of FTR after CABG remains relatively low, mortality following severe complications such as stroke, renal failure, or prolonged ventilation can be substantial.[5,8,15] These findings indicate that survival after CABG is not determined solely by baseline patient risk but also by the effectiveness of perioperative monitoring, early recognition of complications, and institutional capacity to manage postoperative deterioration.[5,8,15] Consequently, FTR has increasingly been recognized as an important quality metric reflecting both patient-related risk factors and health-system performance.[5,8,15]

More recently, advances in artificial intelligence and machine learning have introduced new opportunities to improve risk prediction in cardiac surgery. Traditional statistical models, including logistic regression and Cox proportional hazards analysis, have historically formed the basis of cardiac surgical risk stratification [16]. However, these approaches may be limited by assumptions of linear relationships and may not fully capture complex interactions among multiple perioperative variables.[16] Machine learning algorithms, particularly ensemble methods such as random forests and gradient boosting models, offer the ability to analyze large clinical datasets and detect nonlinear relationships among predictors.[28,29] Recent studies have demonstrated that machine learning models can improve predictive performance for postoperative mortality and complications compared with traditional statistical approaches.[28,29]

Importantly, recent developments in interpretable machine learning techniques have helped address concerns regarding the transparency and clinical applicability of artificial intelligence models. Techniques such as SHapley Additive exPlanations (SHAP) enable the identification and quantification of individual predictor contributions

to model outputs, thereby enhancing interpretability and clinician trust in machine learning–based decision support systems.[28,29] By providing individualized risk predictions, these models may assist clinicians in identifying high-risk patients, optimizing perioperative management strategies, and potentially reducing the incidence of failure to rescue following CABG.[28,29]

The integration of machine learning–based predictive modeling with contemporary innovations in cardiac surgery may represent an important step toward personalized surgical care. Advances in minimally invasive techniques, hybrid coronary revascularization strategies, enhanced recovery pathways, and digital health monitoring are transforming the management of coronary artery disease and may further benefit from data-driven risk stratification approaches.[6,22,28,29] When combined with clinical expertise, machine learning models may facilitate individualized surgical planning and improve allocation of perioperative resources in patients undergoing CABG.[28,29]

Despite these promising developments, several limitations should be considered. Many predictive modeling studies rely on retrospective registry data, and external validation across diverse populations remains necessary before widespread clinical implementation.[16,28,29] Additionally, heterogeneity in study design, patient populations, and analytical methodologies limits direct comparison across studies included in this review.[4–7,16] Ethical considerations, including algorithm transparency, data governance, and equitable access to artificial intelligence technologies, must also be addressed to ensure responsible integration of machine learning into clinical practice.[28,29]

In summary, CABG remains an effective revascularization strategy that provides durable survival benefit in patients with complex coronary artery disease. However, long-term outcomes are influenced by multiple interacting clinical factors, including patient comorbidities, surgical strategy, and perioperative management.[4–7,8,10,14,15] Emerging machine learning–based predictive models offer promising improvements in risk stratification and may enhance individualized decision-making in cardiac surgery.[28,29] Future research should focus on prospective validation of artificial intelligence–based tools, multicenter collaboration, and integration of predictive analytics into routine clinical workflows to improve patient outcomes and reduce failure-to-rescue events following CABG.[28,29]

Conclusion

Coronary artery bypass grafting (CABG) remains an effective revascularization strategy with favorable short-term outcomes, yet long-term survival is strongly influenced by age, left ventricular function, diabetes, renal dysfunction, and cerebrovascular disease. Although overall mortality is low, failure to rescue after major complications remains clinically relevant. Machine learning–based models demonstrate superior predictive performance compared with traditional approaches and provide interpretable, individualized risk assessment. Integrating validated artificial intelligence tools into CABG practice may enhance perioperative decision-making and improve patient-centered outcomes.

Conflict of interest
No conflicts of interest relevant to this manuscript.

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Ethical statement
Ethical approval was not required for this systematic review because it was based on previously published studies and did not involve the recruitment of human participants or the collection of identifiable personal data.

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Původní sdělení | Original research article

The Effect of Sodium Dodecyl Sulfate Concentration on the Integrity of Bovine Jugular Veins for Decellularized Pulmonary Xenografts: A Systematic Review

Atiya Nurrahmah[a], Heroe Soebroto[b], Ketut Alit Utamayasa[c], Arief Rakhman Hakim[b], Ito Puruhito[b]

[a] *Department of Thoracic, Cardiac and Vascular Surgery, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*
[b] *Department of Thoracic, Cardiac and Vascular Surgery, Dr Soetomo General Academic Hospital, Surabaya, Indonesia*
[c] *Department of Child Health, Cardiology Division, Dr. Soetomo General Hospital, Surabaya, Indonesia*

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Tkáňové inženýrství
Vrozená srdeční vada

SOUHRN

Cíl: Cílem této studie bylo podrobně zkontrolovat údaje o tom, jak koncentrace dodecylsíranu sodného (sodium dodecyl sulfate, SDS) ovlivňuje míru zachování extracelulární matrix, její biokompatibilitu, biomechanickou celistvost a účinnost decelularizace bovinních hrdelních žil používaných jako prototypy plicních xenograftů.
Metody: V databázích PubMed, Scopus a Google Scholar jsme vyhledali studie na téma decelularizace s použitím SDS publikovaných do července 2025. Mezi vhodné patřily studie popisující výsledky *in vitro*, *in vivo* a translačního výzkumu s uvedením koncentrací SDS (0,5–1 %). Vyhledávané parametry zahrnovaly míru odstranění DNA, zachování extracelulární matrix, výsledky biomechanického testování, cytotoxicitu a průchodnost štěpu. Vzhledem k heterogenitě výsledků byla provedena jejich syntéza narativní formou.
Výsledky: Celkem bylo vyhledáno 14 studií. Decelularizace byla úspěšná při hodnotách SDS 0,5–1 %. Při použití SDS v koncentraci 0,5 % se zachovalo více kolagenu a elastinu, nicméně nebyly odstraněny všechny buňky. V koncentraci odstranil 1% SDS více DNA, odstranil ale i glykosaminoglykany a do jisté míry došlo i k odstranění růstových faktorů. Biomechanické testy prokázaly, že pevnost v tahu se sice nezměnila, avšak příliš velká expozice vedla k oslabení konstruktů. *In vitro* došlo při použití 1% SDS ke snížení životaschopnosti buněk. Malý počet studií naznačil uspokojivou krátkodobou průchodnost, zdůraznil rizika kalcifikace a trombózy.
Závěr: Použití SDS zajišťuje účinnou decelularizaci bovinních hrdelních žil. Koncentrace 0,5–1 % vyvažují odstranění buněk zachováním extracelulární matrix, ale ani jedna možnost není optimální. Budoucí studie musejí zdokonalit postupy včetně použití enzymatických detergentů a hodnotit dlouhodobé výsledky *in vivo*.
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Keywords:
Bioprosthesis
Blood vessel prosthesis implantation
Congenital heart defect
Decellularized extracellular matrix
Heart valve prosthesis implantation
Jugular veins
Tissue engineering

ABSTRACT

Objective: The aim of this study was to thoroughly examine the data regarding how SDS concentration affects the extracellular matrix preservation, biocompatibility, biomechanical integrity, and decellularization effectiveness of bovine jugular veins used as pulmonary xenograft prototypes.
Methods: We looked for studies on SDS decellularization of bovine jugular veins in PubMed, Scopus, and Google Scholar until July 2025. Eligible studies comprised *in vitro*, *in vivo*, and translational research evaluating SDS concentrations (0.5–1%). The outcomes extracted encompassed DNA removal, extracellular matrix preservation, biomechanical testing, cytotoxicity, and graft patency. Narrative synthesis was conducted because of heterogeneity.
Results: There were fourteen studies in total. SDS at 0.5–1% successfully accomplished decellularization. SDS 0.5% kept collagen and elastin better, however it could have left some cells behind. SDS 1% cleared more DNA, but it also depleted glycosaminoglycans and made it harder for growth factors to stay in place. Biomechanical tests showed that the tensile strength was the same, but too much exposure made the constructs weaker. *In vitro*, cell viability diminished on 1% SDS scaffolds. Limited *in vivo* trials indicated satisfactory short-term patency but emphasized dangers of calcification and thrombosis.
Conclusion: SDS is effective for bovine jugular vein decellularization. Concentrations of 0.5–1% balance cellular clearance with matrix preservation, but neither is optimum. Future study should refine procedures, include enzymatic detergents, and evaluate long-term *in vivo* outcomes.

Address: Heroe Soebroto, MD, PhD, Department of Thoracic, Cardiac and Vascular Surgery, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, e-mail: heroe.soebroto@fk.unair.ac.id
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Introduction

A common feature of congenital heart diseases such as pulmonary atresia and tetralogy of Fallot is right ventricular outflow tract obstruction (RVOTO). A right ventricle–pulmonary artery (RV-PA) conduit, first introduced by Rastelli in 1969, frequently becomes necessary for surgical repair.[1] Despite the widespread availability, homograft's and bovine jugular vein xenografts have a limited supply, and xenografts have been associated to thrombosis, calcification, and immunogenic degeneration.[2,3]

The aim of tissue engineering Is to develop vascular scaffolds that are secure for the body. Decellularized pulmonary homograft's (DPH) demonstrate enhanced long-term patency relative to natural bovine xenografts.[4] Unfortunately, homograft's are frequently not available, especially in regions with limited resources. Developing decellularized pulmonary xenografts (DPX) from bovine jugular veins may provide a cost-effective and affordable alternative.[5–7]

Sodium dodecyl sulfate (SDS) is a hydrophilic detergent that is one of the most widely used to eliminate cells. It dissolves down membranes and removes nuclear material, but it might also disrupt collagen, elastin, and glycosaminoglycans (GAGs).[6,8] The proper dosage of SDS requires a balance between removing cells quickly and keeping the extracellular matrix intact.

This systematic review analyzes the effect of SDS concentration (in particular, 0.5% and 1%) on the decellularization of bovine jugular veins, focusing on: (1) How effectively cellular material is removed aside; (2) maintaining the extracellular matrix (collagen, elastin, GAGs) intact; (3) biomechanical characteristics; (4) cytotoxicity and recellularization potential; (5) preclinical graft patency

Materials and methods

Search strategy

A systematic search was performed in **PubMed, Science Direct,** and **BMC** until July 2025. PRISMA 2020 guidelines was utilized. The keywords were "Sodium Dodecyl Sulfate", "decellularized extracellular matrix", "jugular veins", "bovine jugular veins", and "pulmonary xenograft". Boolean operators („AND", „OR") were applied to optimize the search.

Eligibility criteria

Included were experimental in vitro or in vivo studies and translational reports studying SDS decellularization of bovine jugular veins. Non-bovine studies, non-SDS protocols, case reports, inadequate original data, review artciles, and articles not published in English were excluded.

Data extraction and analysis

The information extracted included SDS concentration, exposure duration, decellularization efficiency, extracellular matrix preservation, biomechanical properties, cytotoxicity, and in vivo outcomes. SYRCLE's risk of bias tool was used to determine the quality of the studies.

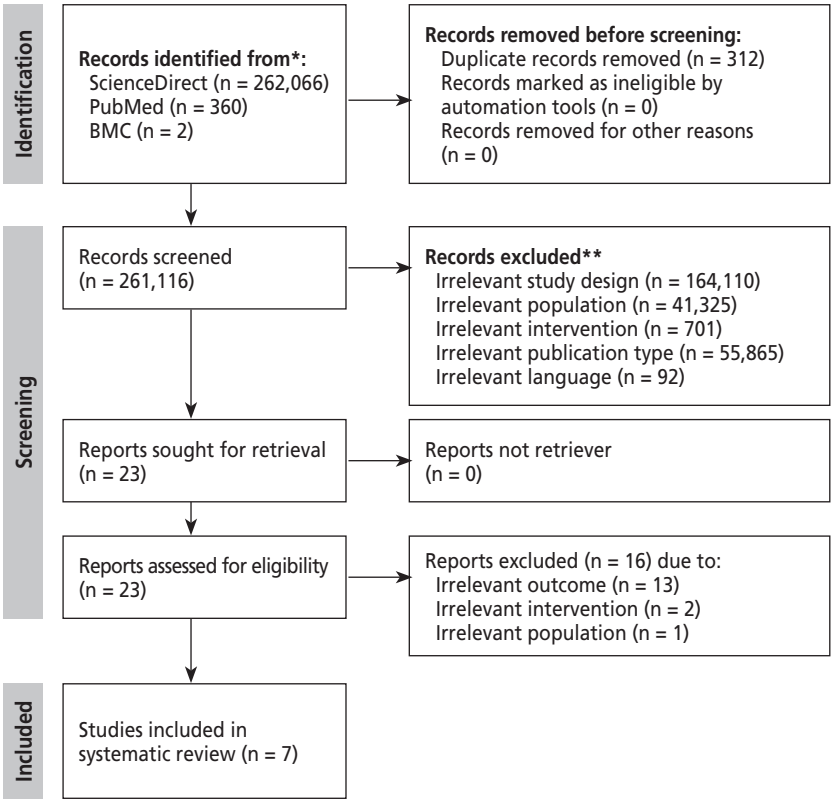


Fig. 1 – PRISMA.
Identification of studies via databases and registers.

Results

Study selection

The systematic search identified 262,428 records: Pubmed (n=360), Science Direct (n=262,066), and BMC (n=2). 312 duplicates were removed; 262,116 records were screened. 261,093 articles were excluded due to irrelevant study design, population, intervention, publication type, or language. Sixteen studies were subsequently removed after full-text screening. Finally, seven studies were included in the systematic review total (**Fig. 1**).[4–5,9–13] Moreover, all included studies were considered high quality studies using SYRCLE's risk of bias tool. **Table 1** describes the outcomes of the studies.

Decellularization efficiency

SDS succeeded in over 90% nuclear clearance across numerous studies. SDS 1% consistently resulted in greater in-scope DNA removal compared to 0.5%, even though residual cellular fragments were occasionally detected in the latter. More clearance makes immunogenicity less, but it also makes ECM damage more likely to occur.[4,9–13]

Extracellular matrix preservation

Histology showed that SDS 0.5% was more effective at maintaining collagen and elastin intact.[9–10,12,13] In contrast, 1% SDS results in GAG depletion and less preservation of growth factors, which could make it more difficult for recellularization.

Biomechanical integrity

The maximum tensile strength and burst pressure of SDS--treated grafts were identical to those of native veins. But prolonged exposure (>14 days) damaged scaffold mechanics.[4,5,11] The best possible results depend on balancing both concentration and duration.

Cytotoxicity and recellularization

MTT assays showed reduced cell viability on 1% SDS scaffolds, suggesting residual cytotoxicity or ECM disrupti-

Table 1 – Outcomes of the studies

Study	Decellularization efficiency	Extracellular matrix preservation	Biomechanical integrity	Cytotoxicity and recellularization	Preclinical outcomes
Bobylev et al. (2024)[4]	Decellularized homografts and SDS-treated bovine conduits showed effective DNA removal with high clearance rates.	Good ECM preservation in decellularized homografts and SDS-treated BJV conduits.	SDS-treated grafts retained mechanical properties similar to native tissues.	No major cytotoxicity reported; SDS-treated conduits functioned well.	SDS-treated homografts showed good early outcomes and hemodynamics.
Hao et al. (2023)[5]	Not primary focus, but used clinically acceptable BJV conduits with prior processing.	ECM status not explicitly detailed but clinical results were acceptable.	Mechanical integrity maintained over medium-term use in clinical settings.	Not reported.	SDS-processed conduits demonstrated mid--term success.
Dalgliesh et al. (2018)[9]	Decellularization efficiency is a key to reducing antigenicity; SDS helps achieve this when optimized.	Proper SDS use helps minimize antigenicity by preserving ECM.	Biomechanical outcomes are favourable when SDS exposure is optimized.	SDS-treated scaffolds showed potential when thoroughly rinsed.	SDS-based processing, when optimized, helps reduce xenograft immune reactions.
Lin et al. (2018)[10]	SDS effectively achieves >90% nuclear clearance.	SDS 0.5% maintained collagen/elastin well; important for scaffold functionality.	SDS preserved mechanical strength with proper exposure duration.	0.5% SDS showed high cell compatibility; 1% requires extended rinsing.	SDS-treated grafts showed positive short--term outcomes; long--term studies ongoing.
Sembiring et al. (2022)[11]	SDS 0.5–1% achieved excellent decellularization; higher concentrations increased removal.	SDS 0.5% showed strong preservation of key ECM elements.	SDS 0.5% maintained tensile strength and structure.	SDS 0.5% supported stem cell attachment and viability.	SDS grafts showed promising animal model results.
Soebroto et al. (2024)[12]	SDS 0.5% effective, though ASB-16 offered additional benefits.	SDS preserved structure, with ASB-16 offering enhanced performance in specific contexts.	Not reported.	SDS performed well, ASB-16 showed additional benefit in specific assays.	*In vitro* study; SDS effects promising but require *in vivo* validation.
Faulk et al. (2014)[13]	SDS effectively removes cellular components while maintaining overall structure with proper use.	SDS preserved matrix elements well under controlled exposure.	SDS-treated scaffolds maintained acceptable mechanical integrity when applied correctly.	With adequate washing, SDS-treated scaffolds supported recellularization.	SDS treatment offers reliable structural preparation for further testing.

on.[12] On the other hand, 0.5% SDS scaffolds facilitated better stem cell attachment and proliferation.

Preclinical outcomes

Short-term patency of SDS-decellularized bovine jugular conduits was shown in animal models; however, at mid-term follow-up, complications like calcification and stenosis were observed.[10] These results imply that SDS by itself might not offer sustained durability.

Alternatives and future directions

Zwitterionic detergents like ASB-16 maintain ECM more effectively but are actually expensive and less accessible.[9] Hybrid methods mixing SDS with enzymatic digestion or nuclease washes could improve outcomes.

In environments with limited resources, SDS-decellularized bovine jugular veins provide a feasible start for the manufacture of locally produced xenografts. But long-term durability is still not proven, and it may be necessary to add anti-calcification or bioactive modifications to the composition.

Discussion

In the context of tissue-engineered pulmonary xenografts, decellularization of bovine jugular veins using sodium dodecyl sulfate (SDS) has shown promise but requires careful optimization of detergent concentration, exposure time, and post-processing steps to ensure safety and clinical applicability. This discussion examines the principal concerns regarding decellularization efficacy, extracellular matrix (ECM) preservation, mechanical stability, cytotoxicity and recellularization potential, preclinical translation, and prospective developments.

Decellularization efficiency

The crucial step to decellularization is getting rid of cellular and nuclear material. Residual DNA levels exceeding 50 ng/mg of dry tissue indicate immunogenic risk, whereas the histological absence of nuclei constitutes a vital quality standard. Numerous studies demonstrate that SDS concentrations ranging from 0.5% to 1% reliably attain over 90% nuclear clearance.[8,13] Protocols utilizing 1% SDS resulted in more significant DNA removal compared to 0.5% SDS, but at the expense of more ECM disruption.

Residual nuclear remnants occasionally observed with 0.5% SDS demonstrate the difficulty of balancing the reduction of immunogenicity with the preservation of ECM[9]. From an immunological point of view, incomplete decellularization poses a risk of retaining antigenic material that could induce graft rejection.[6]

Extracellular matrix preservation

SDS is a strong ionic detergent that dissolves down cellular membranes and changes the structure of ECM proteins. Recent evidence shows that 0.5% SDS preserves collagen I/III and elastin better than 1% SDS, which causes glycosaminoglycan (GAG) loss and less retention of growth factors.[4,13]

Histological and immunohistochemical analyses show that laminin and fibronectin expression diminish following high SDS exposure, thus preventing adhesion and recellularization potential.[10] Composite protocols, such as 0.25% SDS in conjunction with non-ionic detergents, can maintain ECM ultrastructure while allowing effective decellularization.[12]

Biomechanical integrity

Mechanical competence is essential for the long-term sustainability of vascular grafts. Research suggests that SDS-treated bovine veins preserve burst pressure and tensile strength comparable to native tissue when exposure durations are regulated.[15] However, extended SDS treatment (over 14 days) decreases compliance and mechanical stability, potentially undermining in vivo performance.

Therefore, the concentration and the duration of time that detergent is used are two variables that need to be optimized. Brief exposure to 0.5% SDS combined with enzymatic digestion seems to give beneficial results.

Cytotoxicity and recellularization

Residual SDS is difficult to completely remove and represents a major cytotoxic risk. In vitro assays show that scaffolds treated with 1% SDS demonstrate lower cell viability compared to those treated with 0.5% SDS. This is probably because of interactions between the detergent and the proteins.[8,13] On the other hand, scaffolds that were treated with lower concentrations of SDS made it more straightforward for stem cells to attach to them and grow.[4]

Extended washing, perfusion-based rinsing, and chemical neutralization using substances like calcium chloride are examples of mitigation techniques. Hybrid protocols can further reduce cytotoxic effects while increasing recellularization potential by combining SDS with nonionic detergents or enzymatic digestion.[12]

Preclinical translation and immunogenicity

SDS-decellularized bovine jugular veins demonstrated improved hemodynamics and short-term patency in animal models.[15] However, long-term follow up shows complications like calcification, stenosis, and intimal hyperplasia.[15] These results suggest that chronic graft degeneration may not be inhibited by detergent-based decellularization alone.

A significant obstacle to developing immune tolerance is residual antigenicity, especially xenogeneic epitopes.[6] Therefore, to support host integration, adjunctive modifications such as heparinization, growth factor incorporation, and anti-calcification treatments are needed.[10]

Alternative and hybrid approaches

Despite SDS's effectiveness, shortcomings led to research into alternative detergents. Although they are more expensive and less successful at removing nuclear remnants, zwitterionic agents (CHAPS, ASB-16) provide better ECM preservation.[12] Triton X-100 and other nonionic detergents are milder but insufficient for thick vascular tissues.[7]

Simultaneous combining of SDS with DNase, RNase, or nonionic detergents is a hybrid strategy that improves clearance and reduces ECM disruption.[16] Vacuum-assisted

washing and perfusion-based decellularization improve detergent removal and decreased cytotoxicity.[17]

Clinical and translational implications

SDS-decellularized bovine jugular veins provide a practical and affordable substitute for homograft's in limited--resource regions. However, standardized procedures that guarantee safety, reproducibility, and sterility is necessary for clinical translation. One major obstacle is still regulatory compliance, which includes validating DNA removal, ECM integrity, and detergent clearance.[15]

Future clinical trials must evaluate host immune responses, durability, and growth potential in addition to patency, especially in pediatric populations where conduit growth is important.

Conclusion

In conclusion, SDS is an effective, readily available detergent for decellularizing the bovine jugular vein. Concentrations between 0.5 and 1% maintain a balance between clearing cells and keeping the matrix intact. SDS 0.5% helps keep the structure of the cells better, while SDS 1% makes sure that all of the cells are removed while it also makes the matrix more unstable and more toxic to cells.

Further study should:

1. Establish SDS protocols similar with specific times for exposure.
2. Consider the combination with enzymatic or zwitterionic detergents.
3. Review the long-term preclinical and clinical patency outcomes.
4. Establish protocols that are cost-effective and work in areas with limited resources.

Worldwide, children with congenital heart disease could have a bigger opportunity to use pulmonary conduits if SDS-decellularized bovine jugular xenografts become optimized.

Conflict of interest

None declared.

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Protetická endokarditida s abscesem aortálního kořene jako příčina akutního koronárního syndromu

(Prosthetic valve endocarditis with aortic root abscess as a cause of acute coronary syndrome)

Erika Černá[a], Juraj Hrečko[a], Pavel Žáček[b]

[a] *I. interní kardioangiologická klinika, Lékařská fakulta Univerzity Karlovy a Fakultní nemocnice Hradec Králové, Hradec Králové, Česká republika*
[b] *Kardiochirurgická klinika, Lékařská fakulta Univerzity Karlovy a Fakultní nemocnice Hradec Králové, Hradec Králové, Česká republika*

INFORMACE O ČLÁNKU

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Dostupný online: 21. 9. 2026

Klíčová slova:
Akutní koronární syndrom
Infekční endokarditida
Paravalvulární absces
Patogenní mikroorganismy

SOUHRN

Paravalvulární absces mechanické náhrady je vzácná, avšak závažná komplikace infekční endokarditidy. Může vést k dehiscenci protézy, embolizaci, poruše převodního systému, vzniku píštěle nebo mechanické kompresi koronárních tepen. Kazuistika popisuje případ 68letého muže s infekční endokarditidou mechanické aortální náhrady, komplikovanou paravalvulárním abscesem, útlakem kmene levé věnčité tepny a rozvojem akutního koronárního syndromu.

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Keywords:
Acute coronary syndrome
Infective endocarditis
Pathogenic microorganisms
Prosthesis-related infections

ABSTRACT

Paravalvular abscess of a mechanical valve prosthesis is a rare but serious complication of infective endocarditis. It can lead to prosthetic dehiscence, embolization, conduction system disturbances, fistula formation, or mechanical compression of the coronary arteries. This case report describes a 68-year-old man with infective endocarditis of a mechanical aortic valve prosthesis, complicated by a paravalvular abscess, compression of the left main coronary artery, and the development of acute coronary syndrome.

Úvod

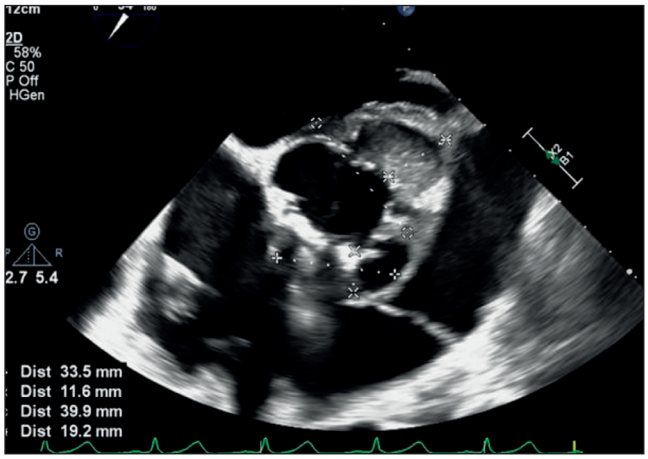
Infekční endokarditida (IE) je zánětlivé onemocnění endokardu. Typicky postihuje pacienty s chlopenní vadou nebo přítomným cizorodým materiálem (např. chlopenní protézy, elektrody kardiostimulátoru). Podle klasické hypotézy patogenní mikroorganismy pronikají ze vstupní brány (dutina ústní, kůže, trávicí trakt) do krevního řečiště, odkud jsou zaneseny do srdce a zachytávají se na postiženém endokardu, kde dochází k jejich následnému množení a tvorbě tzv. vegetací – což jsou útvary tvořené bakteriemi, leukocyty a fibrinem. Lokální a systémové působení bakteriálních toxinů a následná reakce imunitního systému odpovídají za příznaky IE, které jsou často nespecifické. Při postižení chlopenní náhrady může dojít k průniku infekce do okolí protézy – což může vést až k dehiscenci protézy, poruše převodního systému, vzniku píštěle, embolizaci vegetací nebo mechanické kompresi koronárních tepen. Absces je zánětlivá kolekce kolem chlopenní náhrady a představuje vzácnou, avšak závažnou komplikaci IE. Paravalvulární absces vyžaduje včasnou diagnostiku a efektivní cílenou léčbu.

Popis případu

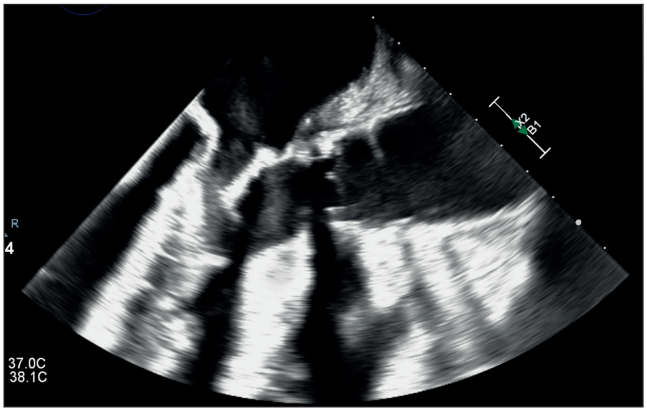
Osmašedesátiletý, plně aktivní muž, s anamnézou náhrady aortální chlopně mechanickou protézou a implantovaným kardiostimulátorem pro atrioventrikulární (AV) blokádu 3. stupně (21 let před přijetím), byl přijat na spádové interní oddělení pro čtyři měsíce trvající recidivující febrilie. Byly vyloučeny běžné infekční zdroje a pro pozitivní nález sta-

Adresa pro korespondenci: MUDr. Erika Černá, I. interní kardioangiologická klinika, Lékařská fakulta Univerzity Karlovy a Fakultní nemocnice Hradec Králové, Sokolská, 500 05 Hradec Králové – Nový Hradec, Česká republika, e-mail: erika.cerna1@fnhk.cz
DOI: 10.33678/cor.2026.085

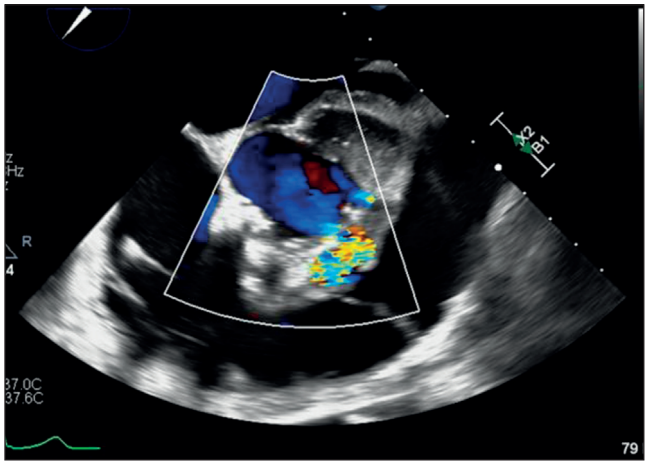
Tento článek citujte prosím takto: Černá E, Hrečko J, Žáček P. Protetická endokarditida s abscesem aortálního kořene jako příčina akutního koronárního syndromu. Cor Vasa 2026;68:605–609.



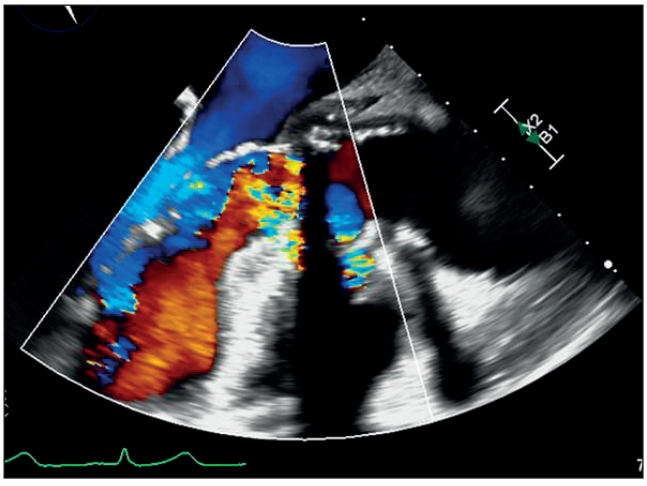
Obr. 1 – Rozsáhlý, prakticky cirkulární absces kořene mechanické aortální náhrady (při TTE vyšetření). TTE – transtorakální echokardiografie.



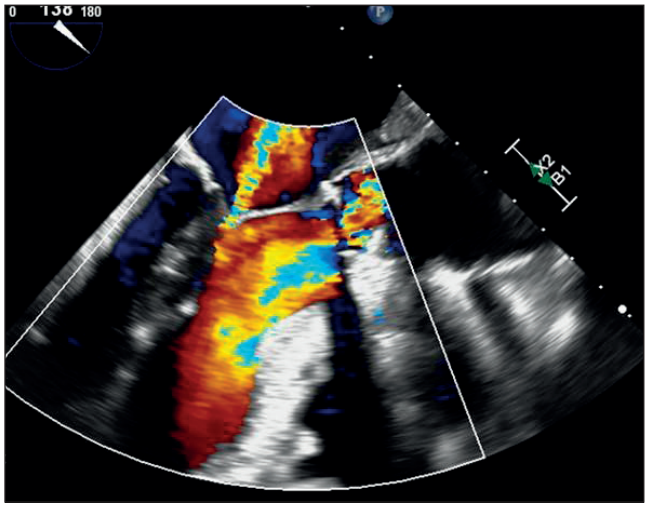
Obr. 4 – Rozsáhlý absces kořene aorty (TEE). TEE – transezofageální echokardiografie.



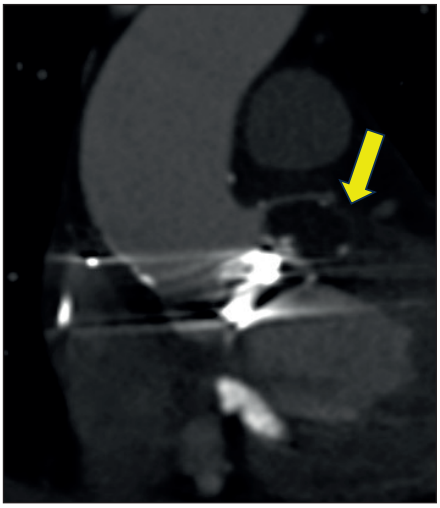
Obr. 2 – Promývané abscesové dutiny aortálního kořene (TTE s barevným dopplerovským mapováním). TTE – transtorakální echokardiografie.



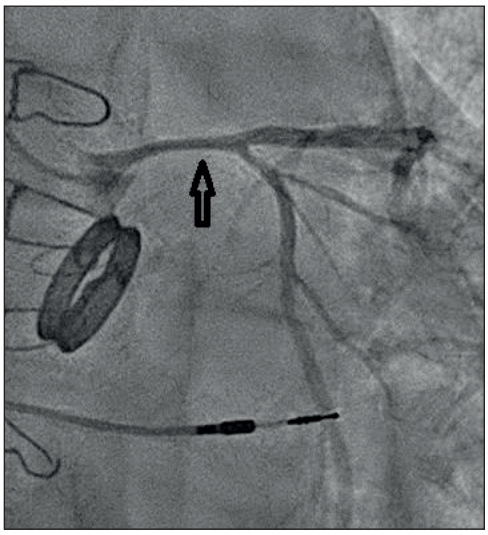
Obr. 5 – Absces s promývanou abscesovou dutinou kořene aorty (TEE). TEE – transezofageální echokardiografie.



Obr. 3 – Významná paravalvulární regurgitace se širokým jetem vyplňujícím prakticky celý výtokový trakt levé komory (TEE s CFM). CFM – colour flow mapping; TEE – transezofageální echokardiografie.



Obr. 6 – Abscesová dutina kořene aorty (CT angiografie). CT – výpočetní tomografie.

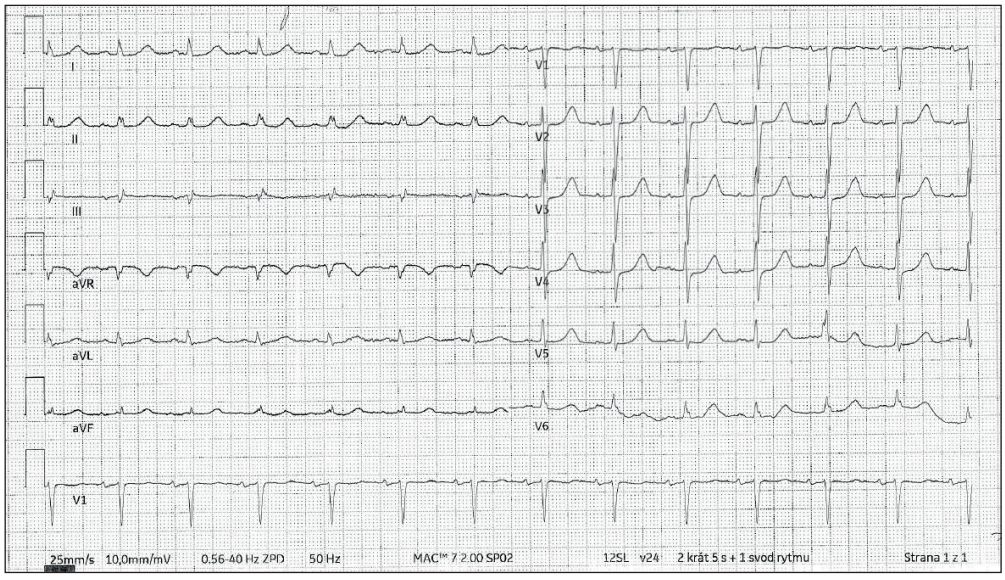


Obr. 7 – Koronarografický nález s obrazem útlaku a elongace kmene levé věnčité tepny.

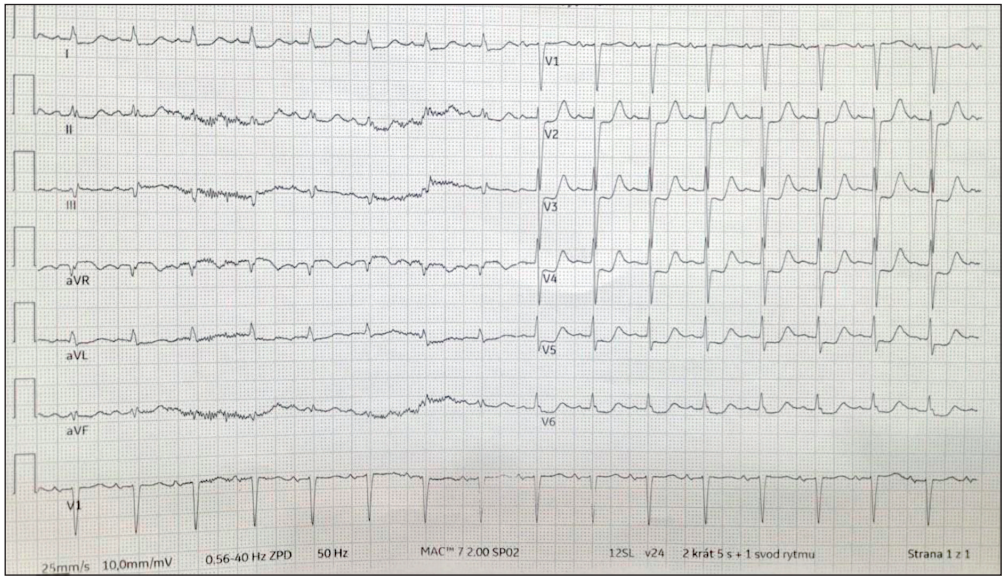
fylokoků v hemokulturách u predisponovaného jedince byl přeložen na naše oddělení s podezřením na infekční endokarditidu.

Při vstupním vyšetření byl auskultačně přítomen klik mechanické chlopenní protézy se systolicko-diastolickým šelestem, laboratorně byla zjištěna elevace zánětlivých parametrů. Odebrané hemokultury opakovaně prokázaly přítomnost *Staphylococcus hominis* a byla zahájena cílená antibiotická léčba flucloxacillinem a rifampicinem. Jícnová echokardiografie odhalila rozsáhlý, prakticky cirkulární absces kořene aorty s promývanou dutinou (33 × 12 mm), zánětlivá infiltrace zasahovala suspektně až do aortomitrální kontinuity (**obr. 1–6**). Na aortální náhradě byla patrna menší vlající vegetace a dále byla prokázána významná paravalvulární regurgitace (**obr. 3, 5**) kolem mechanické protézy. Na elektrodách stimulačního systému v pravostranných oddílech nebylo patrné zjevné zánětlivé postižení.

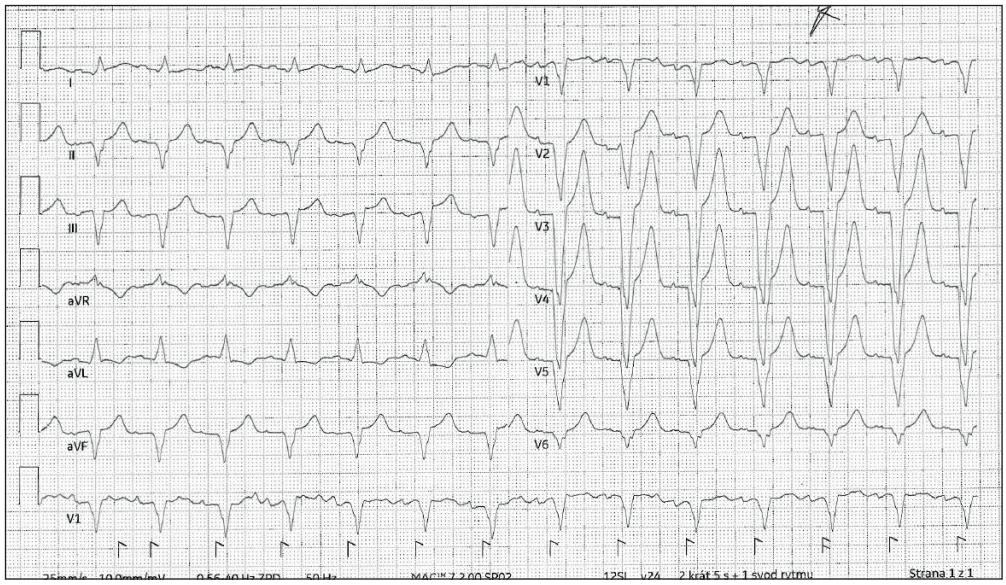
Na základě nálezu byl pacient multidisciplinárním kardiotýmem indikován k časnému operačnímu výkonu. Při



Obr. 8 – Vstupní EKG při přijetí.



Obr. 9 – EKG při první epizodě anginy pectoris s obrazem kmenové ischemie.



Obr. 10 – EKG při pokračujících bolestech na hrudi s obrazem blokády levého Tawarova raménka, těsně před transportem na operační sál.

antibiotické léčbě zánětlivé parametry klesaly a kontrolní hemokultury byly již negativní. Před plánovanou operací se objevily typické anginózní bolesti na hrudi, na EKG byl nejprve obraz kmenové ischemie s následným vývojem blokády levého Tawarova raménka (**obr. 8–10**). Urgentní koronarografie prokázala útlak kmene levé věnčité tepny při jinak normálním nálezu na koronárních tepnách (**obr. 7**). Po korekci supraterapeutických hodnot mezinárodního normalizovaného poměru (INR) pacient podstoupil dlouhý a technicky náročný operační výkon, který byl proveden z resternotomie na mimotělním oběhu, s použitím studené krevní kardioplegie. Byly explantovány pravostranné kardiostimulační elektrody a následně provedena excize původní mechanické chlopně, která byla zcela utržena v jedné třetině obvodu, s toaletou a débridementem destruované okolní tkáně, vlastní aortomitrální kontinuita byla intaktní. Pro nutnost obnovení kontinuity výtokového traktu levé komory (LVOT) při jeho závažném ztrátovém postižení byl implantován aortální homograft. Chirurgický výkon proběhl bez komplikací, pacient byl časně extubován. Další pooperační průběh komplikoval rozvoj přechodné AV blokády 3. stupně s nutností stimulace cestou epikardiálních elektrod, došlo však ke spontánní úpravě rytmu a nebylo nutné implantovat trvalý kardiostimulátor. Kontrolní echokardiografické vyšetření prokázalo dobrý efekt operačního výkonu a pacient byl přeložen k dokončení antibiotické terapie na spádové interní oddělení. Při kontrolním vyšetření s odstupem deset měsíců neměl pacient větší obtíže a echokardiografický nález byl nadále příznivý.

Diskuse

Paravalvulární abscesy u protetických chlopenních náhrad představují jednu z nejzávažnějších forem komplikované infekční endokarditidy. Jejich výskyt odráží rostoucí počet implantovaných mechanických i biologických náhrad (včetně katetrizační náhrady aortální chlopně [TAVI]), což vede k vyššímu absolutnímu počtu případů protetické endokarditidy. Protetická IE tvoří přibližně 20–30 % všech případů endokarditidy ve specializovaných centrech a je spojena s výrazně vyšší mortalitou než endokarditida na nativní chlopni.[1–3] Samotný absces se nejčastěji tvoří v okolí anulu, kde infekce proniká mezi šicí materiál a okolní tkáň. Postižené mohou být mechanické i biologické náhrady, přičemž rozlišujeme časnou (do 12 měsíců od implantace) a pozdní formu protetické infekční endokarditidy. Co se týče infekční endokarditidy na nativní chlopni, je aortální chlopeň a její anulus náchylnější ke vzniku abscesů a přidružených komplikací než mitrální chlopeň a její anulus.[4–6] Zároveň udávaný výskyt perivalvulárních abscesů mezi pacienty s IE je mezi 30–40 %.[4–6]

Mezi závažné komplikace způsobené paravalvulárními abscesy patří periprotetický leak, který je důsledkem destrukce anulu a který může způsobit těžkou regurgitaci a srdeční selhání. Pseudoaneurysmata a fistuly, při kterých mohou vznikat komunikace mezi srdečními oddíly a zhoršovat hemodynamickou stabilitu pacienta. Dále poruchy převodního systému, zejména u aortálních náhrad, kde absces infiltruje membranózní část mezikomorového septa. Vzácně může perivalvulární infekce vést k zevní kompresi koronární tepny a způsobit akutní koronární syndrom.[7] Tento proces může být rychlý a klinicky se projevit jako náhlá těžká ischemie myokardu s obrazem infarktu myokardu s elevacemi úseku ST (STEMI) či infarktu myokardu bez elevací úseku ST (NSTEMI), s kardiogenním šokem nebo náhlou smrtí. Tato vzácná komplikace je popsána spíše v jednotkách případů v konkrétních kazuistikách. Vzhledem k často klinicky němé symptomatologii je diagnostika obtížná.

Transtorakální echokardiografie (TTE) a transezofageální echokardiografie (TEE) jsou primární nástroj pro diagnostiku protetické IE; obě jsou doporučeny pro pacienty s podezřením na protetickou IE.[8–10] Transtorakální echokardiografie má omezenou senzitivitu, zatímco TEE

a moderní CT angiografie významně zlepšují detekci paravalvulárních komplikací u protetických chlopní. CT navíc umožňuje detailní zobrazení rozsahu destrukce a přítomnosti pseudoaneurysmat, což je klíčové pro plánování chirurgické léčby.

Chirurgická léčba zůstává základním pilířem terapie v kombinaci s cílenou intravenózní antibiotickou terapií. Radikální odstranění infikované tkáně a rekonstrukce anulu jsou technicky náročné výkony, zejména u rozsáhlých abscesů. Reoperace u protetické IE s sebou nese vysokou míru chirurgické mortality a dlouhodobé přežití bývá často nepříznivé.[11,12] Neprovedení operace ve včasném termínu je spojováno s časnou úmrtností.[12] Prognóza závisí na rychlosti diagnózy a načasování komplexní léčby.

Závěr

Kazuistika dokumentuje závažné komplikace protetické infekční endokarditidy s tvorbou abscesu kořene aorty s externí kompresí kmene levé věnčité tepny a rozvojem akutního koronárního syndromu. Zdůrazňuje význam časné multimodální diagnostiky a těsné spolupráce kardiologa, kardiochirurga a infektologa při rozhodování o urgentním chirurgickém řešení.

Poděkování
Poděkování patří všem kolegům, kteří se podíleli na péči o pacienta a svými radami pomohli při tvorbě tohoto článku.

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Osobnosti

Zpráva o knize

Zemřel doc. MUDr. Peter Kubuš, Ph.D., dlouholetý primář kardiologického oddělení Dětského kardiocentra



S hlubokým zármutkem jsme přijali zprávu, že dne 4. října 2026 po vážné nemoci zemřel ve věku 50 let doc. MUDr. Peter Kubuš, Ph.D., dlouholetý primář kardiologického oddělení Dětského kardiocentra 2. lékařské fakulty Univerzity Karlovy a Fakultní nemocnice Motol a Homolka.

S Dětským kardiocentrem spojil podstatnou část své profesní dráhy, pracoval zde od roku 2001. Jako dětský kardiolog se následně specializoval především na poruchy srdečního rytmu, jejich invazivní diagnostiku a léčbu a na kardiostimulaci. V letech 2016 až 2025 působil zároveň jako primář kardiologického oddělení.

Vedle klinické práce se dlouhodobě a systematicky věnoval vědecké činnosti. Byl autorem či spoluautorem téměř sedmdesáti odborných publikací evidovaných v databázi Web of Science a jeho práce získaly významný mezinárodní citační ohlas. Publikoval v předních mezinárodních kardiologických časopisech. Ve svém výzkumu se soustředil především na poruchy srdečního rytmu v dětském věku, katetrizační ablace, kardiostimulaci a srdeční resynchronizační léčbu. Významně se zapojoval také do mezinárodních multicentrických studií a byl spoluautorem mezinárodních odborných doporučení v oblasti dětské elektrofyziologie a implantabilních srdečních přístrojů.

V roce 2016 úspěšně ukončil postgraduální studium obhajobou disertační práce na téma Resynchronizace a prosynchronizace při trvalé kardiostimulaci u dětí. V roce 2020 obhájil habilitační práci Elektrický management srdečního selhání u dětí a pacientů s vrozenou srdeční vadou a byl jmenován docentem Univerzity Karlovy pro obor pediatrie. Jako akademický pracovník 2. lékařské fakulty Univerzity Karlovy se podílel také na výuce a vzdělávání dalších generací lékařů.

Pro své kolegy byl respektovaným odborníkem a spolehlivým spolupracovníkem, pro pacienty a jejich rodiny především lékařem, který dokázal spojit vysokou odbornost s lidským a klidným přístupem. S dětskými pacienty uměl navázat přirozený kontakt a získat si jejich důvěru. Právě tato schopnost byla v jeho práci stejně důležitá jako jeho rozsáhlé odborné znalosti a zkušenosti.

Docent Peter Kubuš zanechal výraznou stopu v české dětské kardiologii, v práci Dětského kardiocentra i v životech pacientů a rodin, o které pečoval. Jeho odchod znamená pro naše pracoviště i celý obor velkou ztrátu. Česká dětská kardiologie v něm ztrácí jednoho z mála špičkových odborníků na poruchy srdečního rytmu v dětském věku a my ztrácíme kolegu, se kterým jsme po mnoho let sdíleli každodenní práci Dětského kardiocentra.

Rodině, blízkým, kolegům a všem, které jeho odchod zasáhl, vyjadřujeme upřímnou soustrast.

Čest jeho památce.

doc. MUDr. Ondřej Materna, Ph.D.,
přednosta Dětského kardiocentra 2. lékařské fakulty Univerzity Karlovy a Fakultní nemocnice Motol a Homolka



Jan Pavlíček a kolektiv: Vrozené srdeční vady v klinické praxi. Etiopatogeneze, rizikové faktory, diagnostika a sledování

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Kniha představuje souhrn rozsáhlé problematiky vrozených srdečních vad, které tvoří nejčastější vrozenou anomálii v populaci. Autorům se podařilo velmi přehledně sepsat informace o vrozených srdečních vadách týkající se jejich genetických i negenetických rizikových faktorů, jejich etiopatogeneze, embryologie a klasifikace. Výborné je zařazení moderních poznatků molekulární genetiky, prenatální a postnatální diagnostiky, velmi kvalitní je obrazová dokumentace z oblasti zobrazovacích metod.

V části věnované klinické problematice jsou přehledně uváděny diagnostické postupy, specifická léčba jednotlivých vad, pozornost je věnována také organizaci péče, etickým otázkám, paliativní péči. Celé dílo je přehledně uspořádaný soubor komplexních poznatků, vytvořený špičkovými odborníky v oboru dětské kardiologie, pediatrie a dalších specializací. Je jisté, že bude vynikající učebnicí nejen pro dětské kardiology, ale i pro kardiology i internisty obecně. Jak je konstatováno v předmluvě knihy, díky pokrokům zejména v oblasti prenatální diagnostiky, dětské kardiologie i kardiochirurgie je prognóza dětí narozených s vrozenou srdeční vadou zásadně lepší, než tomu bylo dříve, tato krásná monografie k dalšímu zlepšení jednoznačně přispívá. Kromě díků a gratulace autorům je jistě správné připomenout velmi kvalitní grafické a redakční zpracování této monografie vydavatelstvím Grada.

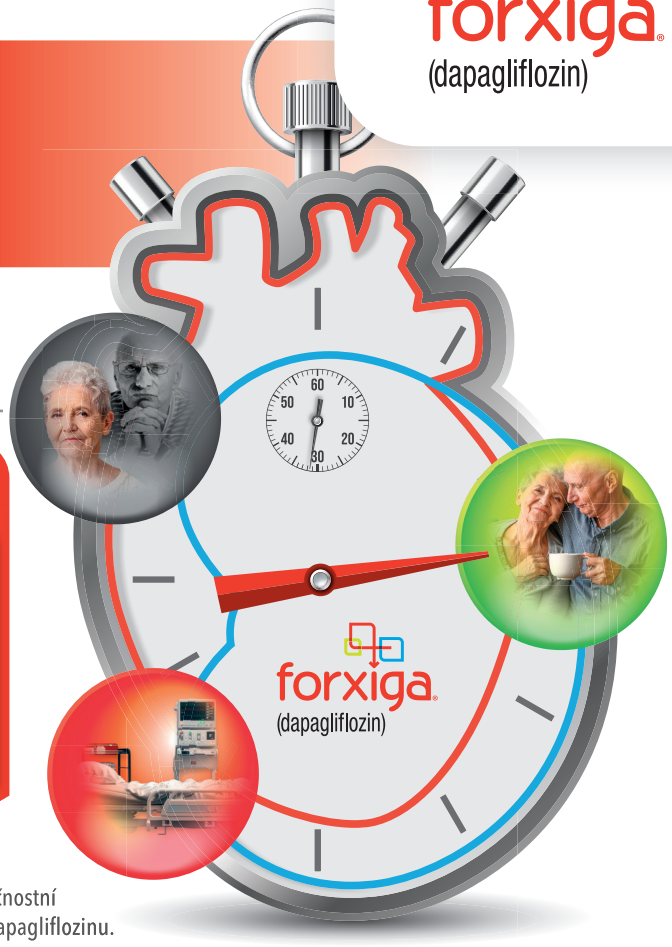
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DM2

SNÍŽENÍ KV ÚMRTÍ[1]

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 placebo[2]

31 % RRR

Sekundární cíl studie DAPA-CKD*

HR 0,69
(95% CI; 0,53–0,88)
p = 0,004

HF

SNÍŽENÍ KV ÚMRTÍ[3]

14 % RRR

Metaanalýza studií DAPA-HF a DELIVER#

HR 0,86
(95%CI: 0,76–0,97)
p < 0,01

Bezpečnost dapagliflozinu v uvedených studiích je srovnatelná s placebem. Celkový bezpečnostní profil dapagliflozinu u pacientů s HF a CKD odpovídal známému bezpečnostnímu profilu dapagliflozinu.

+ **Studie DECLARE:** multicentrická, randomizovaná, dvojitě zaslepená, placebem kontrolovaná 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 účinnostním 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 kontrolovaná 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/1,73m^2 a poměrem albumin/kreatinin v moči (UACR) ≥ 200 až ≤ 5000 mg/g, kteří byli na standartní léčbě (včetně maximálně tolerovaných dávek ACEi nebo ARB). Primární složený cíl studie: ≥50% setrvalé snížení eGFR, onemocnění ledvin v konečném stádiu (ESKD) a renální nebo kardiovaskulární úmrtí. Sekundární cíle: složený renální cíl (≥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 selhaním, která vycházela ze studií DAPA-HF a DELIVER, dapagliflozin vyznamně snížil riziko umrtí z KV příčin 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 umrtí, infaktu 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 redukovanou ejekční frakcí; HR – Hazard Ratio; KV – kardiovaskulární; RRR – relativní redukce rizika.

Reference: 1. KATO, Eri T., Michael G. SILVERMAN, Ofri MOSENZON, et al. Effect of Dapagliflozin on Heart Failure and Mortality in Type 2 Diabetes Mellitus. Circulation [online]. 2019; 139(22), 2528-2536 [cit. 2019-09-30]. DOI: 10,1161/ CIRCULATIONAHA, 119,040130. ISSN 0009-7322. Dostupné z: https://www.ahajournals.org/doi/10,1161/CIRCULATIONAHA,119,040130. **2.** Heerspink HJL et al. N Engl J Med. 2020;383(15):1436-1446. **3.** Jhund PS et al. Nat Med. 2022;28(9):1956-1964.

Zkrácená informace o léčivém přípravku FORXIGA® 10 mg potahované tablety

Kvalitativní a kvantitativní složení: Dapagliflozinum propandiolum monohydricum odpovídající dapagliflozinum 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 přídavná léčba k dietě a fyzické aktivitě ke zlepšení kontroly glykemie - jako monoterapie, pokud je podávání metforminu nevhodné v důsledku intolerance; - jako přídavná léčba k jiným léčivým přípravkům k léčbě DM2. Výsledky studií ve vztahu ke kombinované léčbě s jinými léčivými přípravky, vlivy na kontrolu glykemie 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 inzulinem nebo inzulinovými sekretagogy, lze uvažovat o jejich snížené dávce, aby se snížilo riziko hypoglykemie. 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 pravděpodobné 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. Opatrnosti je zapotřebí u pacientů, u kterých může pokles krevního tlaku vyvolaný 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. Pokud se vyskytnou známky nebo symptomy ketoacidózy, mají být pacienti poučeni, aby si změřili hladiny ketonů. Byla pozorována prodloužená ketoacidóza a prodloužená glukosurie. Po ukončení léčby dapagliflozinem může ketoacidóza trvat déle, než je čas odvozený podle plazmatického poločasu eliminace.* Po uvedení přípravků SGLT2i na trh byly u pacientů hlášeny případy nekrotizující fasciitidy perinea (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 NYHA jsou omezené. Nejsou žádné zkušenosti s dapagliflozinem v léčbě CKD u pacientů bez diabetu, kteří nemají albuminurii. Pacienti s albuminurií mohou mít z léčby dapagliflozinem 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 glykemii 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 hypoglykemie, pokud je dapagliflozin podáván souběžně s deriváty sulfonylmočoviny nebo s inzulinem. **Nežádoucí účinky:** Nejčastěji hlášenými nežádoucími účinky v klinických studiích byly infekce pohlavních orgánů, byly popsány případy fimózy, výskyt hypoglykemií byl srovnatelný s placebem, jejich frekvence se zvýšila při kombinaci se SU či inzulinem. Dalšími častými nežádoucími účinky byly infekce močových cest, závrať, 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:** Nevyžaduje se. **Druh obalu a velikost balení:** Al/Al blistr, 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/1/12/795/007-008, EU/1/12/795/009-010. **Datum revize textu:** 12. 3. 2026.

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

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ČESKÁ KARDIOLOGICKÁ SPOLEČNOST

Česká asociace akutní kardiologie



6. – 8. prosince 2026

HOTEL THERMAL, Karlovy Vary

24. KONFERENCE ČESKÉ ASOCIACE AKUTNÍ KARDIOLOGIE

Bohatý program, zaměřený na akutní a intenzivní kardiologickou péči, bude doplněn třemi 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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