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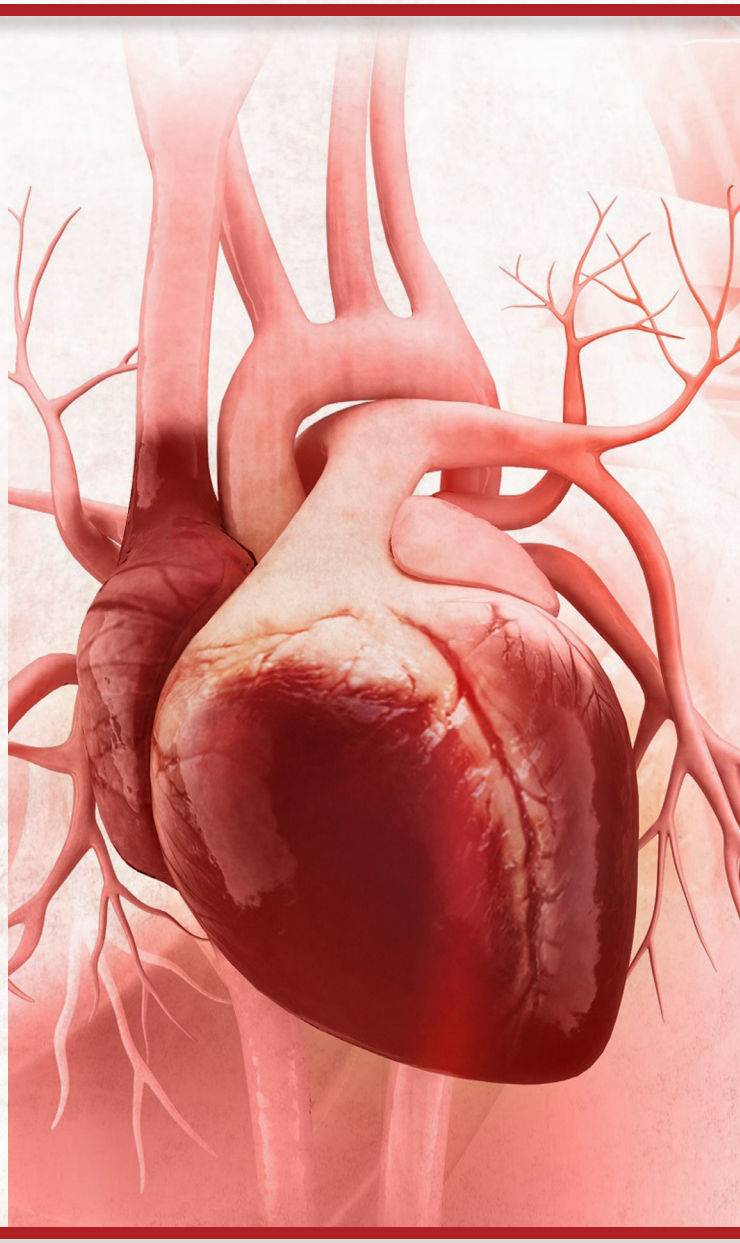

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EDITORIAL

Coronary Artery Aneurysms After Drug-Coated Balloon Angioplasty

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Drug-coated balloons (DCBs) deliver an antiproliferative agent directly to the vessel wall during balloon inflation without leaving a permanent metallic scaffold. This "leave-nothing-behind" approach preserves native vascular anatomy and function while reducing the long-term complications associated with permanent implants. DCB therapy was initially used to treat in-stent restenosis, later expanded to small-vessel and bifurcation lesions, and subsequently applied to *de novo* lesions in larger coronary vessels.[1] Although DCB angioplasty is generally considered safe, coronary aneurysm have occasionally been reported as a rare but potentially important complication. In this paper, we briefly discuss the potential mechanisms underlying coronary aneurysm formation following DCB treatment.

The available evidence on post-DCB aneurysms is derived primarily from case reports, case series, and observational studies, with reported frequencies varying widely (Figure 1). One non-chronic total occlusion (CTO) series reported no aneurysms,[2] whereas another reported an incidence of 0.8%.[3] In contrast, a CTO series reported a substantially higher incidence of 8%.[4] However, because most coronary aneurysms are asymptomatic, their detection depends on planned or clinically indicated follow-up imaging, which is not performed routinely in most patients. Aneurysms may develop relatively early after treatment, although the optimal timing of follow-up imaging remains unknown. In clinical trials, aneurysm formation is rarely defined as a prespecified endpoint, and its low incidence leaves most studies underpowered to detect differences between treatment groups. Moreover, complex lesion subsets are often excluded from clinical trials, further limiting the assessment of patients who may be at greater risk. The available literature is also susceptible to publication bias, selection bias, and surveillance bias, because patients with complex lesions, including CTOs, are more likely to undergo repeat angiography or additional imaging. Furthermore, angiographic findings suggestive of aneurysms may occasionally require intracoronary imaging for confirmation. Some areas of abnormal dilation following DCB angioplasty may represent plaque cavities rather than true aneurysms. One proposed explanation is that plaque regression leaves a cavity within the plaque while preserving the normal architecture of the vessel wall.[2] For these reasons, the true incidence of DCB-related coronary aneurysms remains uncertain and cannot be reliably estimated from the current literature.

Several mechanisms may explain why these aneurysms occur after DCB treatment. First, aneurysm formation may be related to the drug. Two

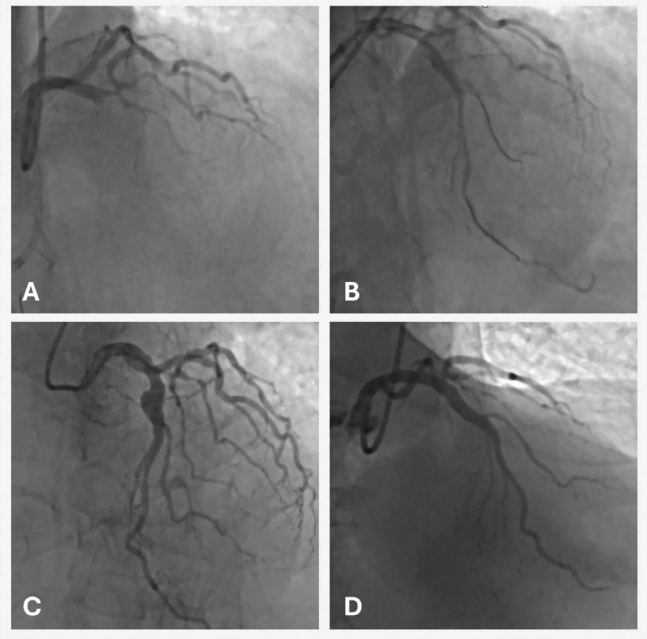

Figure 1. Coronary aneurysm after drug-coated balloons (DCB) treatment of a left anterior descending artery (LAD) chronic total occlusion (CTO). The patient was referred for percutaneous intervention of an LAD CTO (A). The lesion was crossed using antegrade wiring and treated with a DCB. Note the non-flow-limiting dissection at the proximal cap site (B). Follow-up angiography demonstrated aneurysmal dilatation of the treated segment (C). Final angiographic result after implantation of a covered stent (D)

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main classes of antiproliferative agents are used in DCBs. Paclitaxel has long been the predominant agent because its high lipophilicity facilitates rapid arterial uptake and prolonged tissue retention after brief balloon inflation. It is a cytotoxic agent that stabilizes microtubules, arrests the cell cycle in the G2/M phase, and promotes apoptosis of vascular smooth muscle cells.[5] Sirolimus, in contrast, is a cytostatic agent that inhibits the mammalian target of rapamycin pathway and induces cell-cycle arrest in the G1 phase.[5] Its lower lipophilicity and shorter tissue retention initially made balloon-based delivery more challenging. However, advances in carrier and drug-reservoir technologies have enabled the development of sirolimus-coated balloons. Although both agents inhibit neointimal growth, differences in their mechanisms of action and tissue distribution may result in distinct vessel wall responses. Experimental studies suggest that high local concentrations of paclitaxel cause greater apoptosis, smooth muscle cell loss, collagen depletion, macrophage accumulation, and disruption of the internal elastic lamina than sirolimus.[6] Moreover, paclitaxel appears to have a narrower therapeutic window, with excessive tissue concentrations potentially shifting its effects toward vascular toxicity.[6]

Late lumen enlargement (LLE), which is thought to result from vessel enlargement and plaque regression, has been described after DCB treatment of *de novo* coronary lesions.[7] LLE may occur more frequently after treatment with paclitaxel-coated balloons than with sirolimus-coated balloons.[8] However, the same cytotoxic and proapoptotic effects that contribute to positive remodeling may become excessive in some patients, resulting in medial injury, wall thinning, and aneurysm formation. Indeed, almost all published cases of DCB-related aneurysms have occurred after treatment with paclitaxel-coated balloons. This pattern, however, may partly reflect the earlier introduction and much wider use of paclitaxel-coated balloons. Moreover, coronary aneurysms have also been reported after sirolimus-eluting stent implantation.[9,10] Although the metal scaffold and polymer coating may also contribute, the role of sirolimus itself cannot be entirely excluded.

Another proposed mechanism is non-uniform drug transfer resulting from irregular plaque or vessel geometry or heterogeneous drug penetration in the presence of extensive calcification. The resulting heterogeneity in tissue drug exposure and vascular healing may create focal areas of vessel wall weakness, thereby promoting aneurysm formation.[11]

Drug dose, excipient or carrier composition, coating integrity, and tissue transfer efficiency vary among devices. Accordingly, the vascular response to DCB angioplasty may be device-specific rather than drug-specific.

A second potential mechanism is mechanical trauma. DCBs function as drug-delivery devices and are not intended for lesion modification. The lesion should therefore be adequately prepared before DCB application to achieve sufficient expansion and minimize residual stenosis and recoil. Lesion preparation using conventional non-compliant or specialty balloons, as well as advanced plaque-modification techniques such as atherectomy, inevitably results in some degree of vessel wall injury and frequently causes dissection.[12] Dissection is not necessarily an unfavorable finding. It may indicate effective lesion preparation and facilitate drug penetration into the deeper layers of the vessel wall. A higher dissection index has also been associated with more pronounced LLE,[7] potentially reflecting greater vessel wall modification and drug exposure. Concerns arise when the dissection is extensive or extends deeply into the vessel wall. When vascular healing is delayed by antiproliferative therapy, a vessel wall already weakened by medial injury may be less able to withstand intraluminal pressure in the absence of scaffold support, resulting in aneurysmal dilation. In one study, no aneurysms occurred in vessels without dissection or in those with type A dissection, and all coronary aneurysms developed at a previous dissection site, with more than half associated with type C dissections.[4] In our practice, when angiography suggests extensive dissection with deep vessel wall disruption, we have adopted a lower threshold for stent implantation.

Aneurysm formation may also depend on lesion characteristics. The risk may be greater in complex lesions because they often require more intensive lesion preparation. This is particularly relevant in CTO lesions, where vessel wall injury may result from lesion preparation as well as wire-crossing and re-entry techniques that create extraplaque tracks, medial disruption, and long dissections. The presence of

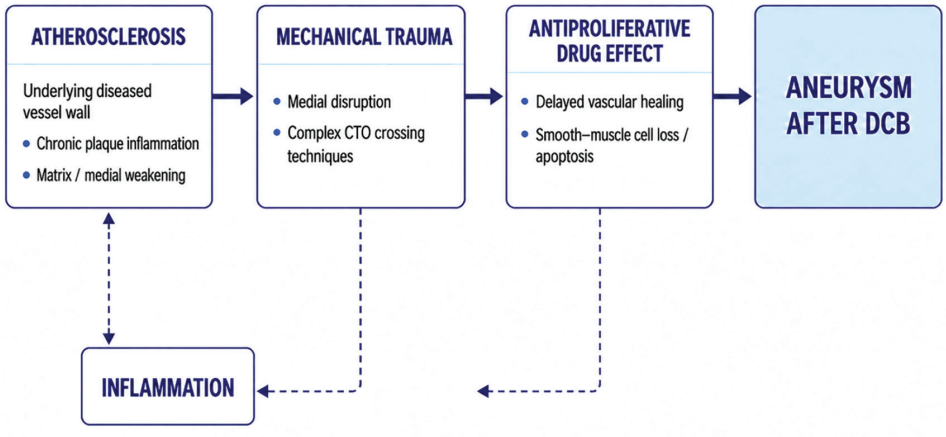

Figure 2. Possible mechanisms of aneurysm formation after DCB angioplasty
CTO: Chronic total occlusion, DCB: Drug-coated balloon

collateral circulation may also make operators more willing to accept larger dissections during CTO procedures and leave them unstented. Some of these dissections may subsequently heal through aneurysmal remodeling.

Inflammation represents a third potential mechanism. Atherosclerosis is characterized by both systemic and local inflammation. Independent of percutaneous coronary intervention, lipid accumulation, chronic inflammation, and matrix-degrading activity can weaken the media and extracellular matrix, thereby contributing to coronary aneurysm formation.[13] Mechanical trauma and the inflammatory response associated with local drug delivery may further contribute to this underlying process. This interaction may be particularly important in patients with acute coronary syndrome, in whom local and systemic inflammatory activity is more pronounced.[14,15] In this setting, the cytotoxic effects of paclitaxel may further impair vascular healing and increase susceptibility to abnormal remodeling (Figure 2).[16]

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ORIGINAL ARTICLE

First Turkish Experience with the PASCAL TEER System

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ABSTRACT

Background: The PASCAL transcatheter edge-to-edge repair (TEER) system was developed for patients with symptomatic severe mitral regurgitation (MR), particularly those at high surgical risk. However, real-world experience with this system remains limited.

Aim: To report procedural success, in-hospital events, and discharge echocardiographic findings from the first Turkish case series of patients treated with the PASCAL system.

Study Design: Retrospective study.

Methods: We retrospectively reviewed consecutive patients who underwent PASCAL-based TEER at a tertiary care center between January 2023 and October 2025. Clinical, procedural, and echocardiographic data were analyzed.

Results: Twenty-three patients underwent PASCAL-based TEER, with 35 devices implanted (11 P10 and 24 advanced closure and enhancement). Procedural success was achieved in all patients according to the prespecified definition. The patient with single-leaflet device attachment had residual MR ≤2+ at discharge and did not require urgent surgery; therefore, the procedure met the predefined success criteria. Two periprocedural complications occurred: one case of single-leaflet device attachment and one episode of decompensated heart failure. No in-hospital deaths occurred. Procedure duration was longer in patients with fibrotic or lipomatous interatrial septal morphology than in those with a normal interatrial septum (118 vs. 53 minutes; p=0.001). Postprocedural pulmonary venous S>D flow was observed in 21 patients (91%). The mitral valve area decreased from 5.13 cm² to 3.70 cm², and the three-dimensional vena contracta area decreased from 0.63 to 0.18 cm² (both p<0.001). Transmitral gradients increased modestly without clinically significant mitral stenosis.

Conclusion: In this small retrospective series, PASCAL-based TEER was technically feasible and was associated with favorable discharge echocardiographic findings. No in-hospital deaths occurred. These findings are preliminary and should be interpreted with caution.

Keywords: Edge-to-edge repair, cardiovascular, interventional, mitral regurgitation, PASCAL, TEER

INTRODUCTION

Severe mitral regurgitation (MR) is a major contributor to heart failure symptoms and is associated with unfavorable clinical outcomes. For patients who are at high or prohibitive surgical risk, transcatheter edge-to-edge repair (TEER) has become an established therapeutic option.[1] Current guidelines recommend TEER for appropriately selected high-risk patients. Nevertheless, additional real-world evidence is needed to better define clinical outcomes and inform device selection in routine practice.

Although the MitraClip system remains the most widely used device, the Edwards Lifesciences PASCAL system offers several unique design features, including independent leaflet grasping, wider paddles, and a central spacer. These features are intended to enhance leaflet coaptation and reduce leaflet stress, potentially decreasing leaflet-related complications. Given the considerable variability in leaflet anatomy and the distinct mechanisms underlying functional and degenerative MR, device selection should be tailored to each patient's anatomical characteristics to optimize procedural outcomes. Consequently, these design features may offer procedural advantages in carefully selected patients.[2]

Although randomized and observational studies have demonstrated the safety and efficacy of the PASCAL system, additional real-world data are needed, particularly from centers with varying procedural volumes, case mixes, and levels of imaging expertise. Reports from our region remain limited. Therefore, we present our initial single-center experience with PASCAL-based TEER for symptomatic MR.

The aim of this study was to describe patient selection, procedural characteristics, in-hospital events, and echocardiographic findings

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at discharge in our initial experience with the PASCAL system, with particular attention to the practical aspects of procedural planning.[3]

METHODS

Study Design and Population

This retrospective, single-center case series included 23 consecutive patients with symptomatic MR grade ≥3+ who underwent TEER using the PASCAL system at VM Medical Park Hospital, İstanbul, Türkiye, between January 2023 and October 2025. All patients were evaluated by a multidisciplinary heart team and were considered to be at high or prohibitive surgical risk based on clinical assessment. Society of Thoracic Surgeons (STS) and EuroSCORE II values were not recorded consistently and were therefore unavailable for analysis. Baseline assessment was performed using transthoracic echocardiography, and two-dimensional (2D) and three-dimensional (3D) transesophageal echocardiography (TEE) were used for procedural planning.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. It was approved by the Institutional Review Board (IRB) of İstanbul Aydın University (approval no: 154/2025, date: 09.07.2025). Written informed consent was obtained from all participants before the procedure.

Inclusion Criteria

Patients were eligible if they had symptomatic grade 3+ or 4+ primary or secondary MR and were considered to be at high or prohibitive surgical risk by the heart team. Anatomical suitability was determined based on the overall mitral valve anatomy rather than a single measurement. Leaflet length and mobility, coaptation gap and depth, calcification, image quality, and the anticipated feasibility of leaflet grasping were evaluated collectively. A posterior leaflet length of approximately ≥9 mm, a coaptation gap of ≤10 mm, and a coaptation depth of ≤11 mm were used as practical reference values, particularly for functional MR. Borderline measurements were accepted when the overall anatomy was considered suitable. Adequate transesophageal echocardiographic image quality was required to ensure clear visualization of the target leaflets and the grasping zone.

Exclusion Criteria

Patients were excluded if any of the following conditions were present: active infective endocarditis, an intracardiac mass or thrombus, rheumatic mitral valve disease, or severe mitral annular calcification that precluded safe device implantation. To minimize the risk of postprocedural mitral stenosis, patients were also excluded if the mitral valve area (MVA) was <4.0 cm^2 or if the baseline mean transmitral gradient was ≥5 mmHg. Additional anatomic exclusion criteria included a posterior leaflet length of <9 mm and severe leaflet calcification within the intended grasping zone that could impair adequate leaflet capture. Patients with known hypersensitivity to device components or contraindications to periprocedural anticoagulation and/or the required postprocedural antithrombotic therapy were also excluded.

Endpoints

The primary endpoint was procedural success, defined as successful PASCAL implantation with residual MR ≤2+ at discharge and no in-hospital death or urgent cardiac surgery. Secondary endpoints included a reduction in MR of at least one grade; changes in the 3D vena contracta area (VCA), MVA, and transmitral gradients; and in-hospital events, including vascular complications, major bleeding, stroke, acute kidney injury, decompensated heart failure, device-related complications, and death. Changes in New York Heart Association (NYHA) functional class and postdischarge outcomes were not evaluated because follow-up data were not consistently available for the entire cohort.

Procedural Technique and Imaging

All procedures were performed under general anesthesia and were guided by fluoroscopy and intraprocedural 2D and 3D TEE using a Philips Affiniti CVx ultrasound system with an X7-2T TEE probe (Philips Healthcare, Andover, MA, USA). TEE was used to guide transseptal puncture, device steering, leaflet grasping, and immediate postimplantation assessment. Procedural characteristics, including the number and type of implanted PASCAL devices and key procedural metrics, were recorded.

Quantitative echocardiographic measurements, including mitral annular dimensions and posterior leaflet length, were obtained using QLAB software (Version 13; Philips Healthcare).

Follow-up and Medical Therapy

Echocardiography was performed at baseline and before discharge according to the institutional protocol. Postdischarge follow-up was incomplete and therefore unsuitable for reliable cohort-level analysis; consequently, these data were not included. Antithrombotic therapy after the procedure was selected according to each patient's underlying indication. Patients who did not require long-term oral anticoagulation received aspirin and clopidogrel for at least 1 month. Those with an indication for oral anticoagulation received oral anticoagulation plus clopidogrel for 3 months, followed by antithrombotic therapy according to the original indication.

Transseptal Puncture Technique

Transseptal puncture was performed under combined fluoroscopic and 2D and 3D TEE guidance. A posterosuperior puncture site on the interatrial septum was targeted to optimize the left atrial device trajectory and alignment with the mitral valve plane.[4]

Mitral Annulus and Leaflet Evaluation

2D and 3D TEE were used for comprehensive assessment of the mitral valve, with 3D TEE preferred for accurate evaluation of the mitral annulus. Measurements were obtained at end-diastole, when annular dimensions are maximal.[5,6] The anatomy of the posterior leaflet guided procedural planning and device selection. Specifically, posterior leaflet length and mobility were assessed using the midesophageal long-axis TEE view (120°-140°) at end-diastole. Patients with a posterior leaflet length of <9 mm were considered anatomically unsuitable for TEER. In patients with restricted posterior leaflet motion despite adequate leaflet length, the PASCAL system was selected because of its independent clasping mechanism, broader paddles, and central spacer.[7]

The estimated number of devices was determined based on the width and segmental extent of the MR jet on baseline TEE, particularly with

respect to commissural involvement.[6] During the procedure, additional devices were implanted incrementally when residual MR jets were present, provided that the mean transmitral gradient remained <5 mmHg. MVA was measured before and after device implantation using planimetry on multiplanar reconstruction (MPR) images derived from 3D TEE datasets.

Three-dimensional Vena Contracta Area Measurement

3D color Doppler full-volume datasets were acquired under electrocardiographic (ECG) gating using an optimized frame rate achieved by narrowing the sector width and reducing the imaging depth, together with optimized color Doppler settings. The Nyquist limit was adjusted (typically by increasing the velocity scale and/or shifting the baseline) to minimize aliasing while maintaining adequate jet definition, and the color gain was set just below the noise threshold. The datasets were cropped to isolate the regurgitant jet and analyzed using MPR with two orthogonal long-axis planes and a corresponding short-axis plane. The imaging planes were iteratively aligned with the narrowest portion of the jet at midsystole, after which the short-axis plane was used to trace the VCA.[8] For multiple jets, VCAs were measured separately and summed. Each measurement represented the average of three cardiac cycles (or ≥5 cycles in patients with atrial fibrillation), while avoiding stitch artifact. Measurements were performed independently by two experienced readers who were blinded to the clinical data, and any discrepancies were resolved by consensus.

Statistical Analysis

Because of the small sample size, the analyses were primarily descriptive. Continuous variables are presented as medians with interquartile ranges (IQRs), and categorical variables as counts and percentages. Independent groups were compared using the Mann-Whitney U test, and paired preprocedural and postprocedural measurements were compared using the Wilcoxon signed-rank test. Multivariable analysis was not performed because the sample size and number of events were insufficient. All statistical tests were two-sided, and a p value of <0.05 was considered statistically significant. Exact p values are reported to three decimal places unless p<0.001. Statistical analyses were performed using Statistical Package for the Social Sciences for Windows, Version 22.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Baseline Characteristics

Baseline characteristics are presented in Table 1. The study included 23 patients, of whom 7 (30%) were women. The median age was 70 years (61-83), and the median body mass index was 27 kg/m^2 (24.0-28.9). Two patients had previously undergone MitraClip implantation. Hypertension was present in 21 patients (91%), diabetes mellitus in 13 (56%), previous myocardial infarction in 16 (70%), heart failure in 18 (78%), and coronary artery disease in 16 (69%). Most patients were classified as NYHA functional class III or IV [class III, 13 (56%); class IV, 2 (9%)]. Medical therapy included beta-blockers in 20 patients (87%), sodium-glucose cotransporter 2 inhibitors in 15 (65%), angiotensin receptor-neprilysin inhibitors in 6 (26%), and furosemide in 18 (78%).

Table 1. Demographic and other characteristics of patients

Variables		Patients [n, median (interquartile), %]
Number		23
Age (year)		70 (61-83)
Gender	Female	7 (30)
	Male	16 (70)
BMI (kg/m^2)		27 (24-28.9)
BSA (m^2)		1.79 (1.7-1.9)
Prior MitraClip		2
Presence of CRT-D		3 (13)
Presence of ICD/pacemaker		4 (17)
History		
Smoking history		3 (13)
Hyperlipidemia		5 (21)
Hypertension		21 (91)
Diabetes mellitus		13 (56)
Myocardial infarction		16 (70)
Heart failure		18 (78)
Presyncope		1 (4)
Syncope		4 (17)
Coronary artery disease		16 (69)
Surgery		4 (17)
Pulmonary arterial hypertension		1 (4)
Chronic obstructive pulmonary disease		1 (4)
NYHA		
I		1 (4)
II		7 (30)
III		13 (56)
IV		**2 (9)**
Use of medication		
Beta blocker		20 (87)
SGLT2 inhibitor		15 (65)
ARNI		6 (26)
Furosemide		18 (78)
Spironolactone		4 (17)
History of CPR		3 (13)
PASCAL device type (device-level denominator, n=35)	P10	11
	ACE	24
Post-procedural need for surgery		0
Complications of procedural		
Clip detachment		1 (4)
Cerebrovascular event		0
Pericardial effusion		0
Bleeding		0
Endocarditis		0
Decompensated heart failure		1 (4)
Death		0

CRT-D: Cardiac resynchronization therapy-defibrillator, ICD: Implantable cardioverter-defibrillator, CPR: cardiopulmonary resuscitation, NYHA: New York Heart Association, SGLT2: Sodium-glucose cotransporter 2

Laboratory and ECG Findings

Baseline laboratory and ECG findings are presented in Table 2. Atrial fibrillation was present in 11 patients (47%), and other conduction and arrhythmic abnormalities are summarized in Table 2. The median N-terminal pro-B-type natriuretic peptide level was 2,913 pg/mL (IQR, 1,102-9,020), and renal function was generally preserved, with a median estimated glomerular filtration rate of 66 mL/min/1.73 m^2 (44-87).

Procedural Characteristics and Device Use

Procedural and echocardiographic data are presented in Table 3. Interatrial septal morphology was normal in 10 patients (43%), fibrotic in 4 (17%), and lipomatous in 9 (39%). A total of 35 PASCAL devices were implanted, including 11 P10 devices (31%) and 24 advanced closure and enhancement devices (69%). The median procedure duration was 78 minutes (50-124). The median procedure duration was 53 minutes (45-67) in patients with a normal interatrial septum and 118 minutes (83-129) in those with fibrotic or lipomatous septal morphology (p=0.001). This comparison was unadjusted, and factors such as case complexity, the number of implanted devices, the presence of intracardiac leads, and operator experience may also have influenced procedure duration.

Safety Outcomes

Two periprocedural complications occurred: one case of single-leaflet device attachment and one episode of decompensated heart failure.

Table 2. Complete Blood Count, biochemical values and ECG findings of patients

Variables	Patients [n, median (interquartile), %]
WBC ($\times10^3$/µL)	6.8 (4.9-11.5)
Hb (g/dL)	11.6 (10.6-13.1)
Hct (%)	35.7 (30.8-39.3)
Plt ($\times10^3$/µL)	228 (211-262)
Total cholesterol (mg/dL)	153 (145-204)
Troponin I (ng/L)	51.2 (22.2-143.4)
NT ProBNP (pg/mL)	2913 (1102-9020)
Uric acid (mg/dL)	6.7 (4.9-8)
Lactate dehydrogenase (U/L)	316 (283-410)
D-dimer (ng/mL)	612 (447-1224)
GFR (mL/min/1.73 m^2)	66 (44-87)
Findings of ECG	
Premature atrial contraction	7 (30)
Premature ventricular contraction	6 (26)
Right bundle branch block	1 (4)
Left bundle branch block	7 (30)
Atrial fibrillation	11 (47)
Supraventricular tachycardia	0
Ventricular tachycardia	5 (21)

ECG: Electrocardiogram, GFR: Glomerular filtration rate, Hb: Hemoglobin, Hct: Hematocrit, NT-proBNP: N-terminal pro-B-type natriuretic peptide, Plt: Platelets, WBC: White blood cells

There were no in-hospital deaths, strokes, major bleeding events, pericardial effusions, cases of endocarditis, or urgent cardiac surgeries. The patient with single-leaflet device attachment had residual MR ≤2+ at discharge and did not require urgent surgery; therefore, the case met the prespecified definition of procedural success.

Echocardiographic and Hemodynamic Outcomes

Functional MR was present in 21 patients (91%) and degenerative MR in 2 patients (9%) (Table 3). Pulmonary venous Doppler findings were recorded for all assessed veins, and the reported flow patterns were not mutually exclusive. S-wave reversal was present before the procedure in 21 patients (91%) but was no longer observed after TEER. An S>D flow pattern was documented after the procedure in 21 patients (91%). The MVA decreased from 5.13 cm^2 (4.92-5.60) to 3.70 cm^2 (3.56-4.10) at discharge ($p<0.001$), and the 3D VCA decreased from 0.63 cm^2 (0.57-0.68) to 0.18 cm^2 (0.14-0.19) ($p<0.001$). Peak and mean transmitral gradients increased modestly (both $p<0.001$), without clinically significant mitral stenosis. Implant locations are reported according to device type and mitral valve segment. The totals exceed the number of patients because some patients received more than one device, and some devices involved adjacent scallops. MR was reduced by at least two grades in 22 patients and by one grade in 1 patient. Procedural success was achieved in all 23 patients.

DISCUSSION

In this initial single-center experience, PASCAL-based TEER was feasible in selected patients with severe MR who were considered to be at high surgical risk. All 23 patients met the prespecified definition of procedural success, defined as successful device implantation with residual MR ≤2+ at discharge and no in-hospital death or urgent cardiac surgery. Two patients experienced periprocedural complications, and no in-hospital deaths occurred. Given the small, uncontrolled cohort, these findings should be interpreted as a description of our early clinical experience rather than as evidence of the comparative safety or efficacy of the PASCAL system.

The overall procedural and echocardiographic findings are consistent with those of previous clinical studies and real-world reports of the PASCAL system.[9] However, the small sample size and observational design of the present study preclude direct comparisons with other devices or treatment strategies.

Beyond technical success, we observed early hemodynamic and echocardiographic improvement. A reduction of at least two MR grades was achieved in 22 patients, whereas one patient experienced a one-grade reduction. Consequently, residual MR was ≤2+ in all patients, with mild residual MR (MR 1+) observed in 22 of the 23 patients. In parallel, quantitative echocardiographic parameters showed meaningful improvement, including a marked reduction in the 3D VCA.

Pulmonary venous Doppler findings also supported the observed reduction in MR. Systolic flow reversal was no longer observed after TEER, and an S>D flow pattern was documented in 21 patients (91%). Because more than one Doppler flow pattern could be recorded among the assessed veins in an individual patient, these findings were not

Table 3. The echocardiography findings of patients

Variables	Patients [n, median (interquartile)]			
Interatrial septum feature				
Normal	10 (43)			
Fibrosis	4 (17)			
Lipomatosis	9 (39)			
Time of procedure (minutes)	78 (50-124)	IAS normal n=10	53 (45-67)	**p=0.001**
		IAS others n=13	118 (83-129)	
LA measurements				
Anterior-posterior diameter (mm)	47 (44-50)			
Medialateral diameter (mm)	48 (44-52)			
Apicobasal diameters (mm)	61 (57-69)			
Left atrial volume (mL)	83.7 (64-95)			
Left atrial volume index (mL/m^2)	46.4 (35.3-56.3)			
Pulmonary venous measurements				
Pre-procedure pulmonary venous S-wave reversal, n (%)	21 (91)			
Post-procedure pulmonary venous S-wave reversal, n (%)	0			
Pre-procedure pulmonary venous S-wave blunting, n (%)	4 (17)			
Post-procedure pulmonary venous S-wave blunting, n (%)	2 (9)			
Preprocedure pulmonary venous S>D	0			
Post-procedure pulmonary venous S>D, n (%)	21 (91)			
Types of mitral valve regurgitation				
Functional	21 (91)			
Degenerative	2 (9)			
Mitral valve measurements				
Annulus measure (mm)	39 (36-42)			
Pre-procedural area (cm^2)	**5.13 (4.92-5.6)**			**p<0.001**
Post-procedural area (cm^2)	**3.7 (3.56-4.1)**			
Anterior leaflet length (mm)	23 (22-24)			
Posterior leaflet length (mm)	14 (12.8-15.5)			
Pre-procedural three-dimensional vena contracta area (cm^2)	**0.63 (0.57-0.68)**			**p<0.001**
Post-procedural three-dimensional vena contracta area (cm^2)	**0.18 (0.14-0.19)**			
Coaptation depth (mm)	11.4 (9-12.3)			
Coaptation length (mm)	3.7 (3-5.2)			
Preprocedure peak gradient (mmHg)	**4 (2.7-4)**			**p<0.001**
Postprocedure peak gradient (mmHg)	**5 (4-7.2)**			
Preprocedure mean gradient (mmHg)	**1.3 (1.1–1.5)**			**p<0.001**
Postprocedure mean gradient (mmHg)	**2.3 (1.9-3)**			
Device/segment location (non-mutually exclusive; 35 devices)				
A1P1	4 (17)			
A2P2	19 (82)			
A3P3	9 (39)			
Decrease in post-procedural mitral regurgitation	23			
Second-degree mitral regurgitation	1			
First-degree mitral regurgitation	22			
Left ventricular measurements				

Table 3. Continued

Variables	Patients [n, median (interquartile)]
Ejection fraction (%)	33.7 (27-52)
Left ventricular end-diastolic diameter (mm)	57 (53-62)
Left ventricular end-systolic diameter (mm)	42 (31-49)
Interventricular septal thickness in diastole (mm)	12 (11-13)
Left ventricular posterior wall thickness in diastole (mm)	10 (9.2-10.7)
Left ventricular length (mm)	75 (69-81)
Left ventricular area (cm^2)	**35 (30-40)**
Left ventricular volume (mL)	131 (106-162)
Left ventricular mass (gr)	278 (224-298)
Left ventricular mass index (g/m^2)	147 (131-168)
Pulmonary artery systolic pressure via tricuspid regurgitation (mmHg)	32 (25-40)

Pulmonary venous Doppler findings indicate the presence of each pattern and are not mutually exclusive across assessed veins. Device/segment locations are reported at the device level; some implants involved more than one adjacent scallop. Values corrected as typographical errors should be verified against the source dataset before final submission. IAS: Interatrial septum, LA: Left atrium

considered mutually exclusive. Therefore, they should be interpreted as supportive evidence, together with the reduction in the 3D VCA, rather than as an independent measure of treatment efficacy.

As expected, transmitral gradients increased modestly after edge-to-edge repair as MR decreased. Importantly, this occurred without evidence of clinically significant iatrogenic mitral stenosis. Overall, mean transmitral gradients remained low, and procedural decisions were guided by maintaining the mean gradient below a predefined intraprocedural threshold (<5 mmHg). Achieving this balance between effective MR reduction and controlled transmitral gradients is particularly important in patients requiring more than one device and highlights the value of a stepwise implantation strategy guided by residual MR jets and transmitral hemodynamics.

The longer procedure duration observed in patients with fibrotic or lipomatous interatrial septal morphology is of practical interest. Difficult transseptal access and a less favorable catheter trajectory may have contributed to this finding.[10,11] Other factors, including mitral valve anatomy, the number and position of implanted devices, previous transseptal procedures, intracardiac leads, case sequence, and operator experience, may also have influenced procedure duration. However, the study was too small to permit a reliable adjusted analysis. Therefore, although septal morphology may be useful for procedural planning, its independent effect on procedure duration requires confirmation in larger studies.

Most patients had functional MR, and the A2-P2 region was the most common implantation site, consistent with routine TEER practice. Because this study reflects our center's early experience with the PASCAL system, increasing familiarity with device steering, independent clasping, transseptal positioning, and coordination between the imaging and interventional teams may have influenced procedure duration. However, the study was not designed to formally evaluate the learning curve.

Study Limitations

Several limitations should be acknowledged. This was a retrospective, single-center study that included only 23 patients, with no control group and multiple echocardiographic comparisons. STS and EuroSCORE II values were not recorded consistently, limiting the objective assessment of surgical risk. Postdischarge follow-up was incomplete; therefore, changes in NYHA functional class, MR severity, rehospitalization, mortality, and reintervention could not be evaluated for the entire cohort. The analysis of the association between interatrial septal morphology and procedure duration was unadjusted and may have been influenced by mitral valve anatomy, the number of implanted devices, intracardiac leads, case complexity, and operator experience. Echocardiographic measurements were obtained at the treating center without independent core laboratory review. In addition, patient-reported outcomes and objective functional assessments were not uniformly available.

CONCLUSION

This initial Turkish experience suggests that PASCAL-based TEER can be performed successfully in a small, carefully selected cohort, with no in-hospital deaths and favorable echocardiographic findings at discharge. The longer procedure durations observed in patients with fibrotic or lipomatous interatrial septal morphology may have implications for procedural planning, although this observation requires confirmation in larger studies with appropriate adjustment for potential confounders. Multicenter studies with systematic surgical risk assessment and longer-term follow-up are warranted.

Ethics Committee Approval: It was approved by the Institutional Review Board (IRB) of İstanbul Aydın University (approval no: 154/2025, date: 09.07.2025).

Informed Consent: Written informed consent was obtained from all participants before the procedure.

Authorship Contributions: Surgical and Medical Practices: S.Ö.Ö., E.A., T.K., H.U., Concept: S.Ö.Ö., M.O., Design: S.Ö.Ö., M.N., T.K., H.U., Data Collection or Processing: S.Ö.Ö., E.A., A.H., Analysis or Interpretation: S.Ö.Ö., M.N., Literature Search: S.Ö.Ö., A.H., M.O., Writing: S.Ö.Ö.

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ORIGINAL ARTICLE

Clinical Determinants of In-Hospital Mortality in a Multicenter Coronary Care Unit Cohort

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ABSTRACT

Background: Cardiovascular diseases remain a major global health concern, and coronary care units (CCUs) provide specialized care for patients with acute cardiovascular conditions.

Objective: This multicenter cohort study aimed to investigate mortality rates in Turkish CCUs and identify predictors of in-hospital mortality.

Study Design: Multicenter, observational cohort study.

Methods: Patients admitted to CCUs across Türkiye with cardiovascular diagnoses were included. Demographic, clinical, laboratory, and outcome data were collected. Regression analyses were performed to identify predictors of in-hospital mortality.

Results: A total of 3,157 patients were included, and the overall CCU mortality rate was 4.3% (n=137). The median age was 65 years (interquartile range, 56-73), and 66.1% of the patients were male. Hypertension (59.8%) and diabetes mellitus (37.5%) were the most common comorbidities. Non-survivors had significantly higher rates of heart failure and chronic kidney disease and lower ejection fractions than survivors. Age, female sex, lower mean blood pressure (BP), elevated serum creatinine, C-reactive protein, and white blood cell count were independent predictors of in-hospital mortality. Mean BP and serum creatinine were the strongest contributors to mortality prediction.

Conclusion: CCU mortality in Türkiye was relatively low. Hemodynamic impairment and renal dysfunction were the primary determinants of in-hospital mortality, highlighting the value of simple clinical parameters for early risk stratification.

Keywords: Coronary care unit, in-hospital mortality, cardiovascular outcomes, mortality predictors, multicenter study

INTRODUCTION

Cardiovascular diseases (CVDs) represent a substantial global public health challenge and remain the leading cause of mortality worldwide. Coronary care units (CCUs) were established specifically to manage CVDs in the late 1960s. Following the initial report by Killip and Kimball[1] demonstrating that the use of a CCU could reduce mortality by nearly 20%, CCUs were widely adopted. Their effectiveness has been demonstrated by an increase in survival rates from 18-20% to 40-46% over several decades of development. Initially focused on the rapid identification and treatment of cardiac arrhythmias, these units subsequently evolved into pivotal research centers dedicated to advancing the treatment of acute coronary syndromes (ACS). Over nearly six decades, the CCU has transformed into a more sophisticated intensive care unit (ICU) that provides comprehensive critical care for patients with a wide range of cardiovascular conditions.[2,3]

Mortality rates in CCUs are influenced by several factors, including patients' preexisting comorbidities, such as diabetes, hypertension, and renal disease, which increase the risk of mortality because of additional cardiovascular risk factors and potential complications. Furthermore, mortality in CCUs is a multifactorial outcome affected by patient characteristics, disease severity, treatment strategies, and the overall quality of healthcare delivery.[4,5] Therefore, evaluating patients' clinical characteristics and factors associated with mortality is essential for improving outcomes and reducing mortality rates in CCUs. Several scoring systems, including APACHE, SAPS II, and GRACE, have been developed to estimate mortality risk in CCUs.[6] However, these scoring systems may not be universally applicable to all CCU populations, and even low scores do not necessarily correlate with lower mortality rates. In addition, differences among patient populations may affect the interpretation of these scores, further complicating mortality risk assessment in CCUs.

International sharing of CCU data, including patient follow-up information, provides valuable insights into mortality outcomes. Variations in demographic characteristics, treatment approaches, and socioeconomic conditions across countries contribute to differences in mortality rates.[7,8] However, previous studies have primarily focused on patients with ACS, highlighting the need for a more comprehensive approach to data collection across diverse patient populations to improve the accuracy of mortality risk assessment in CCUs. Moreover, patients with non-ACS diagnoses, including acute heart failure (HF), arrhythmias, myopericarditis, and cardiogenic shock, constitute a

substantial proportion of the CCU population and may influence survival outcomes.

Türkiye, with a population of approximately 83 million and a well-developed healthcare system, has made substantial progress in improving CCUs. Although CVDs remain the leading cause of death, comprehensive data on mortality rates and predictors in CCUs across all cardiovascular diagnoses, including ACS, remain limited. Accordingly, the MORtality predictors in CCUs in TURKey (MORCOR-TURK) study was designed to characterize Turkish CCUs, evaluate mortality rates among patients with CVDs admitted to these units, and identify predictors of in-hospital mortality. Although the baseline characteristics and overall outcomes of the MORCOR-TURK cohort have been reported previously, the present study provides a focused and more comprehensive evaluation of the determinants of in-hospital mortality, including the relative contribution of individual predictors and their clinical implications for early risk stratification. These findings may help guide clinical decision-making, optimize treatment strategies, and ultimately improve patient outcomes in the critical coronary care setting.

METHODS

Study Design

The MORCOR-TURK study is a prospective, multicenter, observational, non-interventional study. The study was prospectively registered at ClinicalTrials.gov (Identifier: NCT05296694). It included 50 CCUs located across the seven geographical regions of Türkiye.

Study Population

All consecutive patients admitted to the CCUs at 50 centers across Türkiye between September and October 2022 were enrolled. Eligible participants were adults aged 18 years or older of either sex who presented with various cardiovascular emergencies, including ACS, acute HF, arrhythmias, myopericarditis, and cardiogenic shock, and who provided informed consent.

Data collected included demographic and clinical characteristics, hemodynamic status, medical history, laboratory findings, primary diagnoses, in-hospital events, and discharge status. Patients received standard care under the supervision of cardiologists, including medical and interventional therapies. Medications and vital signs were recorded, and adverse events, including arrhythmias, stroke, renal failure, bleeding, and mortality, were documented. No additional medical interventions were performed as part of the study.

Upon admission, routine biochemical tests, cardiac biomarkers (e.g., troponin I and creatine kinase-MB measured at 8-hour intervals), complete blood counts, and lipid profiles were assessed. In addition, all patients underwent two-dimensional M-mode echocardiography. Left ventricular dimensions and wall thickness were measured, and left ventricular ejection fraction (EF) was visually estimated.

Exclusion Criteria

Twenty-four patients who remained in the CCU for less than 4 hours were excluded from the study. In addition, patients admitted to the CCU for reasons other than cardiovascular conditions, including elective procedures such as coronary interventions, peripheral arterial interventions, and transcatheter valve interventions, as well as those who died within 30 minutes despite unsuccessful cardiopulmonary resuscitation (CPR), were excluded (Figure 1).

Center Selection

The process of selecting study centers for the MORCOR-TURK trial was conducted with careful planning. Initially, 50 centers were selected to ensure comprehensive geographic representation based on population density. These centers provided 24-hour CCU care and were distributed across the seven geographical regions of Türkiye.

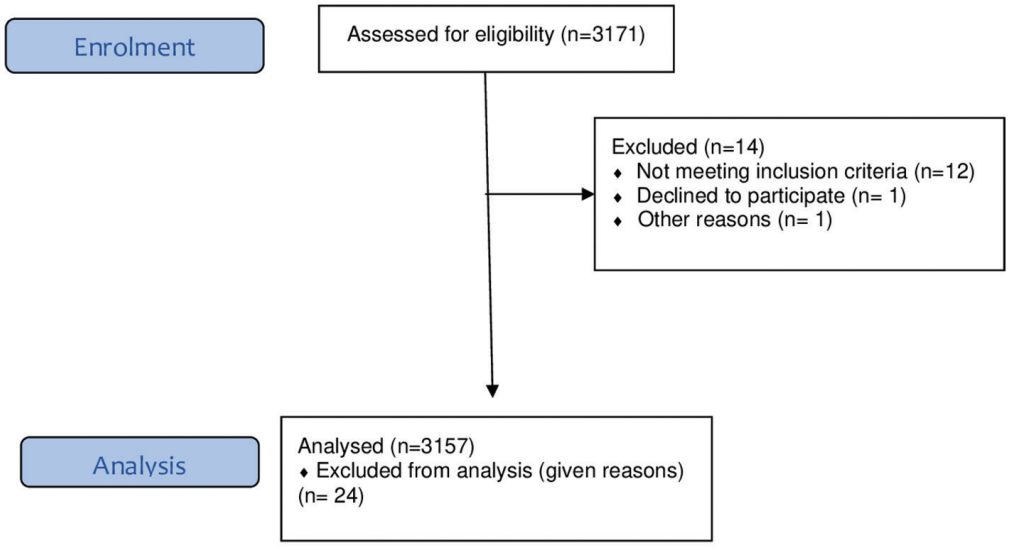

Figure 1. Flow diagram of patient inclusion

Subsequently, a stratified random sampling approach was used to ensure balanced population representation. The final selection of hospitals was intended to be representative of the national healthcare setting in Türkiye based on their geographic distribution and the characteristics of the participating CCUs.

Diagnoses

The diagnosis of ACS was established according to the guidelines of the European Society of Cardiology.[9] ST-segment elevation myocardial infarction (STEMI) was defined by the presence of at least 2 mm of ST-segment elevation in two or more contiguous leads or a new left bundle branch block on a 12-lead electrocardiogram (ECG). Non-STEMI (NSTEMI) was diagnosed in patients with symptoms of myocardial ischemia without ST-segment elevation but with elevated troponin levels. Unstable angina pectoris (USAP) was diagnosed in patients with symptoms of myocardial ischemia and normal troponin levels.

Acute HF was defined as the sudden or gradual onset of HF symptoms. Atrial fibrillation (AF) was diagnosed based on ECG findings of irregular R-R intervals and the absence of distinct P waves. Ventricular tachycardia was defined as premature ventricular complexes persisting for more than 30 seconds on ECG. Bradyarrhythmia was diagnosed when the heart rate was below 60 beats/min and accompanied by any type of atrioventricular block. Cardiogenic shock was defined as persistent hypotension [systolic blood pressure (BP) <90 mmHg or the need for vasopressor support to maintain systolic BP ≥90 mmHg] accompanied by signs of end-organ hypoperfusion, in accordance with contemporary guideline recommendations.

Myopericarditis was diagnosed based on clinical evidence of myopericardial inflammation supported by laboratory findings and imaging modalities, including cardiac magnetic resonance imaging and echocardiography, particularly in patients presenting with typical or atypical symptoms. Coronary angiography and/or percutaneous coronary intervention (PCI) were performed at the discretion of the interventional cardiologist, either immediately, urgently, or electively, to confirm or exclude the presence of coronary artery disease.

In addition, chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 for at least 3 months or a documented history of CKD. The CHA_2DS_2-VA score was calculated for patients with AF to assess thromboembolic risk in accordance with current clinical guidelines.[9] This scoring system is freely available for clinical and research use. Hypertension was defined as a documented history of hypertension or current use of antihypertensive medication. Diabetes mellitus was defined as a documented history of diabetes mellitus, current use of antidiabetic medication, or a previous diagnosis established according to contemporary diagnostic criteria.

Mean arterial pressure was calculated from the admission systolic and diastolic BP measurements using the standard formula: diastolic BP+1/3×(systolic BP-diastolic BP).

Statistical Analysis

Because this was a prospective, nationwide, multicenter observational registry, all consecutive eligible patients admitted during the predefined 1-month study period were included. Therefore, no formal sample size calculation was performed. All statistical analyses were conducted using SPSS version 24 (IBM Corp., Armonk, NY, USA). The primary study endpoint was all-cause in-hospital mortality. Continuous variables are presented as the mean ± standard deviation or median with interquartile range (IQR), depending on the distribution assessed using the Kolmogorov-Smirnov test. Categorical variables are presented as frequencies and percentages.

Comparisons between groups were performed using Student's t-test or the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. To identify predictors of in-hospital mortality, candidate variables were selected based on their clinical relevance and statistical significance. Variables included in the univariate analysis were age, sex, comorbidities (coronary artery disease, hypertension, AF, HF, and CKD), CHA_2DS_2-VA score, admission diagnosis and cardiac rhythm, vital signs (mean BP and heart rate), and laboratory parameters, including serum creatinine, sodium, potassium, calcium, C-reactive protein (CRP), hematocrit, white blood cell (WBC) count, platelet count, and low-density lipoprotein cholesterol.

Variables with a significance level of $p<0.25$ in the unadjusted comparisons between survivors and non-survivors, together with clinically relevant variables, were considered for inclusion in the multivariable logistic regression model. To minimize the risk of multicollinearity, variables that were components of composite risk scores were not entered simultaneously with the corresponding score in the final multivariable model. Specifically, the CHA_2DS_2-VA score was not included in the final model together with its individual components. Missing data were handled using complete-case analysis. Patients with missing values for variables included in a specific analysis were excluded only from that analysis, and multiple imputation was not performed.

A backward stepwise multivariable logistic regression analysis was performed to identify the best predictive model for in-hospital mortality. The explanatory power of the model, as measured by the Nagelkerke R^2, increased substantially from 0.25 to 0.70 after the inclusion of mean BP and serum creatinine. The Akaike information criterion decreased from 180 to 150 following the inclusion of these variables, indicating improved model fit. The Wald test confirmed the significance of mean BP ($p<0.001$), and the likelihood ratio test demonstrated a significant reduction in model fit when mean BP was excluded ($p<0.001$). Receiver operating characteristic (ROC) curve analysis was used to evaluate the model's discriminatory ability. Model performance was assessed using standard discrimination metrics to evaluate its predictive accuracy for in-hospital mortality.

Ethical Considerations

Ethical approval for this study was obtained from the Afyonkarahisar Health Sciences University Clinical Research Ethics Committee for non-interventional clinical studies (date: August 5, 2022; meeting no: 2022/9; approval no: 422). The study was conducted in strict accordance with the principles of Good Clinical Practice and the Declaration of Helsinki. Written informed consent was obtained from all participants or their legally authorized representatives, ensuring the ethical integrity and transparency of the study.

RESULTS

A total of 3,157 patients were included in the study (Figure 1). The most common primary diagnosis was NSTEMI, affecting 1,187 patients (38%), followed by STEMI in 742 patients (23.5%). Other common diagnoses included USAP in 355 patients (11.2%), decompensated HF in 438 patients (14%), and arrhythmias in 272 patients (8.6%). Cardiac arrest was relatively uncommon, occurring in 19 patients (0.6%) (Figure 2). During the 1-month study period, 137 patients died, resulting in an overall in-hospital mortality rate of 4.3%. Among non-survivors, decompensated HF was the most frequent diagnosis, accounting for 39 patients (28.4%). STEMI and NSTEMI were each diagnosed in 31 non-survivors (22.6%).

Non-survivors were significantly older than survivors [median age, 73 years (IQR, 63-83) vs. 65 years (IQR, 56-73); p<0.001]. Mortality was also significantly higher among male patients (66.7% vs. 53.3%, p=0.002). Although the difference did not reach statistical significance, the prevalence of hypertension was higher among non-survivors than among survivors (66.4% vs. 58.7%, p=0.076). The prevalence of diabetes mellitus, smoking, and dyslipidemia was similar between the two groups. Likewise, the prevalence of coronary artery disease was higher among non-survivors but did not differ significantly between groups (54.0% vs. 45.4%, p=0.054). Several baseline comorbidities differed significantly between survivors and non-survivors. Patients who died were more likely to have a history of AF (24.8% vs. 14.9%, p=0.003), HF (55.5% vs. 29.9%, p<0.001), and CKD (32.8% vs. 12.9%, p<0.001). They also had a significantly lower median EF (40% vs. 53%, p<0.001) (Table 1).

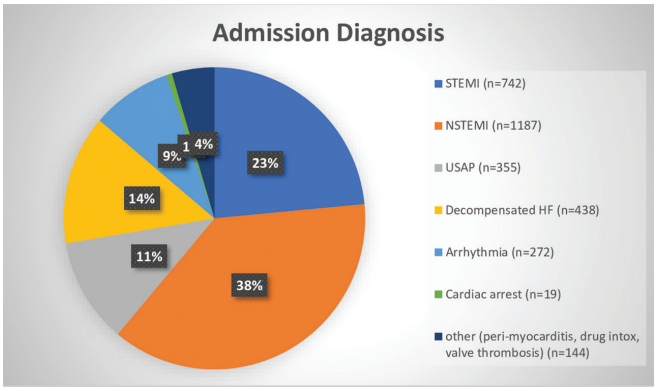

Figure 2. Distribution of admission diagnoses
STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non-ST-segment elevation myocardial infarction, USAP: Unstable angina pectoris

However, the median mean BP was lower in the non-survivor group than in the survivor group [76 (IQR, 66-93) vs. 95 (IQR, 85-105) mmHg, p<0.001], whereas the median heart rate was higher [96 (IQR, 80-110) vs. 80 (IQR, 70-93) beats/min, p<0.001]. Regarding laboratory findings, non-survivors had lower oxygen saturation [94% (IQR, 86-96) vs. 96% (IQR, 93-98), p<0.001], eGFR [39 (IQR, 22.7-78) vs. 79 (IQR, 57-95) mL/min/1.73 m^2, p<0.001], and hematocrit (36.9±6.7% vs. 39.9±6.1%, p<0.001). In contrast, they had higher serum glucose [151 (IQR, 114-212) vs. 123 (IQR, 101-164), p<0.001], serum creatinine (1.6±0.9 vs. 1.3±0.4, p<0.001), potassium (4.7±0.8 vs. 4.4±0.6, p<0.001), WBC count (12.3±5.3 vs. 9.9±3.5, p<0.001), and CRP levels [23.6 (IQR, 10-120) vs. 5.7 (IQR, 1.9-16), p<0.001] (Table 2).

The multivariable analysis identified several independent predictors of in-hospital mortality. Each additional year of age was associated with a 2.4% increase in the odds of in-hospital mortality [odds ratio (OR), 1.024; 95% confidence interval (CI), 1.001-1.048; p=0.040]. Although male patients comprised the majority of the survivor group, female sex emerged as an independent predictor of in-hospital mortality after adjustment for age, comorbidities, and clinical variables (OR, 2.007; 95% CI, 1.150-3.504; p=0.014). Lower mean BP (OR, 0.938; 95% CI, 0.922-0.955; p<0.001), elevated serum creatinine (OR, 1.821; 95% CI, 1.473-2.250; p<0.001), higher CRP levels (OR, 1.007; 95% CI, 1.003-1.012; p=0.001), and higher WBC count (OR, 1.086; 95% CI, 1.022-1.154; p=0.008) were also identified as independent predictors of in-hospital mortality (Table 3).

In addition, ROC curve analysis was performed to evaluate the discriminatory ability of the prediction model. The final multivariable model demonstrated good discrimination for predicting in-hospital mortality [area under the curve (AUC)=0.842]. The optimal predicted probability cut-off was 0.092, corresponding to a sensitivity of 61.7%, a specificity of 90.2%, and a Youden index of 0.519 (Figure 3).

Table 1. Main diagnoses distribution in survivors and non-survivors

	All patients (n=3157)	Non-survivors (n=137)	Survivors (n=3020)	p values
STEMI, n (%)	742 (23.5%)	31 (22.6%)	711 (23.5%)	0.805
NSTEMI, n (%)	1187 (37.6%)	31 (22.6%)	1156 (38.3%)	<0.001
USAP, n (%)	355 (11.2%)	8 (5.8%)	347 (11.5%)	0.041
Decompensated HF, n (%)	438 (14%)	39 (28.4%)	399 (13.2%)	<0.001
Arrhythmia, n (%)	272 (8.6%)	11 (8%)	261 (8.6%)	0.802
Cardiac arrest, n (%)	19 (0.6%)	9 (6.6%)	10 (0.3%)	<0.001
Other, n (%)	144 (4.5%)	8 (5.8%)	132 (4.5%)	0.463

STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non-ST-segment elevation myocardial infarction, USAP: Unstable angina pectoris, HF: Heart failure

Table 2. Baseline characteristics of the study group

	All patients (n=3157)	Non-survivors (n=137)	Survivors (n=3020)	p
Age (years), median (IQR)	65 (56-73)	73 (63-83)	65 (56-73)	<0.001
Sex (male), n (%)	2087 (66.1)	73 (53.3)	2014 (66.7)	0.002
Hypertension, n (%)	1864 (59)	91 (66.4)	1773 (58.7)	0.076
Diabetes mellitus, n (%)	1184 (37.5)	55 (40.1)	1129 (37.4)	0.528
Dyslipidaemia, n (%)	1120 (35.5)	46 (33.6)	1074 (35.6)	0.715
Smoking, n (%)	1955 (61.9)	79 (57.7)	1876 (62.1)	0.322
Family history of CAD, n (%)	1101 (34.9)	37 (27.2)	1064 (35.8)	0.043
CAD, n (%)	1446 (45.8)	74 (54)	1372 (45.4)	0.054
AF, n (%)	483 (15.3)	34 (24.8)	449 (14.9)	0.003
Heart failure, n (%)	978 (31)	76 (55.5)	902 (29.9)	<0.001
Stroke history, n (%)				0.086
No	3015 (95.5)	126 (92)	2889 (95.7)	
Ischemic stroke	125 (4)	9 (6.6)	116 (3.8)	
Haemorrhagic stroke	17 (0.5)	2 (1.5)	15 (0.5)	
Prior major bleeding, n (%)	130 (4.1)	6 (4.5)	124 (4.2)	0.823
Chronic renal disease, n (%)	434 (13.7)	45 (32.8)	389 (12.9)	<0.001
EF (%), median (IQR)	52 (40-57)	40 (30-50)	53 (44-58)	<0.001
Mean blood pressure (mmHg), median (IQR)	94.7 (84.7-105.0)	76 (66-93)	95 (85-105)	<0.001
Heart rate (bpm), median (IQR)	81 (71-94)	96 (80-110)	80 (70-93)	<0.001
Saturation (%), median (IQR)	95 (93-98)	94 (86-96)	96 (93-98)	<0.001
Glucose (mg/dL), median (IQR)	124 (102-166)	151 (114-212)	123 (101-164)	<0.001
Glomerular filtration rate (mL/min), median (IQR)	78 (54-95)	39 (22.7-78)	79 (57-95)	<0.001
Creatinine (mg/dL), mean±SD	0.9±0.4	1.6±0.9	1.3±0.4	<0.001
Sodium (mmol/L), mean±SD	137.6±4.0	137.6±3.9	137.3±5.7	0.318
Potassium (mmol/L), mean±SD	4.4±0.6	4.7±0.8	4.4±0.6	<0.001
White blood cell ($\times 10^3$/µL), mean±SD	10.0±3.7	12.3±5.3	9.9±3.5	<0.001
Haematocrit (%), mean±SD	40.0±6.0	36.9±6.7	39.9±6.1	<0.001
Platelet ($\times 10^3$/µL), mean±SD	243.3±80.5	241.1±115.0	243.4±78.6	0.742
AST (U/L), median (IQR)	27 (19-47)	29 (16-90)	27 (19-46)	0.002
ALT (U/L), median (IQR)	20 (14-32)	24 (12-73)	20 (14-32)	0.001
CRP (mg/L), median (IQR)	6 (2-17)	23.6 (10-120)	5.7 (1.9-16)	<0.001
Troponin (ng/mL), median (IQR)	191 (23-3131)	543 (36-8300)	180 (23-2977)	0.088
CHA_2DS_2VASc score, median (IQR)	3 (1-4)	4 (3-5)	3 (1-4)	<0.001

AF: Atrial fibrillation, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CAD: Coronary artery disease, CHA_2DS_2-VASc: Congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, stroke/transient ischemic attack (2 points), vascular disease, age 65-74 years, sex category (female), CRP: C-reactive protein, EF: Ejection fraction, GFR: Glomerular filtration rate, HF: Heart failure, SD: Standard deviation, IQR: Interquartile range

Table 3. Independent predictors of in-hospital mortality

Variables	Multivariable analysis	
	OR (95% CI)	p
Age (years)	1.024 (1.001-1.048)	0.040
Sex (female)	2.007 (1.150-3.504)	0.014
Mean BP	0.938 (0.922-0.955)	<0.001
Creatinine (mg/dL)	1.821 (1.473-2.250)	<0.001
CRP (mg/L)	1.007 (1.003-1.012)	0.001
WBC ($\times 10^3/\mu L$)	1.086 (1.022-1.154)	0.008

OR: Odds ratio, CI: Confidence interval, BP: Blood pressure, CRP: C-reactive protein, WBC: White blood cell

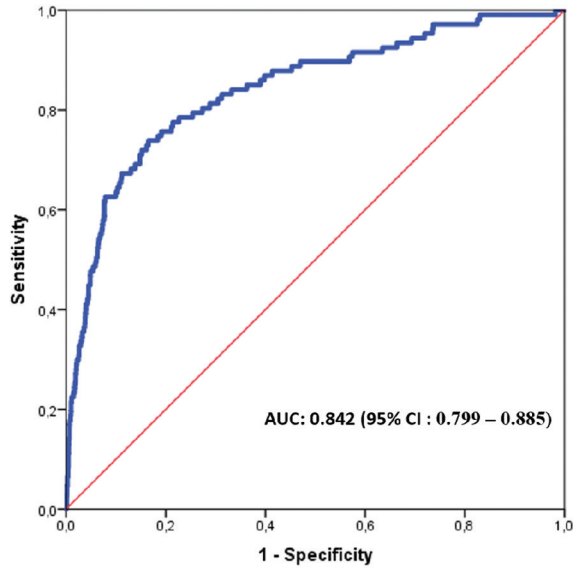

Figure 3. Receiver operating characteristic (ROC) curve of the prediction model
AUC: Area under the curve, CI: Confidence interval

DISCUSSION

In this recent real-world cohort study, we comprehensively evaluated the baseline characteristics, demographic features, clinical profiles, diagnosis distribution, and predictors of in-hospital mortality among patients admitted to CCUs in Türkiye. Although the primary findings of the MORCOR-TURK study have been reported previously, the present analysis provides a focused and in-depth evaluation of mortality predictors and their clinical implications. The overall in-hospital mortality rate was 4.3%, which is consistent with international benchmarks. The study population predominantly comprised male patients with common cardiovascular risk factors, underscoring the ongoing need for targeted preventive strategies in this population. Notably, serum creatinine and mean BP emerged as the strongest predictors of in-hospital mortality. In addition, age, female sex, WBC count, and CRP levels were independently associated with mortality risk. Collectively, these findings provide clinically relevant insights for risk stratification among hospitalized CCU patients. Although the baseline characteristics of the MORCOR-TURK cohort have been reported previously, the present study specifically focuses on in-hospital mortality and its predictors. Whereas the previous report primarily described the demographic and clinical characteristics of the cohort, the current analysis provides a dedicated evaluation of the determinants of in-hospital mortality in a nationwide CCU population. Taken together, our findings suggest that short-term mortality among patients admitted to CCUs is driven primarily by acute hemodynamic compromise and renal dysfunction, whereas demographic and inflammatory factors act as important modifiers rather than primary determinants.

Modern CCUs have achieved substantial advances in patient monitoring, interventional capabilities, and pharmacologic treatment strategies, resulting in a marked reduction in in-hospital mortality among patients with severe CVDs. Previous studies have reported in-hospital mortality rates ranging from approximately 5.6% to 15.2% in heterogeneous CCU populations.[10,11] Notably, our findings demonstrated significant differences in admission diagnoses between survivors and non-survivors, underscoring the critical importance of early recognition and aggressive management of high-risk conditions, such as acute pulmonary edema, decompensated HF, cardiac arrest, and NSTEMI. The high rate of PCI in our cohort further highlights the central role of timely and effective interventional strategies in improving short-term outcomes. Although system-level factors were not directly evaluated, differences in healthcare organization and resource availability may contribute to regional variation in CCU outcomes and should be considered when interpreting patient-level predictors of mortality.

We identified several independent predictors of in-hospital mortality, including age, female sex, mean BP, serum creatinine, CRP, and WBC count. Notably, mean BP and serum creatinine emerged as the strongest predictors, underscoring the importance of hemodynamic stability and renal function in determining patient outcomes. Renal function has been extensively investigated in previous studies, in which acute kidney injury and GFR were identified as independent predictors of adverse events across various patient populations, as well as predictors of mortality in ICUs and CCUs.[12] Mean BP also emerged as a robust predictor of mortality, together with serum creatinine, both of which are key components of established prognostic scoring systems, including APACHE II, SAPS, and MELD. We have previously demonstrated the utility of these parameters in predicting mortality among CCU patients.[6,13] Although established prognostic scoring systems remain valuable, their complexity may limit routine use in busy CCU settings. In this context, readily available and clinically actionable parameters are particularly valuable. The risk model developed in the present study demonstrated good discriminatory performance, with an AUC of 0.842, supporting its potential utility for early risk stratification in CCU patients. The identification of mean BP and serum creatinine as key predictors highlights the value of simple, routinely measured, and potentially modifiable clinical variables for guiding real-world clinical decision-making. Nevertheless, the non-randomized observational design and the exclusion of some CCUs may limit the generalizability of these findings. Future prospective studies are warranted to validate the model and determine whether its integration with established risk scoring systems could further optimize triage and risk stratification in the CCU setting.

In addition to hemodynamic and renal parameters, age, female sex, and markers of systemic inflammation were independently associated with in-hospital mortality in the present study. Advanced age likely reflects reduced physiological reserve and a greater burden of comorbidities, thereby increasing susceptibility to adverse outcomes in the acute CCU setting.[14] The association between female sex and increased mortality risk, despite the higher proportion of male non-survivors in the unadjusted analysis, suggests the influence of confounding clinical factors, such as older age at presentation, greater disease severity, or differences in the recognition and management of cardiovascular conditions. The discrepancy between the unadjusted and adjusted analyses warrants further consideration. Although male patients constituted a greater proportion of the non-survivor group, multivariable adjustment identified female sex as an independent predictor of mortality. This finding may reflect residual differences in age, comorbidity burden, clinical presentation, or disease severity between the sexes. Previous studies have also suggested that women admitted with acute cardiovascular conditions are often older, present with atypical symptoms, and may experience delays in diagnosis or treatment, all of which may adversely affect clinical outcomes. Therefore, the observed association should not be interpreted as a direct biological effect of sex but rather as a marker of complex clinical and healthcare-related factors that warrant further investigation.

Systemic inflammation may represent a common pathophysiological pathway linking these factors. In the acute cardiovascular care setting, an exaggerated inflammatory response often reflects not only the severity of the primary cardiac condition but also the cumulative effects of concomitant organ dysfunction, including HF, renal impairment, and tissue hypoperfusion.[15] Accordingly, elevated inflammatory markers may serve as integrative indicators of overall physiological stress rather than isolated laboratory abnormalities. The independent association between inflammatory burden and short-term mortality observed in our cohort supports growing evidence that inflammation plays a central modulatory role in outcomes among critically ill patients with CVD and underscores the clinical value of incorporating inflammatory markers into early risk stratification in CCU practice.

Although AF was more prevalent among non-survivors, it did not emerge as an independent predictor of in-hospital mortality in the multivariable analysis. This finding may reflect the complex and multifactorial impact of AF in the acute CCU setting, where short-term outcomes are driven primarily by hemodynamic instability, underlying ventricular dysfunction, and concomitant comorbidities. AF contributes to adverse outcomes through the loss of atrial contribution to ventricular filling, impaired cardiac output, and an increased risk of thromboembolic complications, all of which may have a greater influence on long-term prognosis than on immediate in-hospital mortality.[16] Accordingly, long-term follow-up of the MORCOR-TURK cohort may provide additional insights into the sustained impact of AF on mortality and cardiovascular outcomes.

The high prevalence of hypertension and diabetes mellitus highlights the need for targeted preventive and therapeutic strategies for these risk factors in the CCU population. Although diabetes mellitus is a well-established contributor to poor clinical outcomes, its prevalence was similar between survivors and non-survivors in our cohort. However, serum glucose levels were significantly higher among non-survivors. This discrepancy may be attributable to unrecognized dysglycemia or stress-induced hyperglycemia during acute cardiovascular events. It is also possible that the physiological stress associated with cardiovascular emergencies contributes to metabolic disturbances that increase serum glucose levels. Nevertheless, serum glucose did not emerge as an independent predictor of mortality in the present study. Because this study focused on short-term in-hospital mortality, serum glucose levels may have a greater impact on long-term cardiovascular outcomes.

Study Limitations

Despite the valuable insights provided by this nationwide study, several limitations should be acknowledged. First, although the study included a broad geographic representation of CCUs across Türkiye, not all CCU-capable centers were enrolled, which may limit the generalizability of the findings. Differences in institutional resources, the availability of advanced interventional facilities, and operator experience across centers may have influenced patient management and clinical outcomes. Second, although the study was designed as a prospective observational investigation, its non-randomized design precludes causal inference. Although standardized definitions and data collection forms were used, variations in diagnostic practices, admission criteria, and clinical decision-making across centers may have introduced heterogeneity in patient classification and management. In addition, the inclusion of a heterogeneous CCU population that reflected real-world practice beyond ACS may have influenced the relative contribution of individual predictors to short-term mortality. Furthermore, patient recruitment was limited to a 1-month period, which may not have fully captured seasonal variations in admission patterns, disease severity, or mortality rates. Third, several clinically relevant variables could not be comprehensively assessed, including detailed hemodynamic measurements, the timing and intensity of therapeutic interventions, medication dosing, and dynamic changes in laboratory values and vital signs during hospitalization. Furthermore, detailed treatment-related variables, such as the timing of PCI, vasopressor use, mechanical circulatory support, and treatment intensity, were not systematically recorded. Likewise, detailed information regarding the timing, extent, and complexity of coronary angiography, PCI, stent implantation, and surgical procedures was unavailable. Consequently, the direct effects of treatment strategies on survival could not be evaluated. Furthermore, postdischarge outcomes and long-term survival data were not available for the present analysis. Therefore, the findings are limited to in-hospital outcomes and should not be extrapolated to long-term mortality. Although long-term follow-up is planned within the MORCOR-TURK framework, those data were beyond the scope of the present study. Finally, patients who remained in the CCU for less than 4 hours and those who died within 30 minutes despite unsuccessful CPR were excluded according to the predefined study protocol. This may have resulted in a slight underestimation of the in-hospital mortality rate and should be considered a potential source of selection bias.

CONCLUSION

This nationwide study provides comprehensive insights into the predictors of in-hospital mortality among patients admitted to CCUs in Türkiye and contributes to establishing contemporary benchmarks for CCU mortality. Our findings highlight the central role of renal function and hemodynamic status in determining short-term outcomes, underscoring the clinical value of close monitoring of serum creatinine and mean BP in the acute care setting. The proposed risk model, developed using data from a nationwide Turkish CCU cohort, offers a practical framework for early risk stratification and may assist clinicians in prioritizing care and optimizing resource allocation. Although further prospective validation is warranted, these findings support the use of simple, readily available clinical parameters to inform clinical decision-making and may serve as a foundation for future collaborative efforts to improve the quality of CCU care and patient outcomes across diverse healthcare systems. From a practical perspective, these results support a CCU strategy that prioritizes early hemodynamic stabilization and close monitoring of renal function using universally available bedside parameters.

Ethics Committee Approval: Ethical approval for this study was obtained from the Afyonkarahisar Health Sciences University Clinical Research Ethics Committee for non-interventional clinical studies (date: August 5, 2022; meeting no: 2022/9; approval no: 422).

Informed Consent: Written informed consent was obtained from all participants or their legally authorized representatives, ensuring the ethical integrity and transparency of the study.

Authorship Contributions: Concept: İ.E., A.S.Y., F.Kah., S.H., A.M.T., Ş.A., G.Ö.M., M.Ş., Design: İ.E., A.S.Y., F.Kah., S.H., A.M.T., Ş.A., G.Ö.M., M.Ş., Data Collection or Processing: İ.E., A.S.Y., F.Kah., G.T., E.E.K., E.A., M.K., M.M.Ö., A.G.T., S.H., Ö.K., M.G., A.M.T., S.G.N., Ş.A., M.Ö., Ç.K., O.K., A.M.To., M.Öz., Ö.Ku., Ö.Ş., G.Ö.M., Ş.T., M.K.A., M.D., F.Ka., M.Ş., F.Ku., F.A.D., S.E.Ö., M.Y., M.B.T., Y.E.Y., İ.B.Ç., Ş.K., Y.K., A.A., M.U., İ.Y., S.G., B.A., İ.B.I., R.D., İ.H.T., Ö.Ke., Analysis or Interpretation: İ.E., A.S.Y., F.Kah., S.H., A.M.T., Ş.A., G.Ö.M., M.K.A., M.D., M.Ş., F.A.D., İ.H.T., Literature Search: A.S.Y., F.K., A.G.T., S.H., A.M.T., A.M.To., G.Ö.M., M.Ş., F.A.D., Writing: İ.E., A.S.Y., F.Kah., A.G.T., S.H., A.M.T., G.Ö.M., M.Ş., F.A.D.

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ORIGINAL ARTICLE

Efficacy and Safety of Glycoprotein IIb/IIIa Inhibitors Used Concomitantly with Cangrelor in Patients Undergoing Percutaneous Coronary Intervention

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ABSTRACT

Background: Cangrelor, an intravenous and reversible P2Y12 receptor antagonist, is approved for use in patients undergoing primary and non-primary percutaneous coronary intervention (PCI).

Aim: To evaluate the efficacy and safety of glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors initiated during PCI in patients with acute coronary syndrome (ACS) or chronic coronary syndrome (CCS) receiving cangrelor therapy.

Study Design: Retrospective, multicenter study.

Methods: This subgroup analysis of previously reported real-world data on cangrelor use in Türkiye evaluated the effects of GP IIb/IIIa inhibitors on bleeding, ischemic events, and mortality during follow-up in patients receiving cangrelor.

Results: A total of 411 patients were included (mean age: 63.8±12.7 years; 76% male). Of these, 44 patients (10.7%) received GP IIb/IIIa inhibitors in addition to cangrelor (mean age: 68.0±11.3 years; 79% male). Kaplan-Meier analysis showed no significant difference in 12-month overall survival between coronary artery disease groups (log-rank p=0.392). In Firth penalized logistic regression analysis adjusting for age, sex, cardiogenic shock, chronic kidney disease, and femoral vascular access, GP IIb/IIIa inhibitor use was identified as an independent and significant predictor of 48-hour bleeding (odds ratio: 8.44, 95% confidence interval: 3.54-20.18, p<0.001).

Conclusion: This study represents the first large-scale, multicenter retrospective analysis in Türkiye to examine the concomitant use of GP IIb/IIIa inhibitors with cangrelor in a high-risk population of patients with ACS and CCS. The findings suggest that combining GP IIb/IIIa inhibitors with cangrelor does not improve clinical outcomes but significantly increases the incidence of mild-to-moderate bleeding events.

Keywords: Cangrelor, glycoprotein IIb/IIIa inhibitors, percutaneous coronary intervention, acute coronary syndrome, chronic coronary syndrome

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INTRODUCTION

Cardiovascular diseases remain the leading cause of mortality and morbidity worldwide, with acute coronary syndrome (ACS) often representing the first clinical manifestation.[1,2] Current European guidelines emphasize that early percutaneous coronary intervention (PCI) with stent implantation significantly reduces mortality and limits the development of heart failure (HF) in patients with ACS.[3] Achieving rapid and adequate platelet inhibition before coronary intervention is therefore critical for preventing early stent thrombosis, recurrent myocardial infarction, and associated mortality.

Oral P2Y12 inhibitors, including clopidogrel, ticagrelor, and prasugrel, are widely used for this purpose. However, their pharmacokinetic profiles depend on gastrointestinal absorption, which may delay the onset of action and limit their ability to provide rapid and predictable platelet inhibition, particularly in patients at high thrombotic risk.[4,5] Moreover, several conditions frequently encountered in patients with ACS—such as hemodynamic instability, hypotension, nausea and vomiting, the need for endotracheal intubation, delayed gastric emptying, intestinal hypoperfusion, hypothermia, and opioid use—can further impair the bioavailability and pharmacodynamic effectiveness of oral agents, resulting in delayed or inadequate clinical responses.[6,7]

Cangrelor, an intravenously administered, rapidly acting, and reversible P2Y12 receptor antagonist, has been approved for use during PCI and provides potent and predictable platelet inhibition, particularly in clinical scenarios in which oral agents may have delayed or insufficient effects.[8] The safety and efficacy of cangrelor have been evaluated in three randomized controlled trials comparing cangrelor with clopidogrel or placebo in patients undergoing PCI for stable or acute indications who had not previously received a P2Y12 inhibitor. Pooled analyses of these studies demonstrated that cangrelor administration during PCI significantly reduced the composite endpoint of death, myocardial infarction, ischemia-driven revascularization, or stent thrombosis within 48 hours. However, this ischemic benefit was accompanied by an increased incidence of minor bleeding events, without a corresponding rise in life-threatening or fatal bleeding.[9-11]

Glycoprotein IIb/IIIa (GP IIb/IIIa) receptor inhibitors are parenteral agents that prevent platelet aggregation by blocking the binding of fibrinogen or von Willebrand factor to the GP IIb/IIIa receptor, thereby inhibiting platelet cross-linking. Their use has become more selective and is now largely limited to adjunctive therapy during PCI in patients with a high thrombus burden or as "rescue" or "bailout" therapy in the presence of PCI-related complications, such as no-reflow or persistent or recurrent intralesional thrombus.[12]

We recently published the first multicenter study evaluating real-world cangrelor use in Türkiye.[13] In this predefined subgroup analysis, we aimed to assess the efficacy and safety of GP IIb/IIIa inhibitors initiated during PCI in patients with ACS or chronic coronary syndrome (CCS) receiving cangrelor therapy.

METHODS

Study Design and Population

Data were collected between January 20, 2025, and April 1, 2025, from 14 high-volume PCI centers in Türkiye that maintain 24/7 cangrelor administration programs. This retrospective observational study evaluated the records of patients who received cangrelor, with or without concomitant GP IIb/IIIa inhibitors, during the preceding five years. All patients who received cangrelor therapy within the specified period were included in the analysis, regardless of whether GP IIb/IIIa inhibitors were administered.

A total of 411 patients aged ≥18 years with a diagnosis of ACS or CCS who received cangrelor prior to PCI, in accordance with approved indications, were included. Patients with myocardial infarction with non-obstructive coronary arteries or Takotsubo syndrome identified on coronary angiography, and therefore not undergoing PCI, were excluded from the study.[14,15]

Data Collection and Clinical Definitions

Collected data included indications for cangrelor administration, demographic and clinical characteristics, pre- and postprocedural laboratory parameters, procedural details, and in-hospital ischemic events, bleeding events, and mortality outcomes. According to European Society of Cardiology guidelines, patients were categorized into four clinical groups: ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), unstable angina (UA), and CCS.[3]

Stent thrombosis (acute, subacute, or late) was defined as definite, probable, or possible events confirmed either angiographically or clinically.[16] Bleeding events were evaluated at 48 hours and 1 month after the procedure. Bleeding severity was classified using the Bleeding Academic Research Consortium (BARC) and Global Utilization of Strategies to Open Occluded Coronary Arteries (GUSTO) criteria.

According to the BARC classification, type 1 bleeding refers to events not requiring unscheduled diagnostic evaluation, hospitalization, or treatment. Type 2 bleeding includes events requiring non-surgical medical intervention, hospitalization, or escalation of care. Type 3 bleeding is subdivided into three categories: type 3a, overt bleeding associated with a hemoglobin decrease of 3-5 g/dL or requiring transfusion; type 3b, bleeding with a hemoglobin decrease ≥5 g/dL, cardiac tamponade, bleeding requiring surgical intervention (excluding dental, nasal, cutaneous, or hemorrhoidal bleeding), or bleeding requiring intravenous vasoactive therapy; and type 3c, intracranial or intraspinal hemorrhage or intraocular bleeding causing vision loss. Type 4 bleeding refers to coronary artery bypass graft-related bleeding, including perioperative intracranial bleeding, reoperation after sternotomy closure, or significant transfusion requirements. Type 5 bleeding refers to fatal bleeding, with type 5a indicating probable fatal bleeding without confirmatory autopsy or imaging and type 5b indicating definite fatal bleeding confirmed by autopsy or imaging.[17] In the present analysis, BARC type 1-2 bleeding events were classified as minor bleeding, whereas BARC type ≥3 events were considered major bleeding.

According to the GUSTO classification, severe or life-threatening bleeding includes intracranial hemorrhage or bleeding causing hemodynamic compromise requiring intervention; moderate bleeding includes bleeding requiring blood transfusion without hemodynamic deterioration; and mild bleeding includes events not meeting the criteria for severe or moderate bleeding.[18]

Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, a prior diagnosis of hypertension, or current use of antihypertensive medication.[19] Diabetes mellitus was defined as a fasting plasma glucose level >126 mg/dL, a prior diagnosis of diabetes, or use of glucose-lowering medication.[20] HF was defined as the presence of characteristic symptoms accompanied by objective evidence of cardiac dysfunction resulting in reduced cardiac output and/or elevated intracardiac pressure.[21]

Contrast-induced acute kidney injury (CI-AKI) was defined according to Kidney Disease: Improving Global Outcomes guidelines as an increase in serum creatinine ≥0.3 mg/dL within 48 hours after contrast administration, an increase to ≥1.5 times the baseline value within the prior 7 days, or urine output <0.5 mL/kg/h for at least 6 hours.[22]

Procedural Details

Standard coronary angiography was performed using either the transradial or transfemoral approach, according to the operator's preference, using the Seldinger technique. In all patients, a low-osmolar, non-ionic contrast agent, iohexol (350 mg iodine/mL; 755 mOsm/kg H_2O) (Omnipaque-350; GE Healthcare, Rydalmere, Australia), was used.

Following primary PCI (pPCI), saline infusion (0.9% NaCl) was administered according to institutional protocol to reduce the risk of CI-AKI. Patients without HF received isotonic saline at 1 mL/kg/h for 12 hours, whereas those with HF received 0.5 mL/kg/h for 12 hours. The duration of hydration was adjusted by the treating interventional cardiologist based on individual patient risk assessment.

Cangrelor was administered according to current guideline recommendations as an intravenous bolus of 30 µg/kg, followed by a continuous infusion of 4 µg/kg/min. The infusion was maintained for at least 2 hours or for the duration of the procedure, whichever was longer. After discontinuation of cangrelor, transition to an oral P2Y12 inhibitor was performed according to guideline-based recommendations.[3] In patients receiving GP IIb/IIIa inhibitor therapy, tirofiban was administered according to standard practice. A high-dose bolus of 25 µg/kg was given intravenously over 3 minutes, followed by a continuous infusion of 0.15 µg/kg/min. The infusion was typically continued for up to 18 hours at the discretion of the interventional cardiologist.[3] Unfractionated heparin was administered according to current guideline recommendations. An initial intravenous bolus of 70-100 IU/kg was given at the start of the procedure. In patients receiving concomitant GP IIb/IIIa inhibitors, a reduced initial bolus of 60 IU/kg was used. Anticoagulation was monitored using activated clotting time (ACT), when available, and additional boluses were administered as needed to maintain a target ACT of 250–300 seconds (or 200–250 seconds in patients receiving GP IIb/IIIa inhibitors).

Data Management and Follow-up

All numerical variables were cross-checked across participating centers prior to analysis to ensure consistency, and data audits were performed to verify the accuracy of procedural and outcome variables. In-hospital data were retrieved from existing patient records, whereas long-term follow-up data were obtained from hospital databases, telephone interviews, and the national electronic health record system.[23]

Ethics Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Trakya University School of Medicine (approval number: TUTF-GOBAEK-2024/560, date: 20.01.2025). Patient consent was waived due to the retrospective nature of the study.

Statistical Analysis

Continuous variables were summarized as mean±standard deviation or median [interquartile range (IQR)], depending on data distribution. Categorical variables are presented as frequencies and percentages. Event rates were calculated with 95% confidence intervals (CIs) using the Wilson method.

Bleeding rates according to the BARC and GUSTO classifications were summarized based on coronary artery disease presentation (STEMI, NSTEMI, or UA). Time intervals were defined according to the first occurrence of an event, including 48-hour and 30-day intervals with a ±2-day tolerance window. Given the low number of bleeding events relative to the number of predictors (events-per-variable ratio=4.3), Firth's penalized logistic regression was used to identify independent predictors of 48-hour bleeding. The multivariable model included age, sex, cardiogenic shock (Killip class IV), chronic kidney disease, and femoral vascular access. Results are reported as odds ratios (ORs) with profile likelihood-based 95% CIs. As a sensitivity analysis, inverse probability of treatment weighting (IPTW) was performed to assess the robustness of the primary findings. Propensity scores for GP IIb/IIIa inhibitor use were estimated using logistic regression, including age, sex, chronic kidney disease, femoral vascular access, Killip class, diabetes mellitus, hypertension, STEMI presentation, and left ventricular ejection fraction (LVEF) as covariates. The average treatment effect on the treated was estimated using IPTW, with weights trimmed at the 99th percentile to minimize the impact of extreme values. Covariate balance was assessed using standardized mean differences, with <0.1 indicating adequate balance. Weighted outcome analysis was performed using the survey package with robust variance estimation. A two-sided p value <0.05 was considered statistically significant. All analyses were performed using R software version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Among the 411 patients included in the study, the median ages of patients in the STEMI, NSTEMI, UA, and CCS groups were 64, 70, 66, and 59 years, respectively. Patients in the STEMI group presented with higher Killip classes, higher heart rates, and lower systolic and diastolic blood pressures at admission. The prevalence of hypertension was high across all groups. Chronic kidney disease was more prevalent

in the STEMI group, whereas diabetes mellitus was more common in the NSTEMI group. The lowest median LVEF was observed in the STEMI group. Cangrelor was most frequently administered in clinical scenarios involving cardiogenic shock, endotracheal intubation, and nausea or vomiting with impaired oral intake. A total of 44 patients (10.7%) received GP IIb/IIIa inhibitors in addition to cangrelor. The most common indication for GP IIb/IIIa inhibitor use was high thrombus burden in the culprit coronary artery and impaired distal coronary flow [thrombolysis in myocardial infarction (TIMI) 0-1] at the end of the procedure. All patients received aspirin and heparin. In all cases, oral P2Y12 inhibitor therapy was initiated immediately after completion of cangrelor infusion, with clopidogrel being the most frequently used agent (57%). Baseline characteristics, including age, sex, type of coronary artery disease, Killip class, LVEF, diabetes mellitus, and hypertension, were comparable between patients who received GP IIb/IIIa inhibitors and those who did not (all p>0.05) (Table 1).

Although femoral access was more frequently used in patients receiving GP IIb/IIIa inhibitors, median stent diameter (3.0 mm), total stent length (34.3±19.7 mm), median procedural time [39 minutes (IQR: 26-55)], contrast volume [150 mL (IQR: 110-220)], and the rate of complex bifurcation procedures were comparable between the groups (Table 2).

In firth penalized logistic regression analysis adjusting for age, sex, cardiogenic shock, chronic kidney disease, and femoral vascular access, GP IIb/IIIa inhibitor use was the only independent predictor of 48-hour bleeding, corresponding to an approximately eightfold increased risk (OR: 8.44; 95% CI: 3.54-20.18; p<0.001). Notably, neither chronic kidney disease (OR: 0.82; 95% CI: 0.26-2.27; p=0.708) nor femoral access (OR: 1.05; 95% CI: 0.37-3.33; p=0.926) was independently associated with bleeding after adjustment. The remaining covariates also did not reach statistical significance (all p>0.05) (Table 3). In the IPTW sensitivity analysis, adequate covariate balance was achieved after weighting, with all standardized mean differences <0.1. The IPTW-adjusted analysis yielded consistent results, confirming a significant association between GP IIb/IIIa inhibitor use and 48-hour bleeding (OR: 7.97; 95% CI: 3.24-19.62; p<0.001).

When hemodynamic and procedural parameters associated with the decision to use GP IIb/IIIa inhibitors were analyzed, arrhythmia was significantly more common in patients receiving GP IIb/IIIa inhibitors than in those who did not (p=0.011). However, inotropic support, mechanical circulatory support, cardiopulmonary arrest, admission systolic and diastolic blood pressure, heart rate, and number of culprit lesions did not differ significantly between the groups (all p>0.05) (Table 4).

Within 48 hours, the incidence of any bleeding event, major bleeding (BARC ≥3), and blood transfusion was significantly higher in patients receiving GP IIb/IIIa inhibitors compared with those not receiving them (28% vs. 3.8%, p<0.001; 7.0% vs. 1.1%, p=0.028; and 12% vs. 2.7%, p=0.014, respectively) (Table 3) (Figure 1). All major bleeding events were gastrointestinal in origin, whereas minor bleeding events were predominantly related to vascular access sites and the genitourinary system. Regarding bleeding risk indicators and potential contraindications influencing the decision to use GP IIb/IIIa inhibitors, all categories of BARC and GUSTO bleeding scores at 48 hours, chronic kidney disease, and the need for blood transfusion were significantly more frequent in the GP IIb/IIIa inhibitor group than in the non-GP IIb/IIIa group (Table 5).

DISCUSSION

In this study, we evaluated the impact of concomitant use of GP IIb/IIIa inhibitors with the parenteral P2Y12 inhibitor cangrelor on clinical outcomes and bleeding complications in patients undergoing PCI for acute or CCS. The principal finding of our analysis is that the addition of GP IIb/IIIa inhibitors to cangrelor therapy was associated with an approximately eightfold increase in bleeding risk, independent of baseline clinical risk factors, including chronic kidney disease and femoral vascular access, whereas no significant difference in in-hospital mortality was observed.

Cangrelor, currently the only available intravenous P2Y12 inhibitor, has an established role in the management of ACS.[24,25] Although the CHAMPION series of randomized clinical trials demonstrated the efficacy and safety of cangrelor in controlled settings, data reflecting its performance in real-world clinical practice remain limited. In this context, the retrospective multicenter study by Altay et al.[13] provided important real-world evidence regarding cangrelor use in Türkiye, showing that the drug is predominantly used in high-risk patients with ACS and CCS, and describing its indications and clinical outcomes during follow-up.[26,27]

Similarly, real-world data regarding the efficacy and safety of concomitant use of cangrelor and GP IIb/IIIa inhibitors remain scarce. In a meta-analysis by Sethi et al.,[28] which included 20 randomized controlled trials and 7,404 patients with STEMI undergoing pPCI, the effects of GP IIb/IIIa inhibitors on clinical outcomes were compared between patients who did or did not receive preprocedural thienopyridines. The analysis showed that in patients not receiving thienopyridines before PCI, GP IIb/IIIa inhibitors significantly reduced 30-day mortality and target vessel revascularization. In contrast, these benefits were not statistically significant in patients who had received thienopyridines prior to the procedure. However, safety outcomes related to GP IIb/IIIa inhibitors were not reported in detail in this meta-analysis.

In another meta-analysis, Jeremias et al.[29] evaluated 2,937 STEMI patients undergoing pPCI and compared abciximab, a GP IIb/IIIa inhibitor, with placebo in patients who had received preprocedural thienopyridine therapy. The authors reported that abciximab did not reduce mortality or reinfarction rates, either at 30 days or during long-term follow-up. Similar to the previous analysis, safety data were limited.

Importantly, the patient populations included in these meta-analyses differ from those in our study, as all patients in the referenced studies received oral P2Y12 inhibitors, whereas our cohort consisted of patients who could not receive oral P2Y12 inhibitors due to various clinical conditions and were therefore treated with the intravenous P2Y12 inhibitor cangrelor. Among patients receiving GP IIb/IIIa inhibitors in our study, 32 (74%) presented with STEMI. When comparing patients who received GP IIb/IIIa inhibitors with those

Table 1. Patient risk profile by GP IIb/IIIa use

Characteristic	Overall n=411	GP IIb/IIIa (-) n=367	GP IIb/IIIa (+) n=44	p value[1]
Age, median (Q1, Q3)	64 (56, 73)	64 (56, 73)	69 (53, 77)	0.35
Sex, n (%)				0.58
Male	313 (76)	278 (76)	35 (80)	
Female	98 (24)	89 (24)	9 (20)	
CAD type, n (%)				0.11
CCS	33 (8.0)	33 (9.0)	0 (0)	
NSTEMI	100 (24)	88 (24)	12 (27)	
STEMI	268 (65)	236 (64)	32 (73)	
UA	10 (2.4)	10 (2.7)	0 (0)	
Cardiogenic shock (Killip 4), n (%)				0.54
Yes	111 (30)	97 (29)	14 (34)	
No	259 (70)	232 (71)	27 (66)	
Killip class, n (%)				0.35
1	185 (50)	169 (51)	16 (39)	
2	52 (14)	45 (14)	7 (17)	
3	22 (5.9)	18 (5.5)	4 (9.8)	
4	111 (30)	97 (29)	14 (34)	
LVEF (%), median (Q1, Q3)	40 (30, 53)	40 (30, 55)	37 (30, 50)	0.090
Diabetes, n (%)	188 (46)	171 (47)	17 (39)	0.31
Hypertension, n (%)	255 (62)	227 (62)	28 (64)	0.83

[1]Wilcoxon rank sum test; Pearson's chi-squared test; Fisher's exact test
If "Shock" or "Killip" class is not significantly higher in this group, the drug may have been administered for procedural complications rather than clinical severity
STEMI: ST-segment elevation myocardial infarction, CCS: Chronic coronary syndrome, Killip classification (risk assessment of patients after STEMI), Killip class I: Patients without any clinical signs of heart failure; Killip class II: Patients with rales or crackles in the lungs, elevated jugular venous pressure, and S3 gallop; Killip class III: Patients with frank acute pulmonary edema; Killip class IV: Patients with cardiogenic shock or hypotension (systolic blood pressure <90 mmHg) and signs of low cardiac output
LVEF: Left ventricular ejection fraction, NSTEMI: Non-ST-segment elevation myocardial infarction, CAD: Coronary artery disease, UA: Unstable angina, GP IIb/III: Glycoprotein IIb/IIIa. Data are summarized as mean±standard deviation, median (25th percentile; 75th percentile), or n (%)

who did not, no statistically significant differences were observed in Killip class, cardiopulmonary arrest, mortality, or recurrent myocardial infarction, findings that are broadly consistent with those reported in the aforementioned studies.

In the three phase III CHAMPION trials, a total of 24,902 patients undergoing elective or non-elective PCI were randomized to receive cangrelor or clopidogrel, and both clinical efficacy and safety outcomes were assessed.[8] In these studies, 12.7% of patients also received GP IIb/IIIa inhibitors. Among them, abciximab or eptifibatide was administered in 89.2%, whereas tirofiban was used in the remaining 10.8%. The use of GP IIb/IIIa inhibitors was more frequent in the NSTEMI population. Baseline comorbidities, including hypertension, dyslipidemia, diabetes mellitus, prior stroke, HF, and previous myocardial infarction, were more prevalent in patients not receiving GP IIb/IIIa inhibitors. The primary endpoint of the CHAMPION trials was a composite of all-cause mortality, myocardial infarction, ischemia-driven revascularization, or stent thrombosis within 48 hours after randomization. Although the primary endpoint was numerically lower in the cangrelor group compared with the clopidogrel group among patients receiving GP IIb/IIIa inhibitors, this difference did not reach statistical significance.

Regarding safety outcomes, three bleeding classification systems were used: the GUSTO, TIMI, and Acute Catheterization and Urgent Intervention Triage Strategy criteria. Across all three scoring systems, mild and moderate bleeding events were more frequent in patients receiving GP IIb/IIIa inhibitors compared with those who did not, whereas the incidence of severe bleeding was similar between the groups.

In our study, GP IIb/IIIa inhibitors were administered to 44 patients (74% STEMI), primarily in the context of high thrombus burden or as bailout/rescue therapy rather than routine use. Unlike the CHAMPION trials, tirofiban was the only GP IIb/IIIa inhibitor used in our cohort. Baseline characteristics, including age, sex, hypertension, diabetes mellitus, LVEF, and cardiogenic shock, were comparable between patients who did and did not receive GP IIb/IIIa inhibitors.

The clinical outcomes observed in our study were consistent with those reported in the CHAMPION trials, showing no significant differences in major clinical outcomes between patients receiving cangrelor with or without GP IIb/IIIa inhibitors. This study was conducted across 14 high-volume PCI centers in Türkiye, where the femoral approach was used in most procedures. Although radial access is recommended in current

Table 2. Procedural details and complexity indicators

Characteristic	GP IIb/IIIa (-) n=367	GP IIb/IIIa (+) n=44	p value[1]
Vascular access, n (%)			0.003
Femoral	257 (70)	40 (91)	
Radial	110 (30)	4 (9.1)	
Bifurcation procedure (complex), n (%)			0.31
Yes	61 (17)	10 (23)	
No	306 (83)	34 (77)	
Number of stents, n (%)			0.71
0	10 (2.7)	1 (2.4)	
1	227 (62)	23 (55)	
2	99 (27)	14 (33)	
3	22 (6.0)	3 (7.1)	
4	5 (1.4)	1 (2.4)	
5	1 (0.3)	0 (0)	
Total stent length (mm), median (Q1, Q3)	29 (20, 44)	36 (20, 56)	0.29
Procedure duration (min), median (Q1, Q3)	39 (25, 55)	35 (30, 55)	0.72
Contrast volume (mL), median (Q1, Q3)	150 (105, 220)	190 (120, 250)	0.20

[1]Pearson's chi-squared test; Fisher's exact test; Wilcoxon rank sum test
Increased bifurcation, stent length, or procedure duration supports "bail-out" (rescue) use
GP IIb/III: Glycoprotein IIb/IIIa

Table 3. Firth penalized logistic regression for independent predictors of bleeding within 48 hours

Variables	OR (95% CI)	p value
GP IIb/IIIa (+) vs. (–)	8.44 (3.54-20.18)	<0.001
Age (per year)	1.02 (0.99-1.06)	0.185
Female vs. male	1.02 (0.35-2.72)	0.963
Shock (absent vs. present)	0.76 (0.30-2.02)	0.578
Chronic kidney disease	0.82 (0.26-2.27)	0.708
Femoral access	1.05 (0.37-3.33)	0.926

CI: Confidence interval, OR: Odds ratio, GP IIb/III: Glycoprotein IIb/IIIa. Firth penalized logistic regression with profile likelihood CIs

guidelines, the femoral approach remains commonly used in Türkiye, particularly in patients with cardiogenic shock, due to easier vascular access and potential time savings.[30]

Given the relatively small number of bleeding events (n=26), Firth's penalized logistic regression was Firth penalized logistic regression was employed to reduce small-sample bias (events-per-variable ratio=4.3). Six predictors were included in the model: age, sex, cardiogenic shock, chronic kidney disease, femoral vascular access, and GP IIb/IIIa inhibitor use. Despite the inclusion of chronic kidney disease and femoral access-both of which were more prevalent in the GP IIb/IIIa group-GP IIb/IIIa inhibitor use remained the only independent predictor of bleeding, with an approximately 8.44-fold increase in risk. The robustness of this finding was further supported by IPTW analysis, which yielded a consistent estimate (OR: 7.97; 95% CI: 3.24–19.62; p<0.001) after balancing all measured confounders between groups. The agreement between these two distinct analytical approaches-multivariable regression and propensity score weighting-strengthens the conclusion that the observed bleeding risk is attributable to GP IIb/IIIa inhibitor use rather than baseline imbalances. Importantly, the absence of a significant difference in 12-month mortality between the GP IIb/IIIa and non-GP IIb/IIIa groups should be interpreted with caution. Given the relatively small number of patients in the GP IIb/IIIa group (n=44), the study was likely underpowered to detect clinically meaningful differences in long-term outcomes; therefore, a true effect on mortality cannot be excluded. In the CHAMPION trials, GP IIb/IIIa inhibitor use was associated with an approximately 3.5-fold increase in bleeding risk, with most events being mild to moderate in severity, findings that are consistent with those of our study. We speculate that the higher incidence of gastrointestinal bleeding as a major bleeding event may be related to the pharmacologic profile of GP IIb/IIIa inhibitors. Although both agents achieve potent platelet inhibition, GP IIb/IIIa inhibitors are associated with a more pronounced bleeding risk, likely due to their distinct targets, lack of reversibility, and sustained antiplatelet effects after infusion discontinuation. In addition, the higher prevalence of chronic kidney disease in the GP IIb/IIIa group may have further contributed to the increased bleeding risk.

The present study demonstrated that 74% of patients receiving GP IIb/IIIa inhibitors presented with STEMI, and the frequency of arrhythmia was significantly higher in this group, suggesting that these agents are more often used in clinically unstable scenarios. However, the absence of a statistically significant difference between the groups in terms of cardiogenic shock or Killip class indicates that GP IIb/IIIa inhibitors are not exclusively administered in the most severe clinical presentations but may also be used in response to acute procedural complications during PCI.

Table 4. Hemodynamic and interventional decision determinants directly related to GP IIb/IIIa use

Characteristic	Overall n=411	GP IIb/IIIa (-) n=367	GP IIb/IIIa (+) n=44	p value[1]
Inotropic support, n (%)	163 (40)	144 (39)	19 (43)	0.63
Mechanical circulatory support, n (%)	2 (0.5)	2 (0.6)	0 (0)	>0.99
Cardiopulmonary arrest, n (%)	102 (25)	88 (24)	14 (32)	0.26
Arrhythmia, n (%)	90 (22)	74 (20)	16 (36)	0.015
Systolic blood pressure (mmHg), median (Q1, Q3)	100 (80, 125)	100 (80, 125)	100 (82, 115)	0.90
Diastolic blood pressure (mmHg), median (Q1, Q3)	60 (45, 74)	60 (45, 74)	60 (50, 70)	0.82
Admission heart rate (bpm), median (Q1, Q3)	86 (70, 105)	86 (70, 106)	87 (69, 100)	0.47
LVEF (%), median (Q1, Q3)	40 (30, 53)	40 (30, 55)	37 (30, 50)	0.090
Culprit lesion, n (%)				0.22
0	29 (7.1)	29 (7.9)	0 (0)	
1	216 (53)	192 (52)	24 (55)	
2	66 (16)	55 (15)	11 (25)	
3	94 (23)	85 (23)	9 (20)	
4	3 (0.7)	3 (0.8)	0 (0)	
5	3 (0.7)	3 (0.8)	0 (0)	
Bifurcation, n (%)				0.31
Yes	71 (17)	61 (17)	10 (23)	
No	340 (83)	306 (83)	34 (77)	
Number of diseased vessels, n (%)				0.23
0	3 (0.7)	3 (0.8)	0 (0)	
1	169 (41)	152 (41)	17 (39)	
2	139 (34)	125 (34)	14 (32)	
3	95 (23)	84 (23)	11 (25)	
4	4 (1.0)	3 (0.8)	1 (2.3)	
5	1 (0.2)	0 (0)	1 (2.3)	
PCI duration (min), median (Q1, Q3)	39 (25, 55)	39 (25, 55)	35 (30, 55)	0.72
Contrast volume (mL), median (Q1, Q3)	150 (110, 220)	150 (105, 220)	190 (120, 250)	0.20
Number of stents, n (%)				0.71
0	11 (2.7)	10 (2.7)	1 (2.4)	
1	250 (62)	227 (62)	23 (55)	
2	113 (28)	99 (27)	14 (33)	
3	25 (6.2)	22 (6.0)	3 (7.1)	
4	6 (1.5)	5 (1.4)	1 (2.4)	
5	1 (0.2)	1 (0.3)	0 (0)	
Total stent length (mm), median (Q1, Q3)	29 (20, 44)	29 (20, 44)	36 (20, 56)	0.29
DES/BMS, n (%)				0.22
0	4 (1.0)	2 (0.6)	2 (4.5)	
1	377 (94)	336 (95)	41 (93)	
2	11 (2.8)	10 (2.8)	1 (2.3)	
3	6 (1.5)	6 (1.7)	0 (0)	
4	1 (0.3)	1 (0.3)	0 (0)	

[1]Pearson's chi-squared test; Fisher's exact test; Wilcoxon rank sum test
LVEF: Left ventricular ejection fraction, GP IIb/III: Glycoprotein IIb/IIIa, PCI: Percutaneous coronary intervention, DES: Drug-eluting stent, BMS: Bare-metal stent, min: Minimum

Table 5. Bleeding risk and contraindication indicators influencing GP IIb/IIIa use decision

Characteristic	Overall n=411	GP IIb/IIIa (-) n=367	GP IIb/IIIa (+) n=44	p value[1]
Hemoglobin (g/dL), median (Q1, Q3)	13.00 (11.60, 14.60)	13.00 (11.60, 14.70)	12.60 (11.50, 14.60)	0.62
Chronic kidney disease, n (%)	76 (19)	63 (17)	13 (30)	0.047
Dialysis, n (%)	11 (2.7)	9 (2.5)	2 (4.5)	0.34
48-hour bleeding (BARC), n (%)				<0.001
0	383 (94)	351 (96)	32 (73)	
1	16 (3.9)	7 (1.9)	9 (20)	
2	3 (0.7)	3 (0.8)	0 (0)	
3a	5 (1.2)	3 (0.8)	2 (4.5)	
3A	1 (0.2)	0 (0)	1 (2.3)	
5a	1 (0.2)	1 (0.3)	0 (0)	
48-hour bleeding (GUSTO), n (%)				<0.001
0	386 (94)	353 (96)	33 (75)	
1	15 (3.6)	8 (2.2)	7 (16)	
2	7 (1.7)	4 (1.1)	3 (6.8)	
3	3 (0.7)	2 (0.5)	1 (2.3)	
Bleeding site, n (%)				<0.001
Other	25 (6.1)	14 (3.8)	11 (25)	
None	386 (94)	353 (96)	33 (75)	
Transfusion requirement, n (%)	15 (3.7)	10 (2.7)	5 (11)	0.015
Surgery requirement, n (%)	1 (0.2)	1 (0.3)	0 (0)	>0.99
Vascular complication, n (%)	2 (0.5)	1 (0.3)	1 (2.3)	0.20

[1]Wilcoxon rank sum test; Pearson's chi-squared test; Fisher's exact test
BARC: Bleeding Academic Research Consortium, GUSTO: Global Utilization of Strategies to Open Occluded Coronary Arteries, GP IIb/III: Glycoprotein IIb/IIIa

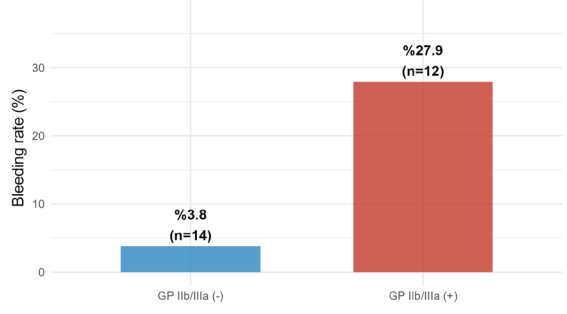

Figure 1. The impact of adding glycoprotein IIb/IIIa inhibitors on bleeding risk in patients treated with cangrelor (rates of any bleeding at 48 hours)

When procedural characteristics were examined, the higher prevalence of chronic kidney disease in the GP IIb/IIIa inhibitor group further supports the notion that this population represents a particularly vulnerable subgroup, predisposed to both thrombotic and hemorrhagic complications. One of the most notable findings of this study was the association between GP IIb/IIIa inhibitor use and bleeding complications. The incidence of any bleeding event was 27.9% in the GP IIb/IIIa inhibitor group compared with 3.8% in the control group. Notably, the significantly higher need for blood transfusion in the GP IIb/IIIa inhibitor group (12% vs. 2.7%) suggests that clinically relevant bleeding events are strongly associated with GP IIb/IIIa inhibitor use.

Study Limitations

The multicenter design and the use of real-world clinical data represent important strengths of this study. The consistency of the primary finding across both Firth's penalized logistic regression and IPTW propensity score analyses further supports the robustness of the results. However, several limitations should be acknowledged.

First, the retrospective design may introduce inherent selection and information biases. Second, due to reimbursement policies in Türkiye, cangrelor use is largely restricted to high-risk patient populations, which may limit the generalizability of the findings to the broader spectrum of coronary artery disease. Third, certain procedural variables that may influence bleeding risk, such as sheath size, were not collected and therefore could not be included in the analysis. Fourth, the relatively small number of patients receiving GP IIb/IIIa inhibitors (n=44) limits the statistical power to detect differences in long-term clinical outcomes, such as 12-month mortality, and the lack of a survival difference should not be interpreted as definitive evidence of no effect. Fifth, despite adjustment for multiple clinical covariates using both multivariable regression and propensity score weighting,

residual confounding from unmeasured variables-such as procedural complexity, thrombus burden severity, and anticoagulation dosing protocols-cannot be excluded and may have influenced the observed associations. Therefore, larger prospective studies encompassing the full spectrum of coronary artery disease presentations are warranted to validate and extend the findings of this analysis.

CONCLUSION

This study represents the first large-scale, multicenter retrospective analysis in Türkiye focusing on the concomitant use of GP IIb/IIIa inhibitors with cangrelor in a high-risk population of patients with ACS and CCS. The findings indicate that, in patients unable to receive oral P2Y12 inhibitors and therefore treated with cangrelor, the addition of bailout or rescue GP IIb/IIIa inhibitors was not associated with improved clinical outcomes, while being associated with an approximately eightfold increase in non-severe bleeding events.

Although chronic kidney disease and femoral vascular access were more prevalent in the GP IIb/IIIa group, neither was independently associated with bleeding after multivariable adjustment, suggesting that the increased bleeding risk is primarily driven by the pharmacological intensity of the combined antiplatelet regimen. In routine clinical practice, when considering the use of this potent antiplatelet combination (cangrelor plus GP IIb/IIIa inhibitors) during primary or non-pPCI, clinicians should carefully balance potential ischemic benefits against the increased bleeding risk. Whenever feasible, radial access should be preferred to minimize bleeding complications, and individualized risk-benefit assessment should guide therapeutic decision-making.

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Trakya University School of Medicine (approval number: TUTF-GOBAEK-2024/560, date: 20.01.2025).

Informed Consent: Patient consent was waived due to the retrospective nature of the study.

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ORIGINAL ARTICLE

Admission Lactate Levels and 1-Month Mortality in Elderly Patients with Non-ST Elevation Myocardial Infarction (NSTEMI) Undergoing Coronary Angiography

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ABSTRACT

Background: Serum lactate is an easily measurable marker that reflects tissue hypoperfusion and systemic stress. Although numerous studies have investigated this topic, no lactate cut-off value associated with mortality has been established for elderly patients with non-ST-segment elevation myocardial infarction (NSTEMI).

Aim: This study aimed to determine the relationship between lactate levels and 1-month mortality and complications in elderly patients with NSTEMI.

Study Design: Retrospective cohort study.

Methods: This study included 110 patients aged ≥65 years who were diagnosed with NSTEMI between August 2024 and August 2025. Baseline lactate levels, duration of hospital stay, 1-month mortality, arrhythmia, cerebrovascular events, recurrent myocardial infarction (MI), contrast-induced nephropathy, deep vein thrombosis/pulmonary embolism, and bleeding events were evaluated.

Results: The mean age was 78.61±8.27 years, and the mean ejection fraction was 46.68±11.52%. The 1-month mortality rate was 16.4%. Admission lactate demonstrated good discriminatory ability for predicting mortality [area under the curve=0.785; 95% confidence interval (CI): 0.651-0.919; p<0.001]. A cut-off value of ≥2.25 mmol/L yielded a sensitivity of 72.2% and a specificity of 72.8%. Patients with lactate levels ≥2.25 mmol/L had significantly higher mortality than those with lower levels (34.2% vs. 6.9%, p<0.001). In the multivariable logistic regression analysis, only lactate levels [odds ratio (OR)=1.35; 95% CI: 1.04-1.76; p=0.023] and fasting glucose levels (OR=1.01; p=0.010) were identified as independent predictors of mortality.

Conclusion: Higher lactate levels were associated with short-term mortality in elderly patients with NSTEMI. Because of its rapid availability and low cost, lactate may serve as a practical and useful marker for early risk assessment in this population.

Keywords: Lactate, myocardial infarction, NSTEMI, elderly patients

INTRODUCTION

Non-ST-segment elevation myocardial infarction (NSTEMI) is the most common form of acute coronary syndrome (ACS) in older adults. The risk of mortality is higher in older patients because of the often atypical clinical presentation, the high prevalence of multiple comorbidities, and the increased occurrence of multivessel disease.[1-4] Therefore, identifying markers associated with mortality in patients with NSTEMI has become increasingly important, and there is a need for inexpensive, easily measurable biomarkers.

Lactate, a metabolic byproduct, provides information about the adequacy of tissue oxygenation and perfusion.[5,6] Its use is particularly common in intensive care units and among patients with shock or sepsis for monitoring treatment response.[6,7] A study of patients with STEMI showed that elevated lactate levels at presentation to the emergency department were associated with higher mortality.[8]

In NSTEMI, another ischemic condition, very few studies have examined lactate levels, particularly in elderly patients with NSTEMI. Therefore, this study aimed to investigate the relationship between lactate levels and 1-month mortality and complications in elderly patients with NSTEMI.

METHODS

Study Design and Setting

This retrospective study was conducted at a Gaziantep City Hospital, the only 24/7 primary percutaneous coronary intervention (PCI) center

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in the city. The ethics committee approval was obtained by Gaziantep City Hospital Non-Interventional Clinical Research Ethics Committee at its meeting numbered 2026/27, decision number 444/2026 and dated: 18.02.2026. Due to the retrospective design of the study, written informed consent was not obtained from the patients.

Selection of Participants

All patients diagnosed with NSTEMI by cardiology specialists who underwent coronary angiography (CAG) between August 2024 and August 2025 were included in the study. Eligible participants were aged ≥65 years. Patients aged ≥65 years were further evaluated by decade of age. Patients with incomplete medical records or unclear 1-month follow-up data after the procedure were excluded.

Measurements and Outcomes

Sociodemographic characteristics, comorbidities, symptoms, hematological and biochemical parameters (complete blood count, glucose, lipid profile, renal function tests, and liver function tests), baseline electrocardiograms, echocardiographic findings [valvular pathologies and ejection fraction (EF)], and CAG findings were reviewed. Duration of hospitalization, 1-month mortality, arrhythmia, cerebrovascular events, recurrent myocardial infarction (MI), contrast-induced nephropathy, deep vein thrombosis/pulmonary embolism, gastrointestinal/genitourinary bleeding, were also evaluated.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as frequencies and percentages (n, %) for categorical variables and as mean±standard deviation or median (minimum-maximum) for continuous variables. Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive value of lactate levels for mortality. Independent samples t-tests were used for comparisons between two groups. Pearson chi-square tests and Fisher exact tests were used to compare categorical variables. A p value <0.05 was considered statistically significant. Variables associated with 1-month mortality were first identified using univariate logistic regression analysis. Variables found to be significant in the univariate analysis were included in the multivariable logistic regression model along with clinically important variables. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Model fit was assessed using the -2 log likelihood and Nagelkerke R^2 statistics. All statistical tests were two-sided, and $p<0.05$ was considered statistically significant.

RESULTS

Table 1 summarizes the sociodemographic and clinical characteristics of the patients included in the study. The mean age was 78.61±8.27 years. By age group, 35.5% of the patients were aged 65-74 years, 36.4% were aged 75-84 years, and 28.2% were aged ≥85 years. No significant difference was observed in the sex distribution between women (52.7%) and men (47.3%) (Table 1).

Regarding comorbidities, hypertension was present in the majority of patients (71.8%), whereas diabetes mellitus was identified in 55.5% of cases. Coronary artery disease was present in 40.0% of patients, whereas peripheral artery disease was observed in 10.9% of cases. A history of coronary artery bypass grafting (CABG) was reported in only 1.8% of patients. Hyperlipidemia was present in approximately half of the patients (50.9%), whereas a history of cerebrovascular disease was reported in 6.4% of cases. Chronic obstructive pulmonary disease was identified in 7.3% of cases (Table 1).

Cardiac function assessment showed that the mean EF was 46.68±11.52%. The majority of patients had sinus rhythm (94.4%), whereas atrial fibrillation (AF) was observed in 5.6% of patients (Table 1).

Regarding hospital admission characteristics, the mean intensive care unit stay was 3.98±3.21 days, and the mean total hospital stay was 6.97±5.71 days. According to the CAG findings, PCI was performed in 59.1% of patients, CABG was planned in 22.7%, 15.5% were managed with optimal medical therapy, and 2.7% received medical therapy alone (Table 1).

When early clinical outcomes were evaluated, the 1-month mortality rate was 16.4%. Within 1 month, contrast-induced nephropathy was observed in 14.5% of cases, and new-onset AF, ventricular tachycardia (VT), or atrioventricular block occurred in 11.8%. During the same period, ischemic cerebrovascular events occurred in 5.5% of cases, whereas hemorrhagic cerebrovascular events occurred in 0.9%. Recurrent MI occurred in 11.8% of cases, whereas deep vein thrombosis/pulmonary embolism (0.9%) and gastrointestinal/genitourinary bleeding (9.1%) were also observed (Table 1).

Table 2 presents the descriptive statistics of the laboratory parameters. Regarding metabolic and acid-base status, the mean lactate level was 2.51±2.27 mmol/L, with values ranging from 0.30 to 14.00 mmol/L. The mean pH was 7.37±0.09, and the mean ionized calcium level was 1.12±0.08 (Table 2).

Renal function assessment showed that the mean urea level was 52.41±24.75, and the mean creatinine level was 1.03±0.39. Among the hematological parameters, the mean white blood cell (WBC) count was 10.16±3.26, the mean platelet count was 252.04±63.20, and the mean hemoglobin level was 12.74±2.05 (Table 2).

Table 3 shows the predictive value of lactate levels for 1-month mortality in the overall study population and across age subgroups, as assessed by ROC curve analysis. In the overall study population, lactate levels demonstrated good discriminatory ability for predicting 1-month mortality [area under the curve (AUC)=0.785; 95% CI: 0.651-0.919; $p<0.001$]. A cut-off value of ≥2.25 mmol/L yielded a sensitivity of 72.2% and a specificity of 72.8% (Table 3).

In subgroup analyses, lactate levels showed good discriminatory ability for mortality in patients aged 65-74 years (AUC=0.884; 95% CI: 0.739-1.000; $p=0.029$), with a sensitivity of 66.7% and a specificity of 75.0% at a cut-off value of ≥2.25 mmol/L. In patients aged 75-84 years, the discriminatory ability of lactate levels was even greater (AUC=0.924; 95% CI: 0.838-1.000; $p<0.001$). At a cut-off value of ≥2.65 mmol/L, the sensitivity was 85.7% and the specificity was 84.8% (Table 3). In contrast, among patients aged ≥85 years, lactate levels showed limited discriminatory ability for predicting 1-month mortality (AUC=0.611; 95% CI: 0.352-0.871), and the association was not statistically significant ($p=0.355$) (Table 3).

Table 1. Distribution of sociodemographic and clinical variables

Variables	n	%
Age		
Mean±SD	78.61±8.27	
Median (min-max)	77.5 (65-101)	
65-74	39	35.5
75-84	40	36.4
≥85	31	28.2
Gender		
Female	58	52.7
Male	52	47.3
HT		
Yes	79	71.8
DM		
Yes	61	55.5
PAD		
Yes	12	10.9
CAD		
Yes	44	40.0
History of CABG		
Yes	2	1.8
Hyperlipidemia		
Yes	56	50.9
Previous cerebrovascular disease		
Yes	7	6.4
COPD		
Yes	8	7.3
Ejection fraction		
Mean±SD	46.68±11.52	
Median (min-max)	50.0 (20-65)	
Mitral stenosis		
None	103	93.6
1st	3	2.7
2nd	3	2.7
3rd	1	0.9
Mitral regurgitation		
None	15	13.6
1st	75	68.2
2nd	19	17.3
3rd	1	0.9
Aortic stenosis		
None	102	92.7
1st	5	4.5
2nd	1	0.9
3rd	2	1.8
Aortic regurgitation		
None	89	80.9
1st	18	16.4
2nd	2	1.8
3rd	1	0.9
Tricuspid regurgitation		
None	28	25.5
1st	70	63.6
2nd	11	10.0
3rd	1	0.9
Rhythm		
Sinus rhythm	102	94.4
AF	6	5.6
Total days in intensive care unit		
Mean±SD	3.98±3.21	
Median (min-max)	3.0 (1-22)	
Total hospital stays		
Mean±SD	6.97±5.71	
Median (min-max)	4.0 (1-32)	
Coronary angiogram results		
Medical	3	2.7
PCI	65	59.1
CABG	25	22.7
Maximal medical treatment	17	15.5
1-month mortality		
Yes	18	16,4
1-month contrast nephropathy		
Yes	16	14.5
1-month new AF/VT/block events		
Yes	13	11.8
1-month cerebrovascular events		
Ischemic	6	5.5
Hemorrhagic	1	0.9
1-month recurrent MI events		
Yes	13	11.8
1-month DVT/PE		
Yes	1	0.9
1-month gastrointestinal/ genitourinary bleeding		
Yes	10	9.1

HT: Hypertension, DM: Diabetes mellitus, PAD: Peripheral artery disease, CAD: Coronary artery disease, CABG: Coronary bypass surgery, PCI: Percutaneous coronary intervention, COPD: Chronic obstructive pulmonary disease, AF: Atrial fibrillation, MI: Myocardial infarction, DVT: Deep vein thrombosis, PE: Pulmonary embolism, SD: Standard deviation, min-max: Minimum-maximum, VT: Ventricular tachycardia

Table 2. Data on laboratory parameters

	Minimum	Maximum	Mean	SD
Lactate (0.5-1.6 mmol/L)	0.30	14.00	2.51	2.27
pH (7.35-7.45)	6.91	7.58	7.37	0.09
Ionized calcium (1.12-1.29 mmol/L)	0.83	1.37	1.12	0.08
HDL-C (mg/dL)	14.00	81.00	47.44	10.79
LDL-C (mg/dL)	22.00	239.00	122.01	36.41
Total cholesterol (mg/dL)	13.00	330.00	194.02	48.31
Triglycerides (mg/dL)	39.00	396.00	132.18	77.89
Sodium (136-146 mmol/L)	128.00	144.00	137.61	3.19
Potassium (3.5-5.1 mmol/L)	3.13	6.29	4.32	0.51
Urea (2-43 mg/dL)	20.00	172.00	52.41	24.75
Creatinine (0.67-1.17 mg/dL)	0.35	2.92	1.03	0.39
Calcium (8.8-10.6 mg/dL)	0.79	10.70	9.07	1.12
ALT (0-50 U/L)	3.00	120.00	22.29	19.91
AST (0-50 U/L)	11.00	425.00	47.50	62.96
Glucose (74-106 mg/dL)	54.00	599.00	184.00	105.66
Albumin (35-52g/L)	23.50	71.00	39.05	5.34
C-reactive protein (0-5 mg/dL)	0.90	140.00	17.64	28.15
WBC (10^9/L)	3.70	21.30	10.16	3.26
Platelet (10^9/L)	81.00	401.00	252.04	63.20
Hb (g/dL)	6.30	16.60	12.74	2.05

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, WBC: White blood cell, Hb: Haemoglobin, SD: Standard deviation

Table 3. Analysis of lactate's predictive value in distinguishing 1-month mortality by age groups and all patients

Variables	AUC	%95 CI	Cut-off	Sensitivity (%)	Specificity (%)	p
Lactate	0.785	0.651-0.919	≥2.25	72.2	72.8	**<0.001**
Lactate (65-74 age group)	0.884	0.739-1.000	≥2.25	66.7	75.0	**0.029**
Lactate (75-84 age group)	0.924	0.838-1.000	≥2.65	85.7	84.8	**<0.001**
Lactate (≥85 age group)	0.611	0.352-0.871	≥1.95	62.5	56.5	0.355

AUC: Area under the curve, 95% CI: Confidence interval

Table 4 compares the clinical outcomes between two groups of patients according to lactate levels: <2.25 mmol/L and ≥2.25 mmol/L. When the length of stay in the intensive care unit was evaluated, the mean stay was longer in the group with lactate levels ≥2.25 mmol/L (4.47±3.77 days vs. 3.72±2.87 days); however, this difference was not statistically significant (p=0.287). Similarly, no significant difference was observed between the two groups in the distribution of CAG outcomes, including medical therapy, PCI, CABG, and optimal medical therapy (p=0.914) (Table 4).

In the evaluation of 1-month mortality, a clear and statistically significant association was found between lactate levels and mortality. The 1-month mortality rate was 6.9% in patients with lactate levels <2.25 mmol/L, whereas it increased to 34.2% in those with lactate levels ≥2.25 mmol/L (p<0.001) (Table 4).

When other early complications were evaluated, the incidence of contrast-induced nephropathy within 1 month did not differ significantly between the two groups (p=0.420). Similarly, no significant differences were observed in the incidence of new-onset AF, VT, or atrioventricular block (p=0.763), cerebrovascular events within 1 month (p=1.000), recurrent MI (p=0.753), deep vein thrombosis/pulmonary embolism (p=1.000), or gastrointestinal/genitourinary bleeding (p=0.310) (Table 4).

Table 4. Comparison of various clinical variables with lactate groups

	Lactate		
Variables	**<2.25 mmol/L n=72**	**≥2.25 mmol/L n=38**	**p**
Total days in intensive care unit			
Mean±SD	3.72±2.87	4.47±3.77	0.287[a]
Coronary angiogram results			
Medical	2 (2.8)	1 (2,6)	0.914[c]
PCI	44 (61.1)	21 (55.3)	
CABG	15 (20.8)	10 (26.3)	
Maximal medical treatment	11 (15.3)	6 (15.8)	
1-month mortality			
No	67 (93.1)	25 (65.8)	**<0.001[b]**
Yes	5 (6.9)	13 (34.2)	
1-month contrast nephropathy			
No	63 (87.5)	31 (81.6)	0.402[b]
Yes	9 (12.5)	7 (18.4)	
1-month new AF/VT/block events			
No	64 (88.9)	33 (86.8)	0.763[c]
Yes	8 (11.1)	5 (13.2)	
1-month cerebrovascular events			
No	67 (93.1)	36 (94.7)	1.000[c]
Ischemic	4 (5.6)	2 (5.3)	
Hemorrhagic	1 (1,4)	0 (0)	
1-month recurrent MI events			
No	64 (88.9)	33 (86.8)	0.753[c]
Yes	8 (11.1)	5 (13.2)	
1-month DVT/PE			
No	71 (98.6)	38 (100)	1.000[c]
Yes	1 (1.4)	0 (0)	
1-month gastrointestinal/genitourinary bleeding			
No	67 (93.1)	33 (86.8)	0.310[b]
Yes	5 (6.9)	5 (13.2)	

[a]: Independent t-test, [b]: Pearson chi-square test, [c]: Fisher's exact test, p<0.05 statistically significant
CABG: Coronary bypass surgery, PCI: Percutaneous coronary intervention, AF: Atrial fibrillation, VT: Ventricular tachycardia, MI:Myocardial infarction, DVT: Deep vein thrombosis, PE: Pulmonary embolism, SD: Standard deviation

Overall, lactate levels ≥2.25 mmol/L were strongly and significantly associated with short-term mortality, whereas no significant association was observed with intensive care unit length of stay or other early complications.

Table 5 presents the univariate and multivariable logistic regression analyses performed to identify factors associated with 1-month mortality. In the univariate analysis, lactate level (OR=1.53; 95% CI: 1.18-1.98; p=0.001), EF (OR=0.94; 95% CI: 0.90-0.98; p=0.009), fasting glucose level (OR=1.01; p=0.013), and WBC count (OR=1.25; 95% CI: 1.08-1.45; p=0.004) were significantly associated with mortality. Although age and creatinine levels approached statistical significance, hemoglobin and C-reactive protein (CRP) levels were not associated with mortality (Table 5).

In the multivariable logistic regression analysis adjusted for age, EF, creatinine, hemoglobin, fasting glucose, CRP, and WBC levels (Table 6), only lactate levels (OR=1.35; 95% CI: 1.04-1.76; p=0.023) and fasting glucose levels (OR=1.01; p=0.010) were identified as independent predictors of mortality. Age, EF, creatinine, hemoglobin, CRP, and WBC levels were not independently associated with mortality in the multivariable model. The model's -2 log likelihood was 67.047, and the Nagelkerke R^2 value was 0.416, indicating moderate-to-good explanatory ability for mortality (Table 6).

Table 5. Univariate binary logistic regression

Variables	OR	95% CL	Wald	p
Lactate	1.53	1.18-1.98	10.353	0.001
Age	1.05	0.99-1.12	2.746	0.097
EF	0.94	0.90-0.98	6.904	0.009
Creatinine	2.64	0.83-8.34	2.720	0.099
Haemoglobin	0.94	0.74-1.19	0.277	0.599
Glucose	1.01	1.00-1.01	6.192	0.013
C-reactive protein	1.00	0.99-1.02	0.106	0.745
White blood cell	1.25	1.08-1.45	8.505	0.004

OR: Odds ratio, EF: Ejection fraction, CL: Confidence limit

Table 6. Multivariable binary logistic regression

Variables	Adjusted OR	95% CL	Wald	p
Lactate	1.35	1.04-1.76	5.200	0.023
Age	1.08	0.97-1.20	2.005	0.157
EF	0.97	0.91-1.02	1.489	0.222
Creatinine	2.06	0.53-8.04	1.088	0.297
Haemoglobin	0.89	0.64-1.23	0.536	0.464
Glucose	1.01	1.00-1.01	6.627	0.010
C-reactive protein	0.99	0.97-1.02	0.201	0.654
White blood cell	1.12	0.91-1.38	1.216	0.270

-2 Log Likelihood: 67,047, Nagelkerke R^2:0,416, OR: Odds ratio, EF: Ejection fraction, CL: Confidence limit

DISCUSSION

Although no significant associations were observed between elevated lactate levels and intensive care unit length of stay, contrast-induced nephropathy, recurrent events, deep vein thrombosis/pulmonary embolism, cerebrovascular events, gastrointestinal bleeding, or genitourinary bleeding, a significant association was found with 1-month mortality.

Lactate is a metabolite produced through anaerobic metabolism and is easily measured in the blood.[9] Blood lactate levels increase in conditions associated with tissue hypoxia and impaired perfusion. The most well-known causes of elevated blood lactate levels are sepsis and septic shock; however, other recognized causes include severe trauma, traumatic brain injury, severe asthma attacks, liver failure, and kidney failure.[5,9,10] More than simply an indicator of hypoxia, lactate may reflect the overall hemodynamic burden and systemic stress response in elderly patients with ACS. During acute myocardial ischemia, impaired coronary perfusion can lead to localized anaerobic metabolism, reduced cardiac output, microcirculatory dysfunction, and sympathetic overactivation.

Lactate is also used to monitor cardiovascular diseases. In MI, the anaerobic pathway is accelerated because of coronary stenosis, resulting in increased lactate production.[11,12] Various studies have investigated lactate monitoring in patients with MI complicated by cardiogenic shock. These studies have shown that lactate monitoring provides valuable information for predicting patient prognosis. An initial lactate level above 2.0 mmol/L has been associated with a poor prognosis, whereas a lactate level below 3.1 mmol/L at 8 hours has been associated with a favorable prognosis.[13-15] In patients with MI without advanced heart failure, lactate levels above 2.5 mmol/L have also been associated with a poor prognosis.[12]

When studies involving the elderly population are examined, a study of older patients admitted to the emergency department reported an association between elevated lactate levels and short-term mortality regardless of infection, with lower mortality observed in patients with lactate levels below 2 mmol/L.[16] Similarly, a study evaluating early mortality after hip fracture in patients aged ≥65 years found that mortality was higher among patients with lactate levels above 2 mmol/L.[17] In the present study, the lactate cut-off value associated with mortality in elderly patients with NSTEMI was 2.25 mmol/L. Notably, lactate remained independently associated with 1-month mortality after adjustment for age, EF, creatinine, hemoglobin, glucose, CRP, and WBC count in the multivariable analysis, supporting its validity as a prognostic marker in this population.

In our study, no significant association was observed between lactate levels and events that may occur after angiography or MI. This finding may be explained by the fact that the study population consisted of frail elderly patients with preexisting cardiovascular disease who routinely received intravenous fluid support after MI to reduce the risk of contrast-induced nephropathy.

Interestingly, lactate did not demonstrate significant discriminatory ability in patients aged ≥85 years. The relatively small sample size in this subgroup may have reduced the statistical power; however, biological and clinical factors may also have contributed to this finding. Patients in this age group are often frailer, have multiple comorbidities, receive multiple medications, and have reduced physiological reserve. All of these factors can influence lactate metabolism and mortality independently of acute ischemic coronary events. Furthermore, non-cardiovascular causes of death are more common in the oldest patients, which may have reduced the prognostic specificity of admission lactate levels for cardiovascular outcomes. Therefore, although admission lactate appears to be a useful marker in patients aged 65-84 years, its prognostic performance in patients aged ≥85 years should be interpreted with caution and validated in larger prospective studies specifically designed for this age group.

Admission lactate levels should be considered an easily obtainable adjunctive biomarker rather than a replacement for established risk stratification tools. Because lactate testing is inexpensive, rapidly available, and routinely performed in emergency departments, it may help identify elderly patients with NSTEMI who are at increased short-term risk before a comprehensive clinical evaluation is completed. However, its prognostic value should ideally be interpreted in conjunction with established clinical, laboratory, and angiographic findings rather than in isolation.

Study Limitations

The primary limitation of our study is that only admission lactate levels were available for analysis. Previous studies have shown that, in patients with acute MI and cardiogenic shock, serial lactate measurements and lactate clearance at 6-8 hours provide stronger prognostic information than a single measurement. SYNTAX and Gensini scores were not calculated from the patients' CAG findings. In addition, validated ACS risk scores, such as GRACE and TIMI, as well as Killip class and frailty assessments, were not routinely available in our retrospective database. As a result, we were unable to assess the incremental prognostic value of lactate beyond these established risk stratification tools. Another limitation is that the relatively small sample size and single-center design may limit the generalizability of our findings. In addition, detailed information on the causes of death was unavailable. Because mortality was assessed as all-cause mortality, we were unable to distinguish among cardiac, non-cardiac, and procedure-related deaths. Consequently, the observed association between admission lactate levels and mortality should be interpreted as reflecting overall short-term mortality rather than specifically cardiovascular mortality.

CONCLUSION

Admission lactate levels were significantly associated with 1-month mortality in elderly patients with NSTEMI. Although lactate appears to have potential value for early prognostic assessment, its role should be interpreted with caution because of the retrospective, single-center design of the study. Larger prospective studies are needed to validate these findings.

Ethics Committee Approval: The ethics committee approval was obtained by Gaziantep City Hospital Non-Interventional Clinical Research Ethics Committee at its meeting numbered 2026/27, decision number 444/2026 and dated: 18.02.2026.

Informed Consent: Due to the retrospective design of the study, written informed consent was not obtained from the patients.

Authorship Contributions: Concept: E.P., Design: E.P., Data Collection or Processing: E.P., Ş.Ç., Analysis or Interpretation: E.P., Literature Search: E.P., Writing: E.P.

Conflict of Interest: No conflict of interest was declared by the authors.

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CASE REPORT

Constrictive Pericarditis as a Rare Cause of Recurrent Miscarriage

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ABSTRACT

Constrictive pericarditis, a rare cause of recurrent pregnancy loss, is a clinical entity characterized by a rigid, fibrotic, thickened pericardium and causes both right and left ventricular diastolic filling deterioration. The underlying etiology is mostly idiopathic, followed by pericardial injury and metabolic and connective tissue diseases. It may follow any pericardial inflammation or effusion, leading to the ultimate development of chronic fibrotic scar tissue and calcification. Endometriosis is a clinical condition defined as functional endometrial glands and stroma outside the uterine cavity. We presented a case of constrictive pericarditis that developed one year after the clinical diagnosis of a pericarditis attack in a 32-year-old woman with recurrent pregnancy loss and endometrioma cyst surgery.

Keywords: Constrictive pericarditis, heart failure, miscarriage

INTRODUCTION

Constrictive pericarditis is characterized by rigid, fibrous, or calcific constrictive thickening of the pericardium, which leads to heart failure. The underlying etiology is often idiopathic (presumably viral), followed by causes such as cardiothoracic surgery and radiation therapy.[1] Pericardial effusion is the most common symptom of pericardial disease during pregnancy. Detected pericardial effusion is generally well-tolerated and often resolves spontaneously postpartum. Acute pericarditis is the second most common cardiac disease requiring medical treatment during pregnancy, while constrictive pericarditis is a rare condition and a potential cardiac cause of recurrent pregnancy loss that is often overlooked. Cardiovascular diseases are a significant complication that should not be overlooked during pregnancy.

CASE REPORT

A 32-year-old woman presented to our cardiology outpatient department with dyspnea on exertion, atypical chest pain, and palpitations. Her medical history revealed that a 6 cm endometrioma was removed from her left ovary 1 year prior, followed by an acute pericarditis attack 2 weeks after the operation. The patient experienced recurrent pregnancy loss in the following period. Her white blood cell count (WBC) and C-reactive protein (CRP) values were slightly increased, and minimal pericardial effusion was observed on echocardiogram. The patient stated that she took medications for approximately a week, after which her complaints subsided; however, she had no follow-up visit. On physical examination, her heart rate was 96 beats/min and regular, and her blood pressure was 110/60 mmHg, with a pulsus paradoxus of 20 mmHg. Additionally, a pericardial knock was auscultated. Basic electrocardiogram showed non-specific T-wave changes. Transthoracic echocardiogram revealed a left ventricular systolic ejection fraction of 45% with inferior and posterolateral wall abnormalities, moderate bi-atrial dilatation, and diastolic septal bounce. Pericardial thickness was 19 mm on the apical four-chamber view, with markedly increased echogenicity, particularly in the mitral annular lateral wall (Figures 1A, B). The inferior vena cava measured 25 mm, with <50% collapsibility during inspiration. Mitral inflow demonstrated an early/atrial ratio of 2.13. Respiratory variability was noted in mitral (>25%) inflow on Doppler echocardiography (Figures 2A, B). On tissue Doppler, the mitral annular septal E' velocity was 17 cm/sec, and the lateral E' velocity was 7 cm/sec, indicating a constrictive physiology (Figures 3A, B). Laboratory findings were normal for WBC, erythrocyte sedimentation rate, CRP, and liver, kidney, and thyroid functions. Testing for connective tissue disease was negative, including antinuclear antibody, rheumatoid factor, and other autoimmune antibodies. Urine analysis was unremarkable. Chest radiography showed egg-shell calcification around the heart on the lateral view (Figure 4A). Chest computed tomography revealed prominent calcified pericardium thickening, particularly around the right ventricular and left ventricular posterior walls (Figures 4B-D). The cardiac team decided to treat the patient with pericardiectomy. The patient underwent off-pump surgery with an uneventful recovery. Video 1 shows the intraoperative view of the calcified pericardium, which felt like a rock. Pathological examination of the surgical specimen revealed

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a fibrotic, thickened, and calcified pericardium. Our patient, who had a successful pregnancy after the operation, was followed up for 3 years. Informed consent was obtained from the patient.

DISCUSSION

Similar to right heart failure, chronic constrictive pericarditis causes recurrent pregnancy losses, decreased cardiac output, venous congestion, and decreased uteroplacental flow. Constrictive pericarditis is the final stage of pericardial inflammation, characterized by thickening of the pericardium that limits ventricular filling and results in heart failure.[2,3] The most common causes are idiopathic causes, previous cardiac surgery, radiation therapy, and connective tissue disorders.[1,4,5] In developing countries, tuberculosis remains the most common cause of constrictive pericarditis.[6] Recurrent miscarriage (RM) is defined as the loss of three or more consecutive pregnancies before 22 weeks of gestation. This condition affects 0.5–3% of all fertile couples.[7] In patients with heart failure, decreased perfusion and venous congestion are the most crucial determinants of liver and kidney dysfunction.[8,9] Similar hemodynamic interactions may occur between the heart and placenta. The limited autoregulatory capacity of the uteroplacental circulation indicates that placental function is directly dependent on maternal cardiac performance.[10] The relationship between maternal hemodynamics and placental function is well-established, having been studied in pregnant women with heart disease and those with pre-eclampsia and in healthy women.[11] Compared with healthy pregnant women, the association between maternal cardiac dysfunction (particularly right ventricular dysfunction) and impaired uteroplacental circulation is clearly shown in a cohort of women with congenital heart disease (CHD) before and during pregnancy; the association is also evident in those with specific types of CHD, such as tetralogy of Fallot.[11,12] Chronic constrictive pericarditis, which produces a clinical picture similar to right heart failure, causes late recurrent pregnancy losses, decreased cardiac output, venous congestion, and decreased uteroplacental flow. Our patient experienced three miscarriages before diagnosis: the first at

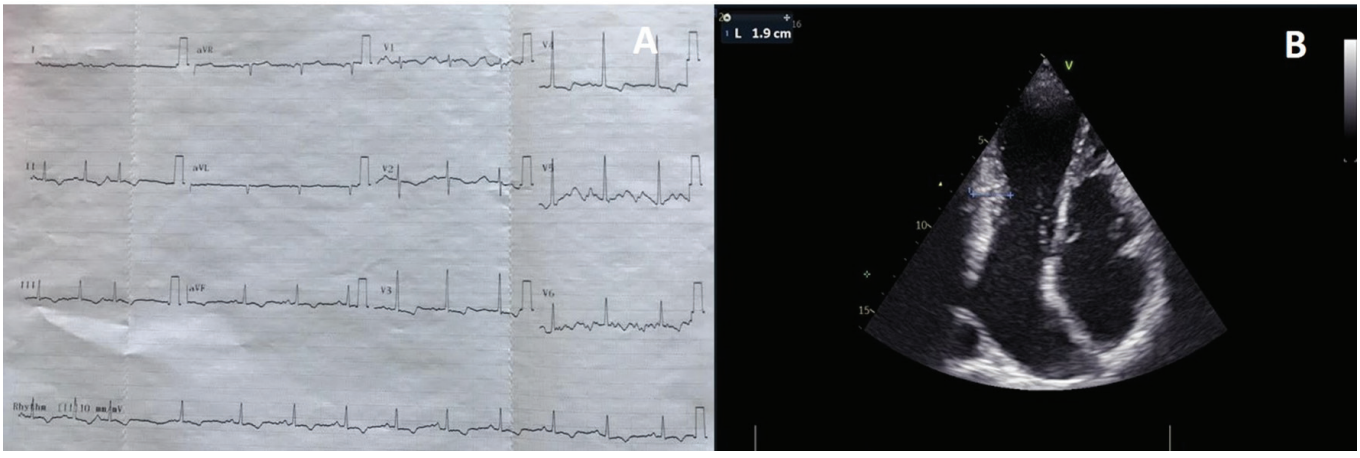

Figure 1. (A) Electrocardiography/electrocardiogram showed non-specific T-wave changes. (B) The pericardial thickness was 19 mm on the apical-4-chamber view

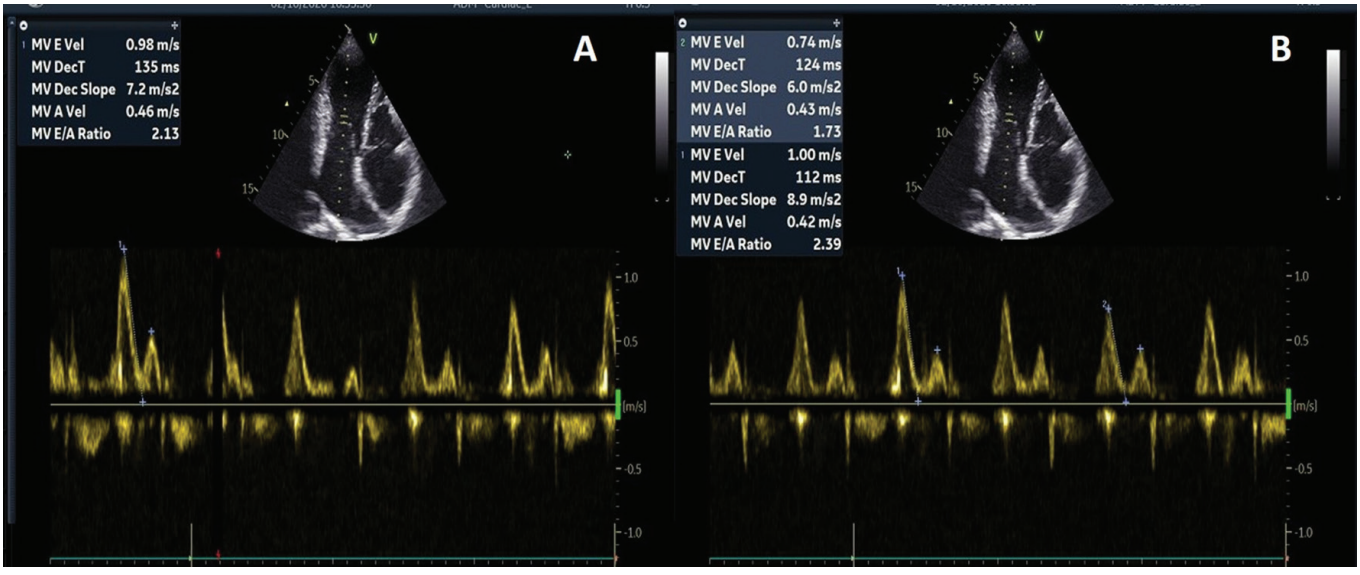

Figure 2. (A) E/A ratio was 2.13 on mitral inflow Doppler. (B) Respiratory variability was observed in mitral (>25%) inflow on Doppler echocardiography
E/A: Early/atrial

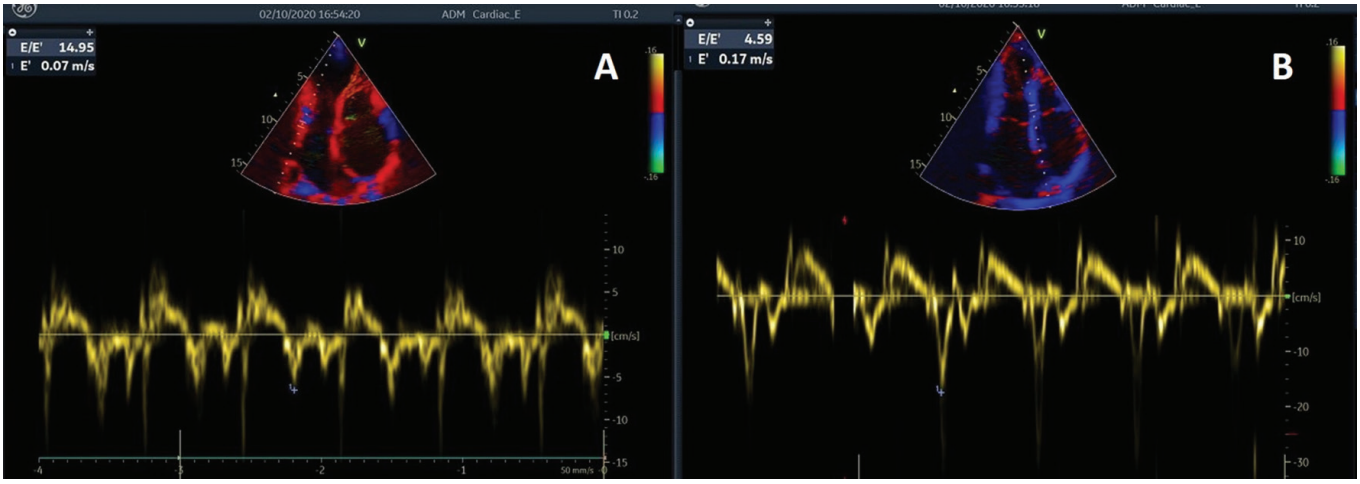

Figure 3. (A) Mitral lateral E' velocity was 7 cm/sec. (B) Mitral annular septal E' velocity was 17 cm/sec on tissue Doppler

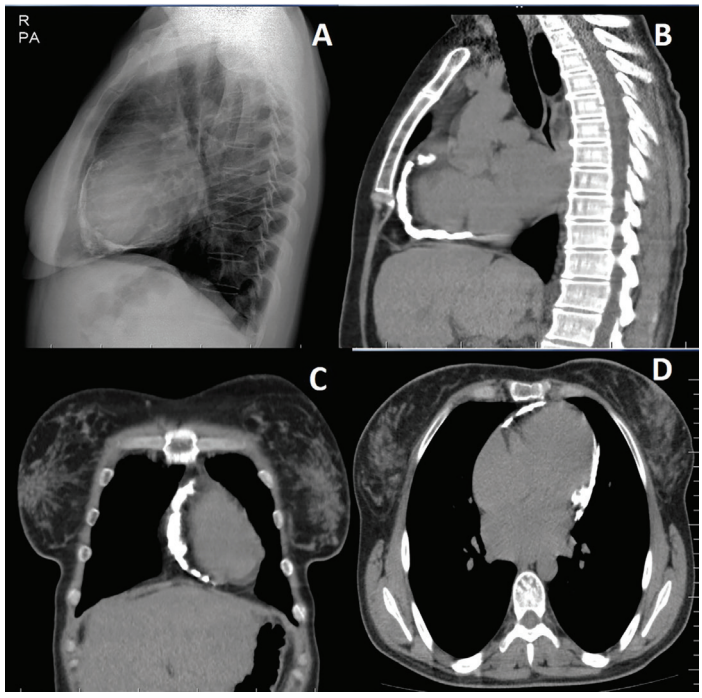

Figure 4. (A) Lateral chest X-ray shows egg-shell pericardial calcification around the heart. (B-D) Transverse computed tomography with sagittal and coronal reconstructions shows diffuse pericardial calcified thickening

10 weeks of a twin pregnancy, the second at 20 weeks, and the last at 14 weeks. Endometriosis is the presence of endometrial glands and stroma outside the uterine cavity. The thoracic cavity is the second most common area of involvement following the abdominopelvic cavity.[13,14] Moreover, spontaneous, recurrent pneumothorax is the most well-known type of catamenial pneumothorax (CP); it occurs in women of reproductive age without underlying lung disease and is associated with their menstrual cycle.[15] Symptoms typically appear at different times of the cycle (i.e., before, during, or after menstruation) and can last from a few hours to 7 days. CP is the most common manifestation of thoracic endometriosis syndrome, which includes hemothorax, hemoptysis, pulmonary nodules, and pneumothorax.[16,17] Several hypotheses regarding the involvement of thoracic tissues exist, including retrograde menstruation, transdiaphragmatic air passage, physiological factors, metastasis, coelomic metaplasia, vascular embolization, vasculogenesis, and immune dysfunction.[18] In accordance with the coelomic metaplasia theory, endometriosis tissue can be found in the pericardium because pericardial tissue is also mesothelial cell-derived.[19] Based on the current patient's medical history, it was hypothesized that endometriosis caused the constrictive pericarditis; however, this diagnosis has not been supported pathologically. The primary cause of the patient's constrictive process

was assessed as inadequate treatment and a lack of follow-up during the pericardial effusion attack. The patient should have received longer medical treatment and should have been followed up on more closely.

CONCLUSION

Cardiovascular diseases can complicate pregnancy. Young women with acute pericarditis should be monitored closely, as inadequate treatment can lead to constrictive pericarditis, which may rarely cause RM.

Informed Consent: Informed consent was obtained from the patient.

Authorship Contributions: Concept: S.A., A.V.Ö., Data Collection or Processing: M.D., Literature Search: S.A., A.V.Ö., Writing: M.D.

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Video 1. Intraoperative view of stony pericardium
https://youtube.com/shorts/FG-fyH5D3Ws

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INTERVENTIONAL CARDIOLOGY PERSPECTIVES

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CASE REPORT

Spontaneous Coronary Artery Dissection Mimicking Stress Cardiomyopathy (Takotsubo Syndrome): A Case Report

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ABSTRACT

Spontaneous coronary artery dissection (SCAD) is a rare but increasingly recognized cause of acute coronary syndrome, particularly in middle-aged women. Its clinical presentation can be highly variable, occasionally mimicking other conditions such as stress cardiomyopathy [Takotsubo syndrome (TTS)]. We report the case of a 59-year-old woman with a history of hypertension who presented with chest pain and echocardiographic findings suggestive of Takotsubo cardiomyopathy. Coronary angiography, however, revealed SCAD in the mid-left anterior descending artery. Given the preserved coronary flow, conservative medical management was pursued. This case underscores the diagnostic challenges and overlapping features of SCAD and TTS and highlights the importance of invasive imaging for accurate diagnosis.

Keywords: Spontaneous coronary artery dissection, Takotsubo cardiomyopathy, acute coronary syndrome, women's heart health, MINOCA

INTRODUCTION

Spontaneous coronary artery dissection (SCAD) is an uncommon but important cause of acute myocardial ischemia, accounting for approximately 1–4% of all acute coronary syndrome (ACS) cases worldwide.[1] It predominantly affects women, especially those in their fourth and fifth decades, making it a critical consideration in the differential diagnosis of chest pain in this population.[1] SCAD is defined by the spontaneous separation of the coronary arterial wall layers, resulting in an intramural hematoma or false lumen that can compromise the true coronary lumen, disrupt blood flow, and potentially lead to myocardial infarction.[2] Unlike conventional ACS, which is usually caused by atherosclerotic plaque rupture, SCAD occurs in the absence of trauma, iatrogenic injury, or significant atherosclerosis, distinguishing it as a unique pathological entity.[3] Its pathophysiology is multifactorial, with predisposing factors including fibromuscular dysplasia (FMD), connective tissue disorders such as Marfan syndrome and Ehlers–Danlos syndrome, hormonal influences, and exposure to extreme physical or emotional stress.[4] These stressors may exacerbate underlying arterial fragility, particularly in the coronary vasculature, triggering or propagating the dissection.[5]

In parallel, stress cardiomyopathy, commonly known as Takotsubo syndrome (TTS), is another rare but increasingly recognized form of ACS that shares clinical and demographic features with SCAD.[6] First described by Sato et al.[7] in Japan over three decades ago, TTS is named after the Japanese "Takotsubo" (octopus trap) because of the characteristic apical ballooning observed on ventriculography during systole. TTS is characterized by transient left ventricular dysfunction, typically triggered by acute emotional or physical stress, which induces a catecholamine surge leading to coronary microvascular dysfunction and direct myocardial injury.[8] The condition predominantly affects postmenopausal women, with up to 90% of cases occurring in females, and is often associated with reversible wall motion abnormalities that extend beyond a single coronary artery distribution.[9] Despite the absence of obstructive epicardial coronary artery disease in most cases, TTS presents with chest pain, electrocardiographic changes, and elevated cardiac biomarkers that closely resemble ACS, complicating early diagnosis.[10] The diagnostic overlap between SCAD and TTS stems from their shared clinical features, female predominance, and potential association with stress-induced triggers.[6] However, while TTS is primarily a microvascular phenomenon, SCAD involves epicardial coronary artery pathology, which can occasionally mimic the regional ventricular dysfunction seen in TTS.[11] This overlap presents a significant diagnostic challenge, as misdiagnosis can lead to inappropriate management. For example, echocardiographic findings of apical ballooning in patients with SCAD may initially suggest TTS, potentially delaying the angiographic evaluation necessary to identify dissection.[12]

The underrepresentation of women in traditional ACS clinical trials further complicates recognition, as sex-specific differences in pathophysiology and presentation remain poorly understood,

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potentially resulting in suboptimal therapeutic approaches.[6] This case report describes an instance of SCAD masquerading as Takotsubo cardiomyopathy in a hypertensive 59-year-old woman, highlighting the importance of maintaining a high index of clinical suspicion and the pivotal role of coronary angiography in resolving diagnostic uncertainty.[13] By examining this case, we aim to contribute to the growing body of evidence on these rare ACS variants, emphasizing the need for tailored diagnostic and therapeutic strategies to optimize patient outcomes in this complex clinical scenario.

CASE REPORT

A 59-year-old woman with a history of well-controlled hypertension presented to the emergency department with acute-onset substernal chest pain radiating to the left arm, accompanied by diaphoresis and shortness of breath. The symptoms began suddenly, without identifiable emotional or physical triggers. On admission, her vital signs were: blood pressure 150/90 mmHg, heart rate 65 beats per minute, respiratory rate 14 breaths per minute, and oxygen saturation 96% on room air. Physical examination was unremarkable, except for mild distress.

Initial electrocardiography showed sinus rhythm with T-wave inversions in leads V4–V6, suggestive of anterolateral ischemia. Serum troponin I was markedly elevated at >50,000 ng/mL (reference: 0.016 ng/mL). Other laboratory parameters, including complete blood count, renal function, and electrolytes, were within normal limits.

Transthoracic echocardiography revealed apical akinesia with ballooning of the left ventricular apex, hypercontractility of the basal segments, and a reduced ejection fraction of approximately 40%, findings highly suggestive of Takotsubo cardiomyopathy (Figure 1).

Given the persistent chest pain and markedly elevated troponin, urgent coronary angiography was performed. This demonstrated a smooth, tapered narrowing in the mid-left anterior descending (LAD) artery, consistent with type 2b SCAD (diffuse and smooth stenosis due to intramural hematoma), without evidence of atherosclerotic plaque or thrombosis (Figure 2). Distal coronary flow was preserved with thrombolysis in myocardial infarction (TIMI) grade 3 perfusion. No percutaneous interventions were required, and the patient was managed conservatively with dual antiplatelet therapy (aspirin and clopidogrel), beta-blockers, and angiotensin-converting enzyme inhibitors for blood pressure control.[1]

The patient's symptoms resolved within 48 hours. Follow-up echocardiography at one week demonstrated normalization of left ventricular function, with an ejection fraction of 60%. She was discharged on medical therapy, along with recommendations for risk factor modification and avoidance of extreme stressors. At three-month follow-up, she remained asymptomatic, with no recurrence of events. Given her complete symptom resolution and absence of recurrent events, repeat vascular imaging, such as coronary computed tomography angiography, was deferred to avoid unnecessary radiation and contrast exposure.

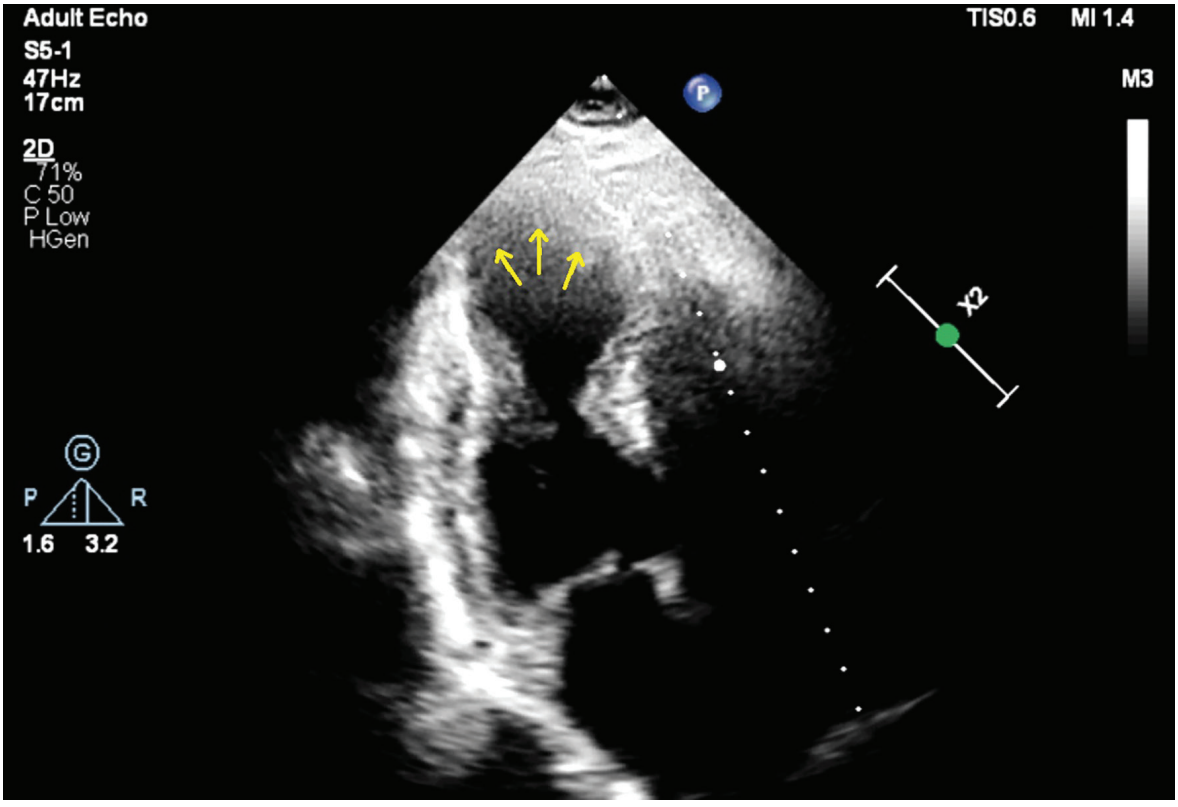

Figure 1. Transthoracic echocardiographic apical four-chamber view showing apical ballooning with akinesia of the apex and hyperkinesis of the basal segments, consistent with a Takotsubo-like pattern

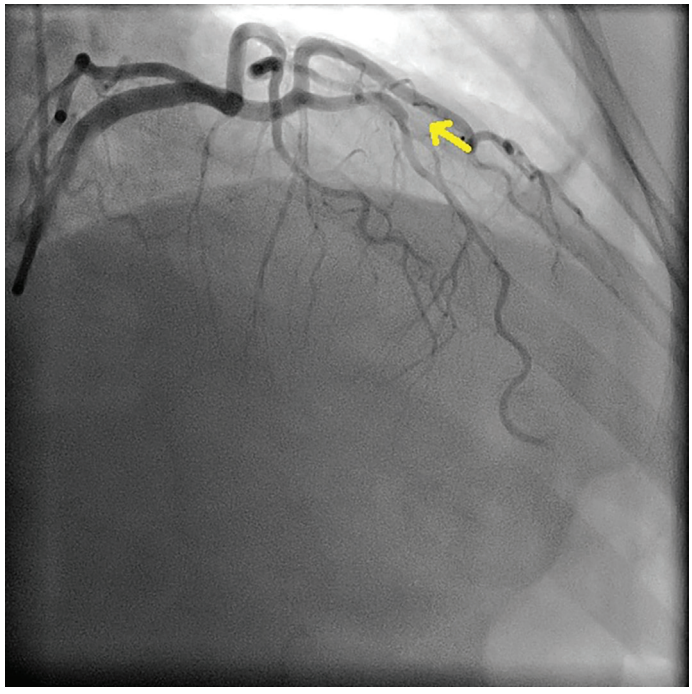

Figure 2. Coronary angiographic views demonstrating smooth narrowing of the mid-left anterior descending artery, indicative of spontaneous coronary artery dissection with preserved distal flow

DISCUSSION

This case illustrates a rare presentation of SCAD mimicking Takotsubo cardiomyopathy (also known as stress cardiomyopathy or TTS), highlighting a diagnostic challenge that can potentially delay optimal management.[13] SCAD is an underdiagnosed cause of ACS, predominantly affecting women aged 40–60 years, and accounts for up to 35% of ACS cases in women under 50.[14] In contrast, TTS is characterized by transient left ventricular apical ballooning in the absence of obstructive coronary artery disease, often triggered by emotional or physical stress, with a similar female predominance (up to 90% of cases).[3,7] The overlap between these conditions may arise from SCAD-induced ischemia triggering TTS-like ventricular dysfunction, as observed in our patient, who exhibited apical ballooning on echocardiography despite mid-LAD artery involvement.[6]

The apical ballooning in this patient is somewhat atypical for isolated mid-LAD SCAD, which typically affects mid-to-distal segments and produces regional wall motion abnormalities rather than the classic TTS pattern.[15] Nevertheless, ischemic insult from SCAD can induce catecholamine-mediated myocardial stunning, mimicking TTS—particularly in patients with hypertension, which may exacerbate microvascular dysfunction and shear stress on arterial walls.[2] A systematic review of SCAD-associated TTS cases reported this coexistence in various scenarios, including the postpartum period, with shared pathophysiological mechanisms such as hormonal fluctuations, inflammatory responses, and vascular fragility (e.g., FMD).[13] Approximately 10–23% of TTS cases undergoing detailed imaging were found to have underlying SCAD, emphasizing the need for diagnostic vigilance.[8] Although cardiac magnetic resonance imaging can differentiate myocarditis from TTS, it was not performed in this case because coronary angiography provided a definitive SCAD diagnosis explaining the wall motion abnormalities.

Differentiating SCAD from TTS is critical because management strategies differ significantly. SCAD often requires antiplatelet therapy, beta-blockers, and monitoring for dissection extension or arrhythmias, whereas TTS generally resolves spontaneously with supportive care.[3] Coronary angiography remains the gold standard for diagnosis, while intravascular imaging modalities such as optical coherence tomography or intravascular ultrasound can provide definitive evidence of intramural hematoma in ambiguous cases.[16] In this patient, preserved TIMI 3 flow supported a conservative approach, consistent with American Heart Association and European Society of Cardiology guidelines, which recommend medical management for hemodynamically stable SCAD without ongoing ischemia, given high spontaneous healing rates (up to 90% at follow-up).[14] Percutaneous coronary intervention is reserved for cases with compromised flow or persistent symptoms due to the risk of dissection propagation.[12]

The association with hypertension in our patient is noteworthy, as it is an established modifiable risk factor for SCAD, potentially mediated by increased arterial wall stress and endothelial dysfunction.[2,17] Other predisposing factors include pregnancy, extreme exercise, and connective tissue disorders, which were absent in this case.[1] The prognosis for SCAD-TTS overlap is generally favorable with early recognition; however, recurrence rates for SCAD can reach 10–30% within 5–10 years, highlighting the need for long-term follow-up and optimization of risk factors.[5] Clinicians should maintain a low threshold for invasive evaluation in middle-aged women presenting with chest pain and TTS-like echocardiographic features, particularly when ACS biomarkers are elevated or traditional risk factors, such as

hypertension, are present.[4,7] Future research, including prospective registries, is necessary to further elucidate the interplay between SCAD and TTS and to refine diagnostic algorithms.[9,13]

CONCLUSION

SCAD can closely mimic Takotsubo cardiomyopathy, posing significant diagnostic challenges. This case underscores the value of coronary angiography in identifying such overlaps and guiding appropriate therapy. Early recognition and conservative management can lead to excellent outcomes, as demonstrated in this patient.

Informed Consent: The patient was informed that the procedures performed would be included in a publication and written consent was obtained.

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SCIENTIFIC LETTER

Early Functional Recovery After PCI: The Underappreciated Role of Early Exercise Stress Testing

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Keywords: Behavioral cardiology, cardiovascular, interventional

Despite major advances in percutaneous coronary intervention (PCI) and contemporary secondary prevention strategies, the early post-procedural period remains a critical phase for functional recovery and reintegration into daily life. Current post-PCI care pathways predominantly focus on ischemia surveillance and pharmacological optimization, whereas structured approaches to objectively restore patients' confidence in physical activity remain inadequately defined.

In this context, early exercise stress testing after uncomplicated PCI may represent more than a diagnostic modality; it may also serve as a practical tool for facilitating functional recovery, improving adherence to cardiac rehabilitation, and supporting an earlier return to work and social participation. The current European Society of Cardiology recommendations emphasize early mobilization and exercise-based rehabilitation; however, they provide limited guidance on objectively assessing readiness for physical activity during the immediate post-PCI period.[1]

Notably, this perspective should be considered hypothesis-generating. Although placebo-controlled studies such as ORBITA demonstrated the limited effects of PCI on objectively measured exercise capacity, these findings do not preclude the possibility that structured post-procedural interventions may influence the behavioral and psychological aspects of recovery.

These studies demonstrate that PCI does not substantially improve objective exercise capacity under blinded conditions. However, functional recovery after PCI extends beyond physiological capacity and encompasses the behavioral, psychological, and confidence-related aspects of physical activity. Early supervised exercise testing may therefore function as a behavioral intervention that bridges the gap between perceived and actual physical capability, rather than as a means of enhancing intrinsic cardiopulmonary performance.

The psychological dimension of recovery is particularly important. Anxiety related to physical exertion and uncertainty regarding cardiovascular safety are common after PCI and may contribute to reduced activity levels and depressive symptoms. Early supervised exercise testing may help reduce these concerns by providing objective reassurance of functional capacity and cardiovascular stability. Considering that depression is consistently associated with impaired quality of life and adverse outcomes in patients with coronary artery disease, strategies that promote psychological well-being are clinically meaningful.[2,3]

Early recovery involves not only symptom control but also return to work and reintegration into society—outcomes that remain underreported despite their importance in contemporary cardiovascular care. In this context, exercise testing may be reframed not solely as a diagnostic tool but also as a structured and supervised method of graded activity exposure.

This concept differs fundamentally from routine ischemia surveillance strategies evaluated in trials such as POST-PCI, in which testing was used to guide repeat revascularization. In contrast, we propose early, selective exercise testing as a recovery-oriented intervention designed to support functional reintegration and enhance patient confidence, rather than to trigger downstream invasive procedures.

However, whether such a strategy improves patient-centered outcomes remains unknown and warrants prospective evaluation.

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We therefore propose that early exercise testing be considered within the framework of "behavioral cardiology," in which objective reassurance may translate into improved activity patterns independent of changes in maximal exercise capacity.

Current guidelines provide limited guidance regarding the timing and role of functional testing in stable patients following successful PCI. This approach would be most applicable to carefully selected, hemodynamically stable patients who have undergone complete revascularization and experienced no procedural complications. Prospective studies evaluating patient-reported outcomes, return to work, and adherence to cardiac rehabilitation are warranted to further define its clinical value.

The limitations of this proposed concept should be acknowledged. Currently, no randomized trials have specifically evaluated early exercise stress testing as a behavioral intervention following uncomplicated PCI. Consequently, the proposed benefits with respect to rehabilitation adherence, return to work, and psychological recovery remain speculative and should be regarded as hypothesis-generating.

In summary, early exercise stress testing after uncomplicated PCI should not currently be viewed as a strategy for routine ischemia surveillance. Rather, it may represent a promising recovery-oriented intervention that warrants prospective investigation in carefully selected patients.

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