e-ISSN: 2148-9211

CARDIOVASCULAR SURGERY AND INTERVENTIONS

Official Electronic Journal of the Turkish Society of Cardiovascular Surgery

VOLUME **13** / ISSUE **1** **MARCH 2026**

galenos Publishing House

www.e-cvsi.org

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Cardiovascular Surgery and Interventions is indexed in **Scilit**, **Türk Medline**, **TR Dizin**, **Türkiye Atıf Dizini** and **SUDOC**.

Owner: Turkish Society of Cardiovascular Surgery

Responsible Manager(s): Şahin Bozok

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Web: www.galenos.com.tr
Publisher Certificate Number: 14521

Online Publication Date: March 2026

e-ISSN: 2148-9211

International scientific journal published triannual.

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DOI: 10.4274/e-cvsi.2025.2105
Cardiovasc Surg Int 2026;13(1):1-6

CARDIOVASCULAR SURGERY AND INTERVENTIONS

Long-term outcomes of aortic valve-sparing root reimplantation surgery (David procedure): A single-center experience

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Received: October 22, 2025 **Accepted:** December 29, 2025 **Epub:** February 02, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Objectives: Aortic valve-sparing root reimplantation (AVSRR) offers distinct advantages, particularly in younger patients with aortic root dilatation and aortic insufficiency (AI), when performed in experienced centers. This study aimed to evaluate the long-term clinical outcomes of AVSRR in a single-center cohort.

Patients and methods: Sixty-one consecutive patients who underwent the David procedure at our center between 2010 and 2025 were analyzed. Preoperative demographics, operative data, and early postoperative and long-term outcomes were evaluated. Survival, freedom from severe AI, and freedom from reoperation at 1, 5, and 10 years were assessed using the Kaplan-Meier method.

Results: In-hospital mortality was 1.6% (n=1); the patient died of multiorgan failure in the early postoperative period. The median follow-up duration was 65 months. Kaplan-Meier survival rates at 1 5, and 10 years were 98.4%. Freedom from severe AI was 96.5%, 90.0%, and 86.4%, while freedom from aortic valve–related reoperation was 98.4%, 91.3%, and 91.3% at 1, 5, and 10 years, respectively.

Conclusion: David procedure has safe long-term outcomes with excellent survival and freedom from aortic valve-related reoperation rates. Experienced high-volume centers are important to achieve optimal results.

Keywords: Aortic valve-sparing root replacement, aortic valve, aortic insufficiency, David procedure.

In young patients with aortic root dilatation, severe aortic regurgitation and good native tissue quality, valve-sparing aortic root reimplantation (David procedure) is preferred over the composite valve graft (Bentall procedure) when performed at experienced centers.[1] Even though the Bentall procedure offers a long-term durable solution, lifelong anticoagulation requirement and associated complications such as hemorrhage and thromboembolism remain a well-recognized drawback, particularly in younger patients.[2,3] Additionally, the use of bioprosthetic valves in Bentall operations—Bio-Bentall procedure—may lead to long-term leaflet degeneration.[3] The David procedure may offer a solution to these issues by preserving native aortic leaflets. A recent meta-analysis showed that the David procedure was associated with less postoperative stroke, reduced early mortality, and higher long-term survival rates compared to Bentall procedure.[4] High-volume, specialized centers are likely to be the cornerstone of long-term success in valve-sparing root replacement (VSRR) due to the procedure's technical complexity. Recent American and European aortic guidelines also recommend considering VSRR in patients—particularly younger ones—with aortic root dilatation and non-diseased or repairable AV leaflets, when performed by experienced surgeons.[5,6] In this study, we aim to present our mid- and long-term outcomes of the David procedure at a single-center.

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Cite this article as: Arslanhan G, Gökçe İ, Baştopçu M, Karaağaç A, Özcan ZS, Koçyiğit M, et al. Long-term outcomes of aortic valve-sparing root reimplantation surgery (David procedure): a single-center experience. Cardiovasc Surg Int. 2026;13(1):1-6

PATIENTS AND METHODS

A total of 61 consecutive patients underwent David procedure between May 2010 and May 2025 at our institution. One patient underwent modified Yacoub (David II) procedure was excluded from the study for the uniformity of the cohort. This patient had asymmetric dilatation of the non-coronary and right coronary sinuses of Valsalva. Therefore, the left coronary sinus of Valsalva was preserved, and a partial root reimplantation was performed. Pre-operative patient demographics, operative details, post-operative outcomes and follow-up data were retrospectively retrieved from institutional and national databases. Preoperative transthoracic echocardiography (TTE) and computed tomography angiography were performed in all patients, and relevant measurements were obtained, including the diameters of the aortic annulus, sinus of Valsalva, sinotubular junction, and ascending aorta. Additionally, perioperative transesophageal echocardiography (TEE) was routinely used in all patients to evaluate the aortic valve intraoperatively. The primary outcomes of the study were mid- and long-term survival, freedom from severe aortic insufficiency (AI) and freedom from reoperation during the 10-year follow-up period.

Surgical Technique

Following induction of general anesthesia and endotracheal intubation, a TEE probe was routinely placed, and the AV was assessed prior to the initiation of the procedure. All surgeries were performed via median sternotomy or mini-J sternotomy. After entering the mediastinum, pericardial stay sutures were placed, and epi-aortic ultrasonography was performed to identify optimal, non-atherosclerotic sites for aortic cannulation and distal aortic cross-clamping. Cardiopulmonary bypass (CPB) was initiated following arterial and venous cannulation. The site of arterial cannulation was determined based on the extent of the procedures, concomitant interventions, anatomical considerations, and the type of sternotomy. Ascending aorta, axillary artery and femoral artery were the choice of arterial cannulation sites. Central venous cannulation via right atrium was used for median sternotomy procedures, whereas peripheral femoral venous cannulation was preferred for mini-J sternotomy. Majority of the operations were performed under systemic moderate hypothermia (28-32 °C). The total of nine patient required total or hemi-aortic arch replacement was operated under deep hypotermic (18 °C) total circulatory arrest (TCA). Additionally, two of the three total aortic arch replacements were performed under TCA combined with antegrade cerebral perfusion (ACP) via axillary artery cannulation. Brachiocephalic artery was cross-clamped or suspended with the vascular tapes to prevent retrograde flow towards the aortic arch. The remaining one patient did not undergo ACP despite performing total aortic arch replacement because this patient was scheduled for hemiarch replacement preoperatively. However, operative evaluation revealed aortic arch aneurysm and total aortic arch replacement decision was made intraoperatively. Aortic arch vessels were reimplanted using island technique and a 26 minutes short TCA duration was achieved. The patient did not encounter any neurologic complication during postoperative period. A suction vent was routinely placed in the right superior pulmonary vein. Aortic cross-clamping was performed, and cardiac arrest was achieved following cardioplegia administration. Cardioplegia was delivered through the coronary ostia in patients with moderate or severe AI. AV leaflets were inspected after aortotomy. Aneurysmal segments of the sinus of Valsalva were resected, the height of left-non-coronary commissure was measured from the base of the interleaflet triangle to the top of the commissure to decide appropriate Dacron graft size (Figure 1A). Straight tubular Dacron grafts were used in all operations while Valsalva grafts can also be preferred. The majority of the grafts used were size 30 or 32. The left and right coronary buttons were subsequently prepared. Dacron graft was implanted into the aortic annulus using horizontally placed, pledgeted, interrupted sutures. A critical nuance at this stage was the vertical placement of sub-annular sutures at the right–non-coronary commissure to avoid injury to the his bundle in the membranous septum (Figure 1B). AV leaflets were then repositioned and reimplanted within the Dacron graft using Prolene sutures (Figure 1C). Coaptation of the AV leaflets were evaluated with saline test to ensure the absence of backward leakage. If any prolapsed aortic valve leaflets were detected at this stage, aortic valve leaflets were repaired using plication technique with Prolene sutures. The left and right coronary buttons were anastomosed to the Dacron graft in sequence using 5/0 Prolene sutures. In patients without hemiarch or total aortic arch replacement, distal anastomosis was performed on the distal ascending aorta under aortic cross clamping (ACC) using 4/0 Prolene sutures. For those undergoing hemiarch or total arch replacement, open distal anastomosis was carried out under TCA with or without ACP. After rewarming and deairing, the patients were weaned off CPB upon achieving optimal hemodynamic conditions. All procedures were completed with chest tube placement and standard layered closure of the surgical incision.

Statistical Analysis

BM SPSS Statistics software package 27.0 was used to perform statistical analyses. Continuous parameters are presented as mean ± standard deviation and median (minimum-maximum), while categorical parameters are shown as counts and percentages. Kaplan-Meier survival analysis was performed to assess 1-, 5-, 10-year survival and freedom of reoperation.

RESULTS

The mean age of the patients was 50.5±13.9 years and 55 (90 %) of the patients were male. The most encountered comorbidities were hypertension in 34 (56%) patients, hyperlipidemia in 10 (16%) patients and diabetes mellitus 9 (15%) patients. The majority of the patients were

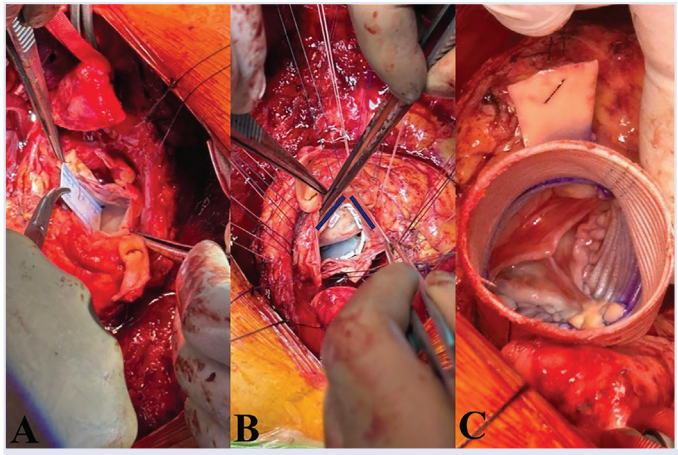

Figure 1. A-Measurement of the height of left-non-coronary commissure, B- Vertical placement of sub-annular sutures at the right–non-coronary commissure, C- Aortic valve leaflet reimplantation within the Dacron graft.

in NYHA Class I with 38 (62%) patients. The mean EUROSCORE II values of the population were 7.1±2.3. The mean diameters of the ascending aorta, sinotubular junction, and sinus of Valsalva were 50.9±9.1 mm, 49.2±6.3 mm, and 51.5±5.8 mm, respectively. In the preoperative echocardiographic evaluation, 26 (43%) patients had severe AI, 16 (26%) had moderate AI, 12 (20%) had mild AI, and 7 (11%) had trace or no AI. Eighteen (30%) patients had bicuspid aortic valve (BAV), six patients (10%) had aortic dissection, and three patients (5%) had Marfan syndrome. The patient demographics were demonstrated in Table 1.

A total of 36 (59%) patients underwent isolated David procedure and concomitant procedures were performed in 25 (41%) patients. The most performed concomitant procedure was coronary artery bypass grafting in nine patients. Aortic leaflet plication was performed in two (3%) patients. After the valve leaflets were reimplanted within the Dacron graft, they were evaluated, and any prolapsed leaflets were repaired using the plication technique. There was a total of three (5%) redo cases. Median sternotomy was the preferred procedural approach in 54 (89%) and mini-J-sternotomy in 7 (11%) patients. The ascending aorta was the site of arterial cannulation in 38 (62%) patients, the femoral artery in 18 (30%) patients, and the axillary artery in 5 (8%) patients. Central venous cannulation was performed in 42 (69%) patients and femoral venous cannulation was preferred in 19 (31%) patients. The mean durations of CPB and ACC were 143±37 minutes and 115±29 minutes, respectively. A total of 9 (15%) cases were performed under TCA with a median duration of 14 (8-76) minutes, and two cases were performed with ACP with a median duration of 45 (40-50) minutes. Operative data is presented in Table 2.

Table 1. Preoperative demographics of the patients (n=61)

Demographics	Mean ± SD or n (%)
Age (years)	50.5±13.9
Female gender	6 (10%)
EUROSCORE II score	7.1±2.3
Comorbidities	
HT	34 (56%)
HL	10 (16%)
DM	9 (15%)
NYHA category	
Class I	38 (62%)
Class II	18 (30%)
Class III	3 (5%)
Class IV	2 (3%)
CTA measures	
Ascending aorta (mm)	50.9±9.1 mm
Sinotubular junction (mm)	49.2±6.3 mm
Sinus of valsalva (mm)	51.5±5.8 mm
Echocardiography	
Aortic insufficiency	
Severe	26 (43%)
Moderate	16 (26%)
Mild	12 (20%)
Trace	5 (8%)
No	2 (3%)
Mean LVEF (%)	60±6
BAV	18 (30%)
Aortic dissection	6 (10%)
Marfan syndrome	3 (5%)

BAV: Bicuspid aortic valve; SD: Standard deviation; HT: Hypertension; HL: Hyperlipidemia; DM: Diabetes mellitus; NYHA: New York Heart Association; CTA: Computed tomography angiography.

The median mechanical ventilation times and intensive care unit stay were 6 (1-39) hours and 20 (14-86) hours, respectively (Table 3). The median duration of hospital stay was 7 (4-20) days. Postoperative atrial fibrillation was encountered in 11 (18%) patients. Complete AV block was seen in two (3%) patients postoperatively and these patients underwent permanent pacemaker implantation. Two (3%) patients needed reexploration for bleeding and one (1.6%) patient required reintubation. Postoperative echocardiography revealed no or trace AI in the majority of the patients. In-hospital mortality was encountered in one (1.6%) patient. The patient was 67 years old and had a history of hypertrophic cardiomyopathy. His death was associated with post-operative multi-organ failure. Sixty patients were followed up for a median of 65 months (1-182 months). There was no late mortality in the entire cohort during follow-up. Kaplan-Meier analysis revealed 1-, 5-, and 10-year survival rates of 98.4% (Figure 2). Follow-up TTE demonstrated mild, trace, or no AI in 51 (87%) of the patients, while six and two patients showed severe and moderate AI, respectively. Freedom from severe AI was 96,5%, 90% and 86.4% in 1, 5 and 10 years, respectively (Figure 3). Four (6.6%) patients required reoperation due to aortic valve dysfunction during the follow-up period. Two of the reoperations were in the BAV group, while the remaining two is in the dissection group. One case in the BAV group

Table 2. Operative data of patients undergoing David procedure (n=61)

Operative data	Mean ± SD or n (%)
Concomitant cardiac procedures	
Cases with concomitant surgery	25 (41%)
Coronary artery bypass grafting	9
Aortic hemiarch replacement	6
Total aortic arch replacement	3
Mitral valve repair	4
Other procedures	8
Redo cases	3 (5%)
Procedural approach	
Midline sternotomy	54 (89%)
Mini-J-sternotomy	7 (11%)
Cannulation sites	
Arterial cannulation	
Ascending aorta	38 (62%)
Femoral artery	18 (30%)
Axillary artery	5 (8%)
Venous cannulation	
Right atrium	42 (69%)
Femoral vein	19 (31%)
CPB time (minutes)	143±37
ACC time (minutes)	115±29
TCA time (minutes)	14 (8-76)
ACP time (minutes)	45 (40-50)

SD: Standard deviation; CPB: Cardiopulmonary bypass; ACC: Aortic cross clamping.

was due to infective endocarditis (IE)-related severe AI and required early reoperation within one month of the initial surgery. The second patient underwent reoperation at 54 months following the initial operation due to severe AI caused by degeneration of the aortic valve leaflets. Among the remaining 16 BAV patients, no additional patients developed severe AI or required reoperation during the follow-up period. The other two cases in the dissection group underwent reoperation for severe AI caused by prolapse or degeneration of the aortic leaflets. The remaining two patients with severe AI did not undergo reoperation. One had severe paravalvular AI that was hemodynamically insignificant and therefore did not require surgery. The other patient was managed with medical therapy. Kaplan-Meier analysis revealed freedom from aortic-valve related reoperation rates of 98.4%, 91.3%, and 91.3% at 1, 5, and 10 years, respectively (Figure 4).

DISCUSSION

This single-center study of the patient cohort undergoing the David procedure establishes that the David procedure can be safely performed in both elective and emergent settings by experienced surgeons in specialized centers, yielding favorable short- and long-term outcomes.

Our in-hospital and long-term mortality rate was low (1.6%). It is also worth noting that there were no in-hospital deaths among the six patients who presented in emergency settings with acute aortic dissection. These statistics are consistent with previous findings in the literature. Beckmann et al.[3] presented data from their large cohort with a 25-year follow-up period, revealing that the overall in-hospital mortality rate was 1.9% in elective settings, while it was 3.8% in the entire population, which included a high proportion of aortic dissection cases. The survival rates at 5 and 10 years in this study were 88% and 77%, respectively. In the series of 465 patients reported by David et al.,[7] the operative mortality was 1%, and the 20-year survival and event-

Table 3. Early and late postoperative outcomes

Mechanical ventilation time (hours)	6 (1-39)
ICU stay (hours)	20 (14-86)
Hospital stay (days)	7 (4-20)
POAF	11 (18%)
Permanent pacemaker implantation	2 (3%)
Postoperative reexploration for bleeding	2 (3%)
Reintubation	1 (1.6%)
Early postoperative AI (n=59)	
Severe	0
Moderate	0
Mild	11 (19%)
Trace	24 (41%)
No	24 (41%)
In-hospital mortality	1 (1.6%)
Survival rate (%) at	
1-year	98.4%
5-year	98.4%
10-year	98.4%
Follow-up AI (n=59)	
Severe	6 (10%)
Moderate	2 (3%)
Mild	21 (36%)
Trace	23 (39%)
No	7 (12%)
Freedom from severe AI at	
1-year	96.5%
5-year	90%
10-year	86.4%
Freedom from aortic valve-related reoperation at	
1-year	98.4%
5-year	91.3%
10-year	91.3%

ICU: Intensive care unit; AI: Aortic insufficiency; POAF: Postoperative atrial fibrillation.

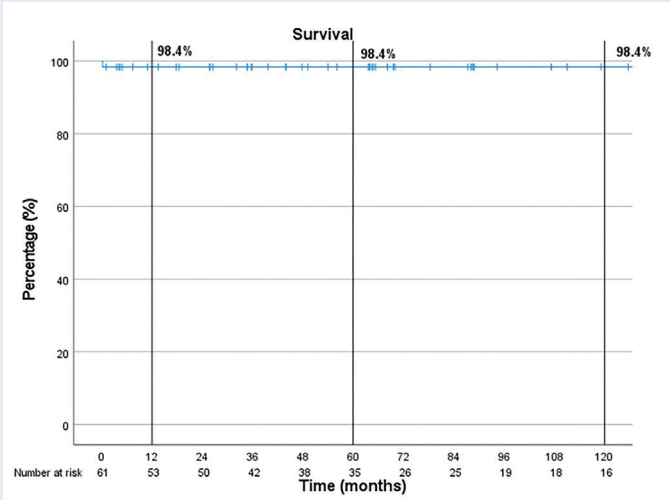

Figure 2. Kaplan-Meier analyses for 1-year, 5-year and 10-year survival.
AI: Aortic insufficiency.

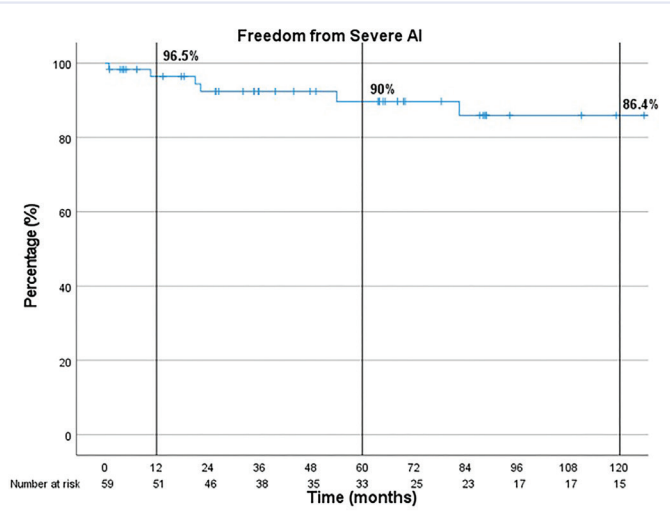

Figure 3. Kaplan-Meier analyses for 1-year, 5-year and 10-year freedom from severe AI.
AI: Aortic insufficiency.

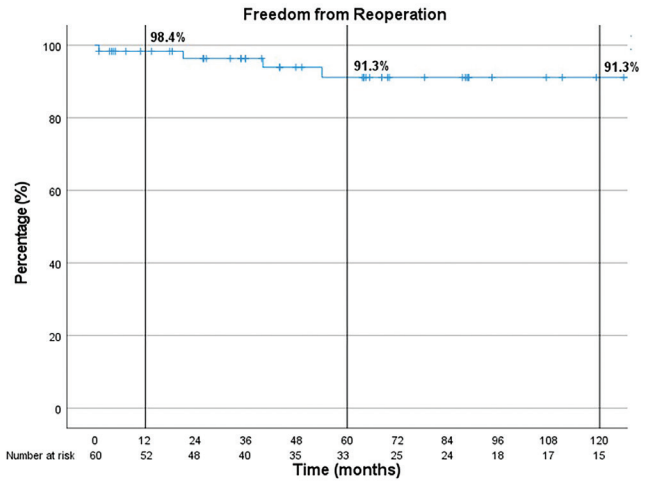

Figure 4. Kaplan-Meier analyses for 1-year, 5-year and 10-year freedom from reoperation.

free survival rates were 75.1% and 69.1%, respectively. Yang et al.[8] also showed that the operative mortality rate in 40 Type A aortic dissection patients who underwent the David procedure was 3%, compared to 13% in the 95 patients who underwent the Bentall procedure. Based on both our data and findings from the literature, we propose that the David procedure is a safe alternative, even in emergent settings, when performed by experienced hands.

When the early postoperative complications were analyzed, our data showed low rates of complications. The POAF rate was 18%, while permanent pacemaker implantation was required in 3.2% of cases. David et al. [9] reported a 22% rate of POAF and a 1.5% rate of permanent pacemaker insertion in their 20-year experience. It is crucial to note that our technique for Dacron graft implantation at the aortic annulus, which involves the vertical placement of sub-annular sutures at the right non-coronary commissure, contributes to the low rates of complications related to the conduction system by preserving important structures in the membranous septum. The overall postoperative reexploration rate for bleeding was 3.2%. In the same study, David et al. [9] reported that 8.7% of the patients underwent reexploration for bleeding or cardiac tamponade. Our overall reexploration rate is extremely low and comparable to the current literature, considering the significant presence of aortic dissection and concomitant procedures in the cohort, including total aortic arch replacement.

Preoperative severe or moderate AI was present in 69% of the patients in our study, while early postoperative echocardiography revealed no severe or moderate AI in our cohort. Furthermore, follow-up echocardiography results showed that only 13% of the patients had severe or moderate AI. Freedom from severe or moderate AI was 94.9% and 73.9% at the 2- and 6-year follow-ups in the report published by Coselli et al.,[2] while it was 98% at 5 years and 96% at 10, 15, and 20 years in David et al.'s[9] 20-year experience. In our cohort, freedom from severe AI was 90% at 5 years and 86.4% at 10 years, which is comparable to the rates reported in the literature. During the follow-up period, four of our patients underwent reoperation due to aortic valve-related causes. All the reoperations were within the first 5 years of follow-up. There was no reoperation in patients with tricuspid aortic valve structure. Two reoperated patients were in the aortic dissection subgroup, while the other two were in the BAV subgroup. On the other hand, our data are consistent with the previously mentioned literature, which highlights the high rate of reoperation within the first 5 years. Freedom from reoperation rates were 98.4% at 1 year and 91.3% at 5 and 10 years in our study. Liebrich et al.[10] published their data, demonstrating 94% and 87% freedom from aortic valve replacement at 5 and 10 years, respectively.[11,12] Beckmann et al.'s[3] data were also similar to those of Liebrich et al.,[10] with 93% and 88% freedom from reoperation rates at 5 and 10 years, respectively. While our numbers were very comparable to those of the two studies, David's series demonstrated higher rates of freedom from reoperation, with 96.9% at 10, 15, and 20 years. Lastly, the incidence of IE after David reoperation warrants discussion. In our cohort, one patient (1.6%) developed IE in the early postoperative period and underwent reoperation one month after the initial surgery, as noted above. In their report on late outcomes of the David procedure, Manganiello et al.[11] documented 5 endocarditis-related reoperations among 19 valve-related reoperations within a 300-patient cohort.

Lastly, comparative studies between the David and Bentall procedures have shown largely similar early and long-term outcomes. Leontyev et al.[12] reported comparable perioperative and late results but a higher incidence of major bleeding in the Bentall group. Similarly, Svensson et al.[13] found no significant differences in 10-year survival or reintervention rates, though severe AI was more frequent after the David procedure in 8 years. A recent meta-analysis by Formica et al.[4] further demonstrated lower early mortality and stroke rates with the David procedure but higher reoperation rates within the first five years.The David procedure can be safely performed in patients with aortic root aneurysms who have non-diseased or repairable aortic valve leaflets, yielding excellent early and late outcomes. High-volume centers and experienced surgeons are essential for achieving optimal results, given the procedure's technical complexity and the need for a high level of expertise. This study is limited by its retrospective design, single-center and single-surgeon experience, and a relatively small cohort size. Although our follow-up extends to 10 years, longer-term data from larger series in the literature—exceeding 20 years—may provide broader generalizability.

Ethics

Ethics Committee Approval: Ethics committee approval was waived due to retrospective design.

Informed Consent: This study was conducted as a retrospective case series, approval from the hospital administration was obtained to access and analyze data from the institutional database.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.A., M.B., A.K., M.K., Ş.Ş., C.A.; Concept: G.A., İ.G., M.B., A.K., Z.S.Ö., Ş.Ş., C.A.; Design: G.A., İ.G., M.B., A.K., Z.S.Ö., M.K., Ş.Ş., C.A.; Data Collection or Processing: G.A., İ.G., M.B., A.K., Z.S.Ö., Ş.Ş.; Analysis or Interpretation: G.A., İ.G., M.B., A.K., Z.S.Ö., Ş.Ş., C.A.; Literature Search: G.A., İ.G., M.B., A.K., Z.S.Ö., Ş.Ş.; Writing: G.A, İ.G., M.B., A.K., Z.S.Ö., Ş.Ş.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Praz F, Borger MA, Lanz J, Marin-Cuartas M, Abreu A, Adamo M, et al. 2025 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J. 2025;46:4635-736. doi: 10.1093/eurheartj/ehaf194.
2. Coselli JS, Hughes MS, Green SY, Price MD, Zarda S, de la Cruz KI, et al. Valve-sparing aortic root replacement: early and midterm outcomes in 83 patients. Ann Thorac Surg. 2014;97:1267-73; discussion 1273-4. doi: 10.1016/j.athoracsur.2013.10.076.
3. Beckmann E, Martens A, Krüger H, Korte W, Kaufeld T, Stettinger A, et al. David's reimplantation technique: single-centre 25-year experience. Eur J Cardiothorac Surg. 2021;60:642-8. doi: 10.1093/ejcts/ezab136.
4. Formica F, Gallingani A, D'Alessandro S, Tuttolomondo D, Hernandez-Vaquero D, Singh G, et al. Long-term outcomes comparison of Bentall-De Bono-versus valve-sparing aortic root replacement: an updated systematic review and reconstructed time-to-event meta-analysis. Int J Cardiol. 2025;419:132728. doi: 10.1016/j.ijcard.2024.132728.
5. Czerny M, Grabenwöger M, Berger T, Aboyans V, Della Corte A, Chen EP, et al. EACTS/STS guidelines for diagnosing and treating acute and chronic syndromes of the aortic organ. Eur J Cardiothorac Surg. 2024;65:ezad426. doi: 10.1093/ejcts/ezad426. Erratum in: Eur J Cardiothorac Surg. 2024;65:ezae235. doi: 10.1093/ejcts/ezae235.
6. Isselbacher EM, Preventza O, Hamilton Black J, Augoustides JG, Beck AW, Bolen MA, et al. 2022 ACC/AHA guideline for the diagnosis and management of aortic disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. Circulation. 2022;146:e334-482. doi: 10.1161/CIR.0000000000001106.
7. David TE, David CM, Ouzounian M, Feindel CM, Lafreniere-Roula M. A progress report on reimplantation of the aortic valve. J Thorac Cardiovasc Surg. 2021;161:890-9.e1. doi: 10.1016/j.jtcvs.2020.07.121.
8. Yang B, Patel HJ, Sorek C, Hornsby WE, Wu X, Ward S, et al. Sixteen-year experience of David and Bentall procedures in acute type a aortic dissection. Ann Thorac Surg. 2018;105:779-84. doi: 10.1016/j.athoracsur.2017.09.029.
9. David TE, David CM, Feindel CM, Manlhiot C. Reimplantation of the aortic valve at 20 years. J Thorac Cardiovasc Surg. 2017;153:232-8. doi: 10.1016/j.jtcvs.2016.10.081.
10. Liebrich M, Kruszynski MK, Roser D, Meisner C, Doll KN, Hemmer WB, et al. The David procedure in different valve pathologies: a single-center experience in 236 patients. Ann Thorac Surg. 2013;95:71-6. doi: 10.1016/j.athoracsur.2012.08.010.
11. Manganiello S, Soquet J, Mugnier A, Rousse N, Juthier F, Banfi C, et al. David procedure: a 21-year experience with 300 patients. Ann Thorac Surg. 2023;115:1403-10. doi: 10.1016/j.athoracsur.2022.04.058.
12. Leontyev S, Schamberger L, Davierwala PM, Von Aspern K, Etz C, Lehmann S, et al. Early and late results after David vs Bentall procedure: a propensity matched analysis. Ann Thorac Surg. 2020;110:120-6. doi: 10.1016/j.athoracsur.2019.10.020.
13. Svensson LG, Rosinski BF, Tucker NJ, Gillinov AM, Rajeswaran J, Roselli EE, et al. Comparison of outcomes of patients undergoing reimplantation versus Bentall root procedure. Aorta (Stamford). 2022;10:57-68. doi: 10.1055/s-0042-1744135.

ORIGINAL ARTICLE

CARDIOVASCULAR SURGERY AND INTERVENTIONS

DOI: 10.4274/e-cvsi.2026.2026-1-3
Cardiovasc Surg Int 2026;13(1):7-12

Colchicine modulates structural and histopathological remodeling in a calcium phosphate-induced rat model of abdominal aortic aneurysm

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Received: January 05, 2026 **Accepted:** February 19, 2026 **Epub:** March 02, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Objectives: Abdominal aortic aneurysm carries a substantial risk of rupture, and no drug therapy has yet been validated to slow aneurysm enlargement. Colchicine, an established anti-inflammatory agent with proven benefit in coronary artery disease, may also modulate vascular remodeling. This study evaluated the impact of colchicine on geometric and histopathological changes in a calcium phosphate ($CaPO_4$)–induced rat model of abdominal aortic aneurysm.

Methods: Twenty-two male Wistar albino rats were randomized into three groups: Sham-operated controls (n=6), $CaPO_4$-induced abdominal aortic aneurysm (aneurysm, n=8), and $CaPO_4$–induced abdominal aortic aneurysm treated with colchicine (n=8). Experimental aneurysms were induced by periadventitial application of 0.5 mol/L calcium chloride and phosphate-buffered saline to the infrarenal aorta. The treatment group received colchicine 0.5 mg/kg/day for 30 days. On day 30, morphometric measurements of lumen diameter and aortic cross-sectional area, together with semiquantitative histological scores for Caspase-3, Caspase-9, elastic fiber fragmentation, and calcium accumulation, were obtained.

Results: Compared with sham animals, aneurysm rats exhibited marked increases in lumen diameter and aortic area, higher Caspase-3 and Caspase-9 expression, pronounced elastin fragmentation, and greater calcium deposition. Colchicine significantly reduced lumen diameter and aortic area versus untreated aneurysm rats and lowered Caspase-3 and Caspase-9 scores while attenuating elastin fragmentation. In contrast, calcium scores remained elevated in both aneurysm and colchicine groups relative to sham, without a significant difference between the two aneurysm groups.

Conclusion: Colchicine partially limited early aneurysmal remodeling by improving geometric parameters and mitigating apoptosis and elastin degradation, whereas vascular calcification was not substantially modified. These data support further investigation of colchicine as a potential adjunctive therapy in abdominal aortic aneurysm.

Keywords: Abdominal aortic aneurysm, colchicine, calcium phosphate model, elastin degradation, apoptosis.

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Cite this article as: Kemahlı MB, Tunca NU, Bilen Ç, Akokay P, Metin K, Gençpınar T, et al. Colchicine modulates structural and histopathological remodeling in a calcium phosphate-induced rat model of abdominal aortic aneurysm. Cardiovasc Surg Int. 2026;13(1):7-12

Abdominal aortic aneurysm (AAA) is a progressive dilation of the abdominal aorta associated with a high risk of rupture and mortality. Despite major advances in surgical and endovascular management, there remains no approved pharmacological therapy capable of effectively preventing aneurysm expansion.[1] This therapeutic gap has directed attention toward anti-inflammatory and tissue-protective agents targeting the molecular mechanisms of aneurysm formation.[2]

The pathogenesis of AAA involves chronic inflammation, degradation of extracellular matrix components (particularly elastin), loss and apoptosis of vascular smooth muscle cells, and medial calcification.[3,4] Calcium-phosphate-based experimental models in rodents reproduce these features rapidly and reproducibly, making them useful for evaluating potential pharmacological interventions.[5] Such models demonstrate accelerated aneurysmal dilatation, elastin fragmentation, macrophage infiltration, and calcium deposition within a short experimental window.

Colchicine is a long-established anti-inflammatory alkaloid that acts by disrupting microtubule polymerization and thereby suppressing various inflammatory processes. Through its cytoskeletal effects, colchicine can reduce leukocyte migration, attenuate oxidative stress, and stabilize vascular tissue responses to injury.[6,7] In addition to its traditional clinical indications such as gout and pericarditis, low-dose colchicine has demonstrated cardiovascular benefits by reducing systemic inflammation and improving vascular outcomes in large randomized controlled trials.[8,9] These broad anti-inflammatory and cytoprotective actions suggest that colchicine may also exert protective effects in the development of AAA.

Therefore, this study aimed to investigate the effects of colchicine on structural remodeling, elastin integrity, apoptosis, and medial calcification in a calcium phosphate ($CaPO_4$)-induced AAA model in rats.

METHODS

A total of 22 male Wistar albino rats weighing approximately 300 g were used in this experimental study. Animals were housed in standard laboratory conditions (22±2 °C, 55±10% humidity, 12-hour light/dark cycle) with free access to food and water. All procedures were approved by the Dokuz Eylül University Animal Experiments Ethics Committee (protocol no: 32/2021, date: 02.08.2021) and performed in accordance with institutional and international guidelines for animal care. Rats were randomly assigned into three groups:

Sham group (n=6): Surgical exposure without aneurysm induction.

AAA group (n=8): Calcium phosphate-induced aneurysm.

Drug group (AAA + colchicine treatment group) (n=8): Aneurysm induction followed by colchicine therapy.

Surgical Procedure

Anesthesia was induced by intraperitoneal administration of ketamine (50 mg/kg) and xylazine (10 mg/kg). After sterile preparation, a midline laparotomy was performed, and the infrarenal abdominal aorta was exposed by gentle retroperitoneal dissection. Experimental AAA performed in the AAA group and drug group was created using the modified $CaPO_4$ periadventitial injury technique. The exposed aorta was first wrapped with a sterile sponge saturated with 0.5 mol/L $CaCl_2$ for 10 minutes, followed by application of a phosphate buffered saline-soaked sponge for 5 minutes, promoting localized $CaPO_4$ crystal formation and medial injury.

In the Sham group, the same procedure was performed using a 0.9% NaCl-soaked sponge for 15 minutes. After application, the abdomen was closed in layers and animals were monitored until recovery.

Rats in the treatment group received colchicine 0.5 mg/kg/day, administered by oral gavage once daily beginning on the day of aneurysm induction and continued throughout the 30-day follow-up period, as specified in the approved ethical protocol. Sham and AAA groups did not receive any pharmacological treatment.

Tissue Collection and Processing

On postoperative day 30, all rats were re-anesthetized using the same ketamine-xylazine protocol as for the index surgery. A midline laparotomy was reopened, and the infrarenal abdominal aorta, including the segment subjected to periadventitial chemical injury, was carefully dissected free from surrounding tissues and excised en bloc. Animals were then euthanized by exsanguination under deep anesthesia.

The harvested aortic specimens were immediately immersed in 10% neutral buffered formalin and fixed for 48-72 hours. After fixation, tissues were dehydrated through graded ethanol, cleared in xylene, and embedded in paraffin blocks according to routine histological procedures. Transverse sections of 5 µm thickness were obtained using a rotary microtome and mounted on poly-L-lysine-coated glass slides for histological and immunohistochemical evaluation.

Histopathological and Immunohistochemical Evaluation

For general structural assessment and morphometric measurements, sections were stained with hematoxylin&eosin (H&E). Two additional special stains were used for targeted evaluation of wall components:

Van Gieson's staining was employed to visualize elastic fibers and to grade elastic fiber fragmentation in the aneurysmal segment. Elastin integrity was scored semiquantitatively on a four-point scale (1-4), where higher scores indicated more pronounced disruption and loss of elastic lamellae.

Alizarin Red staining was used to detect medial calcium deposition. Calcification was evaluated semiquantitatively under light microscopy and graded on a 0-3 scale, from no visible deposits (0) to extensive, diffuse calcification involving large areas of the vessel wall (3).

Apoptotic activity within the aortic wall was assessed immunohistochemically using primary antibodies against Caspase-3 and Caspase-9. After antigen retrieval and blocking of endogenous peroxidase, sections were incubated with the primary antibodies, followed by a biotinylated secondary antibody and a streptavidin-peroxidase detection system. The reaction was visualized with a chromogenic substrate and counterstained with hematoxylin.

Caspase-3 and Caspase-9 immunoreactivity was scored semiquantitatively on a 0-3 scale (0= no staining, 1= mild, 2= moderate, 3= strong and diffuse staining). Each slide was evaluated independently by two observers who were blinded to group allocation, and the mean of their scores was used for statistical analysis. The histopathological outcomes reported in the manuscript (elastic fiber fragmentation,

calcium accumulation, Caspase-3, and Caspase-9) correspond directly to these scoring systems.

Morphometric Analysis

Morphometric measurements were performed on H&E-stained cross-sections using a computer-assisted image analysis system (ImageJ software, National Institutes of Health, Bethesda, MD, USA). For each animal, images were acquired at standardized magnification from the region of maximal dilation of the infrarenal aorta. At least three non-overlapping sections per animal were analyzed, and the mean value was used for further comparisons.

In line with the final study dataset, two primary morphometric parameters were evaluated:

Lumen diameter-defined as the maximal internal diameter of the aortic lumen measured perpendicular to the long axis of the vessel.

Aortic area-defined as the total cross-sectional area of the aortic wall and lumen within the external contour of the vessel.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous morphometric variables were assessed for normality using the Shapiro-Wilk test and expressed as mean ± standard deviation. Normally distributed variables were compared among the three experimental groups using One-Way Analysis of Variance. When a significant overall difference was detected, pairwise group comparisons were performed with Student's t-test. Because the study had an exploratory design and included a limited number of animals, no formal adjustment for multiple pairwise testing was applied; therefore, raw p-values were reported.

Histopathological scoring variables were evaluated as ordinal data and summarized using the median with interquartile range. Group differences were examined using the Kruskal-Wallis test. For parameters demonstrating significant global differences, pairwise comparisons were carried out with the Mann-Whitney U test. Similar to continuous variables, no correction for multiple comparisons was used, and raw p-values were presented. A p-value <0.05 was considered statistically significant.

RESULTS

Lumen diameter differed significantly among the three groups. The aneurysm group exhibited a notable increase in lumen diameter compared with the sham group (p=0.005), consistent with aneurysmal dilatation following $CaPO_4$-induced injury. Colchicine treatment substantially limited this enlargement, resulting in significantly smaller lumen diameters relative to untreated aneurysm rats (p<0.001). No significant difference was observed between the sham and colchicine groups (p=0.195).

Aortic area showed a similar pattern. Aneurysm formation led to a marked increase in aortic area compared with the sham group (p<0.001). Colchicine-treated rats demonstrated significantly smaller aortic areas than untreated aneurysms (p<0.001). All pairwise comparisons among the three groups reached statistical significance (p<0.001 for all), indicating clear differences in structural expansion across conditions (Table 1).

Caspase-3 expression was considerably higher in the aneurysm group compared with the sham group (p=0.001). Colchicine treatment reduced Caspase-3 levels significantly when compared with untreated aneurysm animals (p=0.003). A significant difference was also present between the sham and colchicine groups (p=0.019).

Caspase-9 scores increased markedly following aneurysm induction, with significantly higher values in the aneurysm group than in the sham group (p=0.002). Colchicine administration resulted in significantly lower Caspase-9 scores compared with untreated aneurysms (p=0.006). The sham and colchicine groups also differed significantly (p=0.009).

Elastic fiber fragmentation was substantially greater in the aneurysm group than in the sham group (p=0.001). Colchicine treatment attenuated elastin degradation, producing significantly lower fragmentation scores than those seen in untreated aneurysm animals (p<0.001). The sham versus colchicine comparison showed a trend toward increased fragmentation in the treatment group but did not reach statistical significance (p=0.058).

Aneurysm induction resulted in increased calcium accumulation, with significantly higher scores in the aneurysm group compared with the sham group (p=0.003). Colchicine-treated rats displayed higher calcium levels than shams (p=0.015). However, no statistically significant difference was detected between the aneurysm and colchicine groups (p=0.116) (Table 2, Figure 1).

DISCUSSION

In this experimental study, we investigated the effects of colchicine on structural and histopathological alterations in a calcium phosphate-induced AAA model in rats. The principal findings of our study were that colchicine attenuated aneurysmal dilatation, limited aortic wall expansion, reduced apoptotic activity, and mitigated elastic fiber degradation. These results collectively suggest that colchicine exerts a measurable protective influence on the aortic wall during $CaPO_4$ induced aneurysm formation.

The marked differences observed in lumen diameter and aortic area across the experimental groups indicate that structural remodeling occurred rapidly in this $CaPO_4$-induced model. The finding that

Table 1. Morphometric comparison

Parameter	Sham	Aneurysm	Drug	p-values			
				ANOVA	Sham-aneurysm	Sham-drug	Aneurysm -drug
Lumen diameter	651.75±93.23	788.57±56.05	581.70±95.31	**<0.001**	**0.005**	0.195	**<0.001**
Aortic area	434068.55±81284.07	835417.32±28269.16	626651.69±75027.21	**<0.001**	**<0.001**	**<0.001**	**<0.001**

Morphometric parameters were expressed as mean ± standard deviation. Group differences were evaluated using One-Way Analysis of Variance (ANOVA). Pairwise comparisons were performed with Student's t-test. Significant p-values are shown in bold. A p-value <0.05 was considered statistically significant.

Table 2. Comparison of histopathological scores

Parameter	Comparison	Group 1 median (Q1-Q3)	Group 2 median (Q1-Q3)	p-value
Caspase-3	Sham *vs.* aneurysm	1.0 (1.0-1.0)	3.0 (2.75-3.0)	**0.001**
	Sham *vs.* drug	1.0 (1.0-1.0)	2.0 (1.0-2.0)	**0.019**
	Aneurysm *vs.* drug	3.0 (2.75-3.0)	2.0 (1.0-2.0)	**0.003**
Caspase-9	Sham *vs.* aneurysm	0.5 (0.0-1.0)	3.0 (2.0-3.0)	**0.002**
	Sham *vs.* drug	0.5 (0.0-1.0)	2.0 (1.0-2.0)	**0.009**
	Aneurysm *vs.* drug	3.0 (2.0-3.0)	2.0 (1.0-2.0)	**0.006**
Elastic fiber fragmentation	Sham *vs.* aneurysm	1.0 (1.0-1.0)	3.0 (3.0-4.0)	**0.001**
	Sham *vs.* drug	1.0 (1.0-1.0)	1.5 (1.0-2.0)	0.058
	Aneurysm *vs.* drug	3.0 (3.0-4.0)	1.5 (1.0-2.0)	**<0.001**
Calcium accumulation	Sham *vs.* aneurysm	0.5 (0.0-1.0)	2.0 (2.0-3.0)	**0.003**
	Sham *vs.* drug	0.5 (0.0-1.0)	1.5 (1.0-2.0)	**0.015**
	Aneurysm *vs.* drug	2.0 (2.0-3.0)	1.5 (1.0-2.0)	0.116

Pairwise comparisons of apoptotic markers (Caspase-3 and Caspase-9), elastic fiber fragmentation, and calcium accumulation among Sham, aneurysm, and drug-treated groups. Data are expressed as median (Q1-Q3). Comparative analyses were performed using the Mann-Whitney U test. Multiple comparison adjustment was not applied due to the exploratory nature of the study. A p-value <0.05 was considered statistically significant.

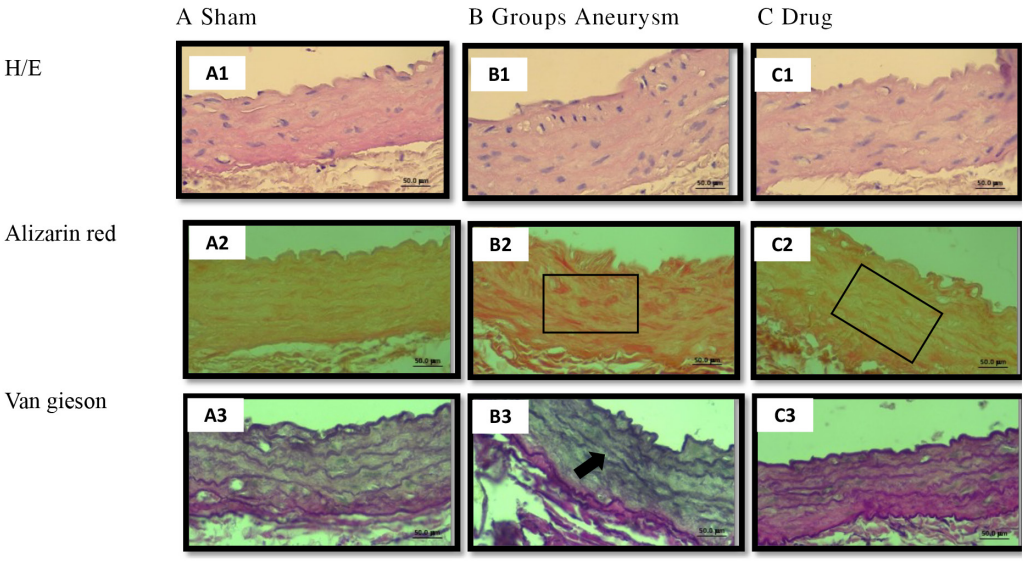

Figure 1. Histological sections of groups (hematoxylin&eosin stain, 40X) A1- Sham group, B1- Aneurysm group, C1- Drug group. Histological sections of groups (alizarin red stain, 40X): A2- Sham group, B2- Aneurysm group, C2- Drug group. Calcium accumulation in the groups is shown in the square. Histological sections of groups (Van Gieson stain, 40X): A3: Sham group, B3- Aneurysm group, C3- Drug group. Deteriorations in elastic fibers in the tunica media layer were seen with the black arrov.

colchicine-treated animals exhibited values closer to physiological dimensions suggests that the drug may interfere with the processes driving pathological wall expansion. Similar attenuation of aneurysmal growth with colchicine has been reported in recent preclinical studies, supporting the notion that pharmacological intervention can modify early aneurysmal remodeling of the aortic wall.[10] Nevertheless, contrasting findings also exist, and some models have shown limited structural response to colchicine treatment, highlighting that its effects may vary depending on the underlying mechanism of aneurysm induction.[11]

Aneurysm induction resulted in marked elastic fiber fragmentation, reflecting the early deterioration of medial architecture typical of experimentally induced AAAs.[12] Preservation of elastin is fundamental to maintaining aortic wall stability.[13] In the present study, colchicine-treated animals demonstrated substantially lower elastin fragmentation scores compared with untreated aneurysm rats, suggesting that the drug may exert a stabilizing effect on the medial layer of the vessel wall. This aligns with recent reports indicating that elastin degradation is a critical driver in aneurysm progression and that pharmacological modulation of inflammatory and proteolytic pathways may help preserve medial elastin structure.[12]

Apoptotic signaling is regarded as an important contributor to structural deterioration in AAA, and experimental models consistently demonstrate increased activation of caspase-dependent pathways in aneurysmal

segments.[14] In our study, aneurysm induction was associated with higher Caspase-3 and Caspase-9 scores, indicating activation of intrinsic apoptotic mechanisms within the aortic wall. Colchicine treatment reduced both caspase markers, implying a potential attenuation of apoptotic activity in the aortic tissue. These findings are in line with previous reports showing that modulation of apoptosis-related pathways can influence the structural trajectory of aneurysm development without necessarily restoring cellularity itself.[15,16]

Calcium deposition increased markedly after aneurysm induction in our model, consistent with prior work showing that medial mineralization accompanies chemically induced aortic injury and structural degeneration.[17,18] In the present study, colchicine-treated animals demonstrated calcium scores that were significantly higher than those of sham rats and only modestly lower than those of untreated aneurysm animals, with no statistically significant difference between the latter two groups. These findings suggest that colchicine did not substantially influence early vascular calcification within the 30-day observation period, possibly because mineral deposition may progress relatively independently of short-term anti-inflammatory or cytoskeletal-modulating treatments in this model.

Colchicine has regained prominence in recent years following major cardiovascular outcome trials. Studies in patients with myocardial infarction and in those with stable coronary artery disease have demonstrated that colchicine significantly reduces major adverse cardiovascular events, thereby increasing interest in applying the drug to other chronic vascular pathologies.[19,20] In recent years, colchicine has also been investigated for AAA; several experimental studies have suggested that it may slow aneurysm development, often through mechanisms involving attenuation of cellular stress responses, preservation of elastic fiber integrity, or reduction of inflammasome-related signaling.[10,21,22] However, not all studies have shown consistent results, and some experimental models have reported no significant suppression of aneurysm expansion, implying that its efficacy may depend on model type, treatment timing, and dosing regimen.[11]

In this context, the present $CaPO_4$-induced model provides complementary structural and histopathological insights into colchicine's effects during aneurysm formation. The smaller lumen diameters and reduced aortic areas observed in the colchicine group, together with lower Caspase-3 and Caspase-9 scores and markedly decreased elastin fragmentation, suggest that the drug may partially limit early structural deterioration. In contrast, the lack of a significant reduction in calcium deposition indicates that calcification in this model may be more resistant to short-term colchicine treatment. Overall, these findings suggest that colchicine may serve as an adjunctive pharmacological strategy aimed at stabilizing the aneurysmal aortic wall, although its effects may not extend uniformly across all components of AAA pathobiology.

This study has several limitations. First, mechanistic pathways were not directly assessed, and therefore no conclusions can be drawn regarding the molecular processes through which colchicine may influence aneurysm remodeling. Second, only a single colchicine regimen was evaluated, leaving the dose–response relationship and the effects of alternative treatment schedules undetermined. Third, the $CaPO_4$ model represents an acute chemically induced injury that does not fully recapitulate the chronic and multifactorial nature of human AAA, which may limit translational extrapolation. Finally, the sample size was modest, reducing the power to detect more subtle differences between subgroups and warranting confirmation in larger experimental cohorts.

In this experimental $CaPO_4$-induced AAA model, colchicine treatment was associated with reduced lumen diameter, smaller aortic area, lower apoptotic activity, and attenuated elastin fragmentation compared with untreated aneurysm animals. These findings suggest that colchicine can mitigate early structural deterioration of the aortic wall, although mineralization remained largely unaffected. While the mechanistic basis of these effects was not directly assessed, the overall pattern supports a potential role for colchicine as an adjunctive strategy in limiting early aneurysmal remodeling. Further studies incorporating alternative dosing strategies, longitudinal assessment, and chronic AAA models are needed to clarify its therapeutic relevance and translational potential.

Ethics

Ethics Committee Approval: All procedures were approved by the Dokuz Eylül University Animal Experiments Ethics Committee (protocol no: 32/2021, date: 02.08.2021) and performed in accordance with institutional and international guidelines for animal care.

Informed Consent: This experimental study did not involve human participants; therefore, informed consent was not required.

Acknowledgments

For transparency, the authors note that an artificial intelligence–assisted language model (ChatGPT, OpenAI) was utilized to support text editing and language correction. This assistance was limited to linguistic refinement; all scientific content, critical analysis, and final editorial decisions were made exclusively by the authors.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.B.K., Ç.B., P.A.; Concept: T.G., K.M.; Design: S.B.; Data Collection or Processing: P.A.; Analysis or Interpretation: P.A.; Literature Search: M.B.K., N.U.T.; Writing: M.B.K.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Puertas-Umbert L, Almendra-Pegueros R, Jiménez-Altayó F, Sirvent M, Galán M, Martínez-González J, et al. Novel pharmacological approaches in abdominal aortic aneurysm. Clin Sci (Lond). 2023;137:116794. doi: 10.1042/CS20220795.
2. Mo B, Ding Y, Ji Q. NLRP3 inflammasome in cardiovascular diseases: an update. Front Immunol. 2025;16:1550226. doi: 10.3389/fimmu.2025.1550226.
3. Zhang S, Cai Z, Zhang X, Ma T, Kong W. A calcium phosphate-induced mouse abdominal aortic aneurysm model. J Vis Exp. 2022. doi: 10.3791/64173.
4. Yamanouchi D, Morgan S, Stair C, Seedial S, Lengfeld J, Kent KC, et al. Accelerated aneurysmal dilation associated with apoptosis and inflammation in a newly developed calcium phosphate rodent abdominal aortic aneurysm model. J Vasc Surg. 2012;56:455-61. doi: 10.1016/j.jvs.2012.01.038.

5. Tian K, Malik F, Zhao S. Animal models for abdominal aortic aneurysms: where we are and where we need to go. Animal Model Exp Med. 2025;8:573-7. doi: 10.1002/ame2.12572.

6. Leung YY, Yao Hui LL, Kraus VB. Colchicine--update on mechanisms of action and therapeutic uses. Semin Arthritis Rheum. 2015;45:341-50. doi: 10.1016/j.semarthrit.2015.06.013.

7. Dalbeth N, Lauterio TJ, Wolfe HR. Mechanism of action of colchicine in the treatment of gout. Clin Ther. 2014;136:1465-79. doi: 10.1016/j.clinthera.2014.07.017.

8. Ma Z, Chen J, Jin K, Chen X. Colchicine and coronary heart disease risks: a meta-analysis of randomized controlled clinical trials. Front Cardiovasc Med. 2022;9:947959. doi: 10.3389/fcvm.2022.947959.

9. Buckley LF, Libby P. Colchicine's role in cardiovascular disease management. Arterioscler Thromb Vasc Biol. 2024;44:1031-41. doi: 10.1161/ATVBAHA.124.319851. Erratum in: Arterioscler Thromb Vasc Biol. 2024;44:e208. doi: 10.1161/ATV.0000000000000172.

10. Chen M, Yang D, Zhou Y, Yang C, Lin W, Li J, et al. Colchicine blocks abdominal aortic aneurysm development by maintaining vascular smooth muscle cell homeostasis. Int J Biol Sci. 2024;20:2092-110. doi: 10.7150/ijbs.93544.

11. Phie J, Thanigaimani S, Huynh P, Anbalagan R, Moran CS, Kinobe R, et al. Colchicine does not reduce abdominal aortic aneurysm growth in a mouse model. Cardiovasc Ther. 2022;2022:5299370. doi: 10.1155/2022/5299370.

12. Cai D, Chen SY. Elastin in the pathogenesis of abdominal aortic aneurysm. Cells. 2025;14:1597. doi: 10.3390/cells14201597.

13. Niestrawska JA, Regitnig P, Viertler C, Cohnert TU, Babu AR, Holzapfel GA. The role of tissue remodeling in mechanics and pathogenesis of abdominal aortic aneurysms. Acta Biomater. 2019;88:149-61. doi: 10.1016/j.actbio.2019.01.070.

14. Sinha I, Sinha-Hikim AP, Hannawa KK, Henke PK, Eagleton MJ, Stanley JC, et al. Mitochondrial-dependent apoptosis in experimental rodent abdominal aortic aneurysms. Surgery. 2005;138:806-11. doi: 10.1016/j.surg.2005.07.011.

15. Weaver LM, Loftin CD, Zhan CG. Development of pharmacotherapies for abdominal aortic aneurysms. Biomed Pharmacother. 2022;153:113340. doi: 10.1016/j.biopha.2022.113340.

16. Qian G, Adeyanju O, Olajuyin A, Guo X. Abdominal aortic aneurysm formation with a focus on vascular smooth muscle cells. Life (Basel). 2022;12:191. doi: 10.3390/life12020191.

17. Klopf J, Fuchs L, Schernthaner R, Domenig CM, Gollackner B, Brostjan C, et al. The prognostic impact of vascular calcification on abdominal aortic aneurysm progression. J Vasc Surg. 2022;75:1926-34. doi: 10.1016/j.jvs.2021.11.062.

18. Wang Y, Krishna S, Golledge J. The calcium chloride-induced rodent model of abdominal aortic aneurysm. Atherosclerosis. 2013;226:29-39. doi: 10.1016/j.atherosclerosis.2012.09.010.

19. Tardif JC, Kouz S, Waters DD, Bertrand OF, Diaz R, Maggioni AP, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. N Engl J Med. 2019;381:2497-505. doi: 10.1056/NEJMoa1912388.

20. Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TSJ, et al. Colchicine in patients with chronic coronary disease. N Engl J Med. 2020;383:1838-47. doi: 10.1056/NEJMoa2021372.

21. Hu J, Xu J, Zhao J, Liu Y, Huang R, Yao D, et al. Colchicine ameliorates short-term abdominal aortic aneurysms by inhibiting the expression of NLRP3 inflammasome components in mice. Eur J Pharmacol. 2024;964:176297. doi: 10.1016/j.ejphar.2023.176297.

22. Zhao Y, Shen QR, Chen YX, Shi Y, Wu WB, Li Q, et al. Colchicine protects against the development of experimental abdominal aortic aneurysm. Clin Sci (Lond). 2023;137:1533-45. doi: 10.1042/CS20230499.

ORIGINAL ARTICLE

CARDIOVASCULAR SURGERY AND INTERVENTIONS

DOI: 10.4274/e-cvsi.2026.2115
Cardiovasc Surg Int 2026;13(1):13-19

The predictive value of the inflammatory prognostic index (IPI) for early adverse outcomes following carotid artery surgery

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Received: November 19, 2025 **Accepted:** January 24, 2026 **Epub:** February 20, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Objectives: The inflammatory prognostic index (IPI), a composite biomarker incorporating C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), and serum albumin (ALB), has recently emerged as a marker of systemic inflammation. This study aimed to investigate the predictive capacity of IPI for early adverse outcomes following carotid artery surgery. A retrospective cohort study was conducted in a single tertiary center.

Patients and methods: Medical records of 286 patients who underwent carotid artery surgery between January 2021 and December 2024 were retrospectively reviewed. Patients were stratified into two groups according to early postoperative outcomes: those with adverse events (major cerebrovascular accident, myocardial infarction, or 30-day mortality) and those without. Preoperative CRP, NLR, and ALB levels were collected to calculate the IPI using the formula (CRP×NLR)/ALB. Comparative analyses were performed between groups. Multivariate logistic regression identified independent predictors of adverse outcomes, and receiver operating characteristic (ROC) analysis was used to determine the optimal IPI cut-off point.

Results: Adverse outcomes were observed in 20 patients (7%). The adverse group showed significantly higher IPI and CRP values, along with lower serum ALB levels, compared to the favorable group. In multivariate analysis, IPI emerged as the only independent predictor of adverse outcomes. ROC analysis identified an IPI threshold of 0.27, which predicted adverse outcomes with high sensitivity but moderate specificity.

Conclusion: This study is the first to demonstrate that IPI is an independent predictor of early adverse outcomes following carotid artery surgery. Given its simplicity and cost-effectiveness, IPI may serve as a practical biomarker for preoperative risk stratification and clinical decision-making in vascular surgery

Keywords: Inflammatory prognostic index, biomarker, poor outcome, carotid artery surgery.

Carotid artery surgery (CAS), remains a cornerstone in the management of significant carotid artery stenosis, aiming to reduce the risk of ischemic stroke—one of the leading causes of morbidity and mortality worldwide.[1] Approximately one-third of ischemic strokes are attributed to carotid artery stenosis.[2] While CAS is an effective strategy for stroke prevention, it is not without risks. In high-risk patients, the incidence of postoperative stroke or death can exceed 10%.[3] To optimize the risk-benefit ratio of CAS, guidelines recommend maintaining perioperative (intraoperative and postoperative) stroke or death rates below 6% for symptomatic and 3% for asymptomatic patients.[4] Achieving these targets, however, is challenged by the lack of standardized tools capable of reliably predicting adverse outcomes following the procedure.

Atherosclerosis is widely recognized as a chronic inflammatory process.[5] The formation and progression of atherosclerotic plaques are largely governed by inflammatory and immune mechanisms.[5] Numerous biomarkers reflecting systemic inflammation and immune status have been shown to be associated with outcomes following oncologic and cardiovascular surgery.[6,7] Among these, complete blood count-derived markers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-

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Cite this article as: Güven H, Çetintaş D. The predictive value of the inflammatory prognostic index (IPI) for early adverse outcomes following carotid artery surgery. Cardiovasc Surg Int. 2026;13(1):13-19

lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) have demonstrated potential prognostic value for predicting outcomes in vascular surgery, including CAS.[6,8,9]

The inflammatory prognostic index (IPI), a novel composite marker combining C-reactive protein (CRP), NLR, and serum albumin (ALB) levels, has recently emerged as a promising prognostic tool.[10] Calculated as IPI = CRP×NLR/ALB, this index provides an integrative measure of a patient's inflammatory and immune status. Initially introduced by Dirican et al.[10] to predict prognosis in patients with non-small cell lung cancer, the IPI has since demonstrated prognostic potential in various clinical settings. For example, it has demonstrated prognostic potential in various cardiovascular conditions, such as new-onset atrial fibrillation, mortality after coronary artery bypass grafting, and 90-day outcomes after acute ischemic stroke (AIS).[11] Furthermore, the potential role of IPI in vascular surgery has been evaluated, for example, in predicting perioperative mortality after type A aortic dissection surgery.[12]

However, while IPI has been investigated mainly in the context of long-term survival or in relation to other inflammatory indices, its role in predicting early adverse outcomes (within 30 days) following CAS has not yet been investigated. Although a recent study highlighted the prognostic potential of SII for early side effects following CAS,[8] the potential of IPI to predict adverse outcomes after CAS, including similar studies focused on inflammation, has not been investigated. This knowledge gap underlines the necessity of further exploring the IPI as a predictive tool for early complications after CAS.

The primary objective of this study is to investigate the role of preoperative IPI levels in predicting early adverse outcomes (defined as stroke, myocardial infarction [MI], or death within 30 days) in patients undergoing CAS.

PATIENTS AND METHODS

Study Design and Patient Selection

This retrospective observational cohort study included 286 patients who underwent CAS for significant carotid artery stenosis at the department of cardiovascular surgery of a tertiary referral hospital in Türkiye between January 2021 and December 2024. The study enrolled adult patients who underwent elective, first-time, isolated CAS with complete and accessible medical records. Exclusion criteria included the absence or incompleteness of medical data, emergency procedures, re-operations, combined carotid and coronary artery surgeries, and the presence of active infections, malignancies, hematological or immunological disorders, as well as end-stage renal or hepatic diseases. Based on postoperative outcomes, patients were categorized into two groups: The adverse outcome group (n=20), comprising those who experienced adverse events such as major cerebrovascular accident (CVA), MI, or 30-day mortality, and the favorable outcome group (n=266). Clinical data, including demographic characteristics, comorbidities, laboratory test results, derived indices, intraoperative details, and postoperative complications, were retrieved from the hospital's electronic medical records system, documented for analysis, and subsequently compared between these two groups. Patients receiving preoperative antiplatelet therapy (e.g., aspirin or clopidogrel) were enrolled, and bleeding/hematoma rates were compared between patients receiving antiplatelet therapy and those not receiving antiplatelet therapy.

Ethical approval for the study was obtained from the University of Health Sciences Türkiye, Bursa City Hospital Scientific Research Ethics Committee (approval number: 2025-2/6, date: 22.01.2025). The study was performed in accordance with the ethical principles of the Declaration of Helsinki.

Preoperative Management

The indications for surgical intervention were defined as the presence of ≥50% internal carotid artery (ICA) stenosis in symptomatic patients and ≥70% ICA stenosis in asymptomatic patients, following the criteria established by the North American Symptomatic Carotid Endarterectomy (CAS) Trial and the Society for Vascular Surgery guidelines.[13,14] The degree of ICA stenosis was initially assessed through color Doppler ultrasound and subsequently confirmed using advanced angiographic techniques, including computed tomography angiography and digital subtraction angiography. All patients scheduled for surgery were prescribed 100 mg/day of oral acetylsalicylic acid (ASA) as an antiplatelet therapy prior to the procedure.

Surgical Technique

All surgical procedures were performed under general anesthesia with intraoperative monitoring using near-infrared spectroscopy. An oblique incision was made along the anterior border of the sternocleidomastoid muscle. After exposing the carotid bifurcation, the common carotid artery (CCA), ICA, and external carotid artery (ECA) were isolated using vascular tapes. These arteries were visually inspected, and clamps were applied sequentially (ICA, CCA, and ECA) following intravenous administration of heparin at a dose of 150 IU/kg, targeting an activated clotting time of ≥250 seconds. Depending on the surgeon's preference, different surgical techniques were employed, including conventional CAS with either Dacron or saphenous vein patch closure, primary closure (without patch), traditional or modified eversion CAS, and saphenous vein graft bypass or interposition for the ICA. Upon removal of the atherosclerotic lesion, the clamps were released in reverse order (ECA, CCA, and ICA). Protamine was administered intravenously to neutralize heparin. Hemostasis was achieved, and the wound was closed in standard fashion. The effect of surgical techniques on clinical outcomes was evaluated by statistical analysis

Postoperative Management and Follow-up

Following surgery, all patients were initially monitored in the intensive care unit (ICU). In the absence of major complications, they were transferred to the general ward on the first postoperative day. Dual antiplatelet therapy, consisting of 100 mg/day ASA and 75 mg/day clopidogrel, was initiated six hours postoperatively in the absence of significant bleeding. Discharged patients were scheduled for routine follow-up visits at one week, then at one, two, three, six, and twelve months, and annually thereafter. At each visit, patients underwent physical examination and routine Doppler ultrasonography. Patients were monitored for at least 30 days postoperatively, except for those who experienced mortality.

Laboratory Analysis

Blood samples were collected after a minimum of six hours of fasting, using vacutainers for peripheral venous access. The collected samples were placed in tubes containing anticoagulants and promptly transported to the laboratory. Automated biochemical and hematological analyzers were utilized to measure the laboratory

parameters, which included glucose, hemoglobin A1c, total cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, ALB, CRP, hemoglobin, hematocrit, platelet count, white blood cell count, neutrophil count, and lymphocyte count. In addition, several derived indices were calculated: The NLR, PLR, systemic immune-inflammation index (SII), and IPI. Given that composite inflammatory indices are derived from basic laboratory parameters, alternative multivariable model structures were explored during the analysis phase. These included models incorporating clinical variables combined with a single inflammatory index. The final model was selected based on clinical relevance and overall model performance. SII was calculated using the formula "platelet×NLR", while IPI was determined as "CRP×NLR/ALB".

Statistical Analysis

Data analysis was conducted using IBM SPSS Statistics version 24 (IBM Corp., Armonk, NY, USA). The normality of distribution for continuous variables was assessed using the Shapiro-Wilk test. Continuous variables that followed a normal distribution were compared between groups using the Student's t-test, while the Mann-Whitney U test was employed for variables that did not follow a normal distribution. Categorical variables were analyzed using the chi-square test. Variables identified as significant in univariate analysis ($p<0.1$) were further evaluated using multivariate logistic regression to identify independent predictors of poor outcomes. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cut-off value(s) for significant variables, with sensitivity and specificity values calculated based on the area under the curve (AUC). To assess potential multicollinearity among variables included in the multivariable logistic regression model, variance inflation factor (VIF) values were calculated. A VIF value <5 was considered indicative of the absence of significant multicollinearity.

Given the shared components among inflammatory indices, IPI was retained in the final model due to its superior discriminatory performance.

Normally distributed continuous variables were presented as mean ± standard deviation, whereas non-normally distributed variables were reported as median (minimum-maximum). Categorical variables were expressed as numbers (percentages). A p-value of less than 0.05 was considered statistically significant.

RESULTS

In this study, the overall population had a mean age of 65.9±8.7 years (ranging from 42 to 88 years), with 36% of the participants being female. Among the cohort, 63% had a history of previous cerebrovascular events (CVE), including amaurosis fugax, transient ischemic attack, and minor or major stroke. Contralateral ICA occlusion was present in 13 patients (4.5%). The overall incidence of the composite 30-day adverse outcome was 7% (20 out of 286 patients). The primary poor outcomes assessed in this study were major CVA, MI, and mortality, which were observed in 13, 2, and 5 patients, respectively.

Comparative analysis of the preoperative demographic and clinical characteristics between the adverse outcome group and the favorable outcome group demonstrated no statistically significant differences for any of the assessed parameters, indicating that the groups were comparable in terms of baseline characteristics (Table 1).

When intraoperative and postoperative variables were analyzed, the median lengths of stay in the ICU and the overall hospital stay were significantly longer in the adverse outcome group compared to the favorable outcome group. Prolonged ICU and hospital stays were observed as a consequence of major postoperative complications and were not included as predictive variables in the risk assessment analyses.

No significant differences were identified between the two groups for any other intraoperative or postoperative variables assessed (Table 2).

Table 1. Preoperative basic demographic and clinical characteristics

Variable	Adverse outcome group (n=20)	Favorable outcome group (n=266)	p-value
Age (year)	67.1±6.4	65.8±8.9	0.380
Gender (female)	7 (35%)	96 (36%)	0.922
Weight (kg)	81.3±15.3	76.6±14.5	0.201
Height (cm)	170.0±4.8	170.5±5.1	0.658
BMI (kg/m²)	28.1±5.2	26.4±5.1	0.162
Smoking	8 (40%)	92 (35%)	0.624
Antiplatelet therapy (%)	9 (45%)	82 (39 %)	0.312
HT	14 (70%)	159 (60%)	0.367
DM	9 (45%)	112 (42%)	0.800
HL	8 (40%)	96 (36%)	0.726
CAD	11 (55%)	127 (48%)	0.531
PAD	6 (30%)	52 (20%)	0.262
COPD	2 (10%)	16 (6%)	0.479
Previous CVE	15 (75%)	164 (62%)	0.234
Contralateral ICA occlusion	2 (10%)	11 (4%)	0.225

BMI: Body mass index; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; CVE: Cerebrovascular event; DM: Diabetes mellitus; HL: Hyperlipidemia; HT: Hypertension; ICA: Internal carotid artery; PAD: Peripheral artery disease.

Table 2. Intraoperative and postoperative data

Variable	Adverse outcome group (n=20)	Favorable outcome group (n=266)	p-value
Clamp time (min)	24 (13-75)	24 (10-90)	0.905
Operation time (min)	58 (45-142)	60 (32-197)	0.762
Duration of ICU stay (hour)	180 (48-360)	18 (4-72)	<0.001
Duration of hospital stay (day)	12 (2-32)	4 (2-10)	<0.001
Vocal cord paralysis	1 (5%)	7 (3%)	0.536
Bleeding/hematoma	0 (0%)	14 (5%)	0.293
Major CVA	13 (65%)	0 (0%)	NS
MI	2 (10%)	0 (0%)	NS
30-day mortality	5 (25%)	0 (0%)	NS
Surgical techniques			0.896
CEA with patch	10 (%50)	130 (48.9%)	
CEA without patch	6 (30%)	77 (28.9%)	
Eversion	3 (15%)	37 (13.9%)	
Saphenous vein graft	1 (5%)	22 (8.3%)	

CVA: Cerebrovascular accident; ICU: Intensive care unit; MI: Myocardial infarction; CEA: Carotid Endarterectomy; NS: Not specified.

Evaluation of the laboratory test results and derived indices revealed that the mean serum ALB level was significantly lower, while the median values of CRP and the IPI were significantly higher in the adverse outcome group compared to the favorable outcome group. No other laboratory parameters showed statistically significant differences between the two groups (Table 3).

Following the univariate analysis, variables with p values less than 0.1 were considered potential risk factors and were included in the multivariate logistic regression analysis. In this regression model, only IPI retained statistical significance as an independent predictor of poor outcome, while other variables were excluded due to lack of significance. VIF analysis demonstrated no significant multicollinearity among the included variables, with all VIF values remaining below the predefined threshold (Table 4).

Table 3. Laboratory parameters

Variable	Adverse outcome group (n=20)	Favorable outcome group (n=266)	p-value
Glucose (mg/dL)	116.9±25.1	117.4±22.1	0.941
Hemoglobin A1c (%)	6.0±1.0	6.1±1.0	0.686
Total cholesterol (mg/dL)	207.7±46.0	196.3±49.8	0.334
LDL cholesterol (mg/dL)	131.1±24.3	130.9±34.9	0.968
Triglyceride (mg/dL)	178.4±68.3	170.6±62.4	0.627
Albumin (g/L)	37.0±4.9	42.1±6.4	<0.001
CRP (mg/L)	4.5 (1.4-16.3)	2.8 (0.3-31.6)	0.004
Hemoglobin (g/dL)	12.7±2.0	12.6±1.9	0.952
Hematocrit (%)	38.4±6.2	38.5±8.1	0.966
Platelet count (10^3/µL)	274.2±104.7	264.9±97.8	0.702
WBC count (10^3/µL)	9.3±3.0	8.2±2.5	0.116
Neutrophil count (10^3/µL)	6.7±2.5	5.6±1.9	0.085
Lymphocyte count (10^3/µL)	1.3±0.7	1.4±0.8	0.393
NLR	5.5 (2.2-16.6)	4.0 (1.1-25.6)	0.061
PLR	248 (73-694)	203 (33-1461)	0.325
SII	1452 (406-4802)	1067 (189-6930)	0.070
IPI	0.73 (0.13-3.43)	0.26 (0.02-4.00)	<0.001

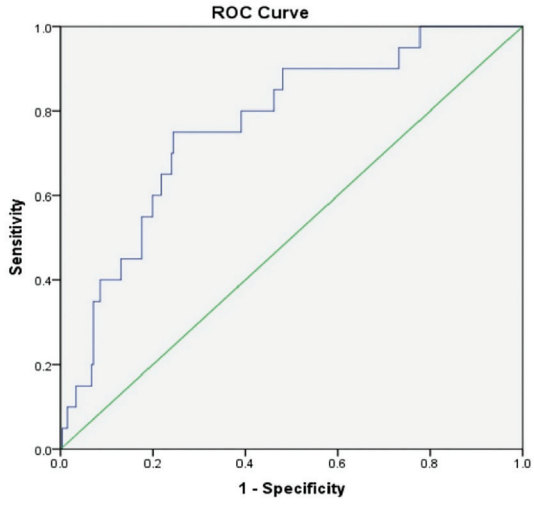
CRP: C-reactive protein; IPI: Inflammatory prognostic index; LDL: Low-density lipoprotein; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index; WBC: White blood cell.

ROC curve analysis identified an IPI cut-off value of 0.27 as the optimal threshold for predicting poor outcomes, with a sensitivity of 85% and a specificity of 48% (AUC=0.767 [95% confidence interval: 0.666-0.869]) (Figure 1).

DISCUSSION

Our study demonstrates that the IPI is a significant prognostic biomarker for predicting early adverse outcomes following CAS. IPI, which integrates CRP, NLR, and serum ALB levels, provides a comprehensive reflection of the patient's inflammatory and immune response. Our findings revealed that higher IPI values were significantly associated with poor outcomes (p<0.001). Specifically, the median IPI value was 0.73 (0.13-3.43 in the adverse outcome group, compared to 0.26 (0.02-4.00) in the good outcome group.

Our analysis showed that traditional risk factors, including age, gender, body mass index, smoking status, hypertension (HT), diabetes mellitus, hyperlipidemia, coronary artery disease, peripheral artery disease, and chronic obstructive pulmonary disease, did not significantly differentiate between patients with poor and good outcomes (p>0.05).



Optimum cut-off value	Area under the curve (AUC)	Sensitivity	Specificity	P value
0.27	0.767 (0.666–0.869)	85%	48%	<0.001

Figure 1. Receiver operating characteristic (ROC) curve analysis.

Table 4. Multivariate logistic regression analysis to determine the independent predictors

Variable	Beta	Standard error	Wald	Expected beta	95% CI for expected beta (upper-lower)	p-value
Neutrophil	0.444	0.865	0.264	1.560	0.286-8.494	0.607
NLR	0.000	0.171	0.000	1.000	0.716-1.397	0.999
SII	0.000	0.000	0.085	1.000	0.999-1.001	0.771
CRP	0.073	0.107	0.459	1.075	0.871-1.327	0.498
Albumin	0.227	0.125	3.324	1.255	0.983-1.603	0.068
IPI	-0.189	0.056	11.329	0.828	0.742-0.924	0.001

CI: Confidence interval; CRP: C-reactive protein; IPI: Inflammatory prognostic index; NLR: Neutrophil-to-lymphocyte ratio; SII: Systemic immune-inflammation index. Variance inflation factor values for all variables included in the model were <5.

For instance, the prevalence of HT was 14 (70%) in the adverse outcome group versus 14 (70%) in the good outcome group (p=0.367). This finding indicates that conventional risk factors may be limited in predicting individual patient outcomes, highlighting the potential of inflammatory biomarkers to bridge this gap. The comparison of bleeding and hematoma rates according to preoperative antiplatelet therapy was included as a secondary safety analysis, given the routine use of antiplatelet agents in patients undergoing CAS. The proportion of patients receiving preoperative antiplatelet therapy was 31% (82/266) in the favorable outcome group and 45% (9/20) in the adverse outcome group (p=0.312, Table 1). In our cohort, preoperative antiplatelet therapy was not associated with an increased risk of bleeding or hematoma formation (p=0.293, Table 2). This finding should be interpreted as descriptive and exploratory, and it does not suggest any modification of current perioperative antiplatelet management strategies.

In our study, there is no statistically significant difference was found between patients in the adverse outcome group (n=20) and the good outcome group (n=266) in terms of carotid clamp time (median 24 [13-75] min *vs.* median 24 [10-90] min, p=0.905) and operative time (median 58 [45-142] min *vs*. median 60 [32-197] min, p=0.762). We also evaluated the impact of different surgical techniques (conventional carotid endarterectomy, patch closure, eversion techniques, and saphenous vein grafting) on clinical outcomes. Although no significant difference was found between techniques (0.896, Table 2), the potential impact of this factor on outcomes cannot be excluded. Future studies should further examine the prognostic value of surgical techniques in conjunction with IPI. However, regarding other perioperative and postoperative outcomes, ICU stay (median 180 [48-360] hours) and hospital stay (median 12 [2-32] days) were found to be statistically significantly longer in the adverse outcome group. This suggests that major complications that constitute the definition of adverse outcome (major CVA 65%, MI 10%, 30-day mortality 25%- seen only in the adverse outcome group) result in patients staying in the ICU and hospital for longer periods. The significantly longer ICU and hospital stays observed in the adverse outcome group should be interpreted as downstream consequences of major postoperative complications rather than as preoperative or intraoperative predictors. This temporal distinction is essential to avoid misinterpretation of length-of-stay variables as causative factors.

Chronic systemic inflammation is known to play a pivotal role in the pathogenesis of atherosclerosis and vascular diseases.[15] Numerous studies have reported the prognostic value of inflammatory markers in predicting adverse outcomes following CAS.[16,17] Although major CVA and MI have different pathophysiological mechanisms, both are influenced by the inflammatory nature of atherosclerosis. As composite indices integrate multiple inflammatory and nutritional parameters, they were interpreted as summary markers rather than independent substitutes for their individual components. As an indicator of systemic inflammation and immune status, IPI may reflect the common inflammatory pathways of these complications.[18] Therefore, IPI is thought to offer prognostic value for both conditions. In our univariate analysis, ALB level was found to be significantly lower in the adverse outcome group (p<0.001). ALB is a negative acute phase reactant that decreases in the inflammatory response and has been reported to affect the prognosis of AIS.[19] The median value of CRP was found to be significantly higher in the adverse outcome group (p=0.004). CRP is a well-known positive acute phase reactant of inflammation and is associated with the risk of cardiovascular events.[19,20] According to the univariate analysis results, many other laboratory parameters such as glucose, HbA1c, total cholesterol, LDL cholesterol, triglyceride, hemoglobin, hematocrit, platelet count, leukocyte count, lymphocyte count, NLR, PLR and SII did not show any statistically significant difference between the two groups (p>0.05).

The most critical finding is the multivariate analysis result. In multivariate analysis, only IPI was found to be a significant and independent predictor of adverse outcome (p=0.001), while other markers with univariate significance or p<0.1, including CRP and ALB, lost their statistically significance. This result indicates that IPI (as an index combining CRP, NLR and ALB) can independently predict early poor outcomes after CAS better than markers such as CRP or ALB alone or other derived indices such as SII, and the association of the components of IPI with inflammatory status supports the linkage of inflammation with postsurgical outcomes.

ROC curve analysis was used to evaluate the prognostic performance of IPI in predicting early poor outcomes after CEA. The AUC value obtained was 0.767, indicating that IPI has a moderate discriminatory power. The determined cut-off value of 0.27 can correctly identify the majority of patients with poor outcomes with a sensitivity of 85%. The identified IPI cut-off value demonstrated high sensitivity but limited specificity, indicating that while it may be useful as a screening tool for early risk identification, it is not suitable as a standalone marker for guiding major perioperative clinical decisions. Instead, IPI should be integrated with established clinical, radiological, and procedural factors to support comprehensive perioperative risk assessment. However, the specificity of this cut-off value was found to be 48%, indicating that approximately half of the patients without poor outcomes could be classified as false positives.

These findings reveal that IPI has a high sensitivity and low specificity profile. Such a marker may have clinical value as a screening tool, especially for the early identification of high-risk patients. However, the high false positive rate due to low specificity may limit the use of IPI as a sole decision-making tool and suggest that it should be supported by more specific tests.

Although postoperative adverse events following CAS are predominantly influenced by mechanical and procedural factors—including plaque manipulation, embolic phenomena, and perioperative hypoperfusion—systemic inflammation may contribute indirectly by reflecting overall patient vulnerability and impaired physiological reserve. In this context, the IPI should not be interpreted as a mechanistic driver of postoperative complications, but rather as a composite marker of systemic inflammatory and nutritional status that may complement traditional risk assessment strategies.

Furthermore, while more specific biomarkers of plaque-related inflammation (such as hs-CRP, matrix metalloproteinases, or lipoprotein-associated phospholipase A_2) may provide greater biological specificity, these parameters are not routinely measured in standard clinical practice. The use of IPI, derived from widely available laboratory parameters, therefore represents a pragmatic approach to preoperative risk stratification rather than a substitute for plaque-specific inflammatory assessment.

The simplicity and cost-effectiveness of IPI, which is derived from routinely measured blood parameters, make it a practical tool in clinical practice. Identifying high-risk patients based on preoperative IPI values can enable proactive perioperative management strategies, such as intensive monitoring or the consideration of anti-inflammatory therapies in patients with high IPI.

This study has several limitations. First, its retrospective design introduces inherent biases, such as selection and information bias, which may affect the generalizability of the findings. Second, being a single-center study conducted in a tertiary referral hospital, the results may not be directly applicable to other populations or healthcare settings. Third, the inflammatory markers used to calculate the IPI, including CRP, NLR, and serum ALB, were derived from routine laboratory measurements, which may be subject to inter-laboratory variability. Fourth, the study focused exclusively on early (30-day) adverse outcomes, potentially overlooking the long-term prognostic value of IPI. Fifth, the exclusion of patients with active infections, malignancies, hematological or immunological disorders, and end-stage renal or hepatic diseases may limit the applicability of the findings to broader patient populations. Sixth, although multivariate analysis was used to adjust for potential confounding factors, the possibility of residual confounding cannot be completely ruled out. Finally, despite demonstrating high sensitivity, IPI had moderate specificity, leading to a substantial number of false positives, which limits its use as a standalone diagnostic tool. The relatively small number of adverse events limits the statistical power of multivariate analyses and raises the possibility of model overfitting. Therefore, the results of the regression analysis should be interpreted with caution and regarded as exploratory rather than definitive.

In this study, we demonstrated that higher preoperative IPI values were significantly associated with early adverse outcomes following CAS. Specifically, higher preoperative IPI values were associated with an increased risk of major CVE, MI, and 30-day mortality. Our findings suggest that IPI, a composite marker derived from routinely measured inflammatory parameters (CRP, NLR, and ALB), provides a simple and cost-effective tool for risk stratification in patients undergoing CAS. However, due to its moderate specificity, IPI may serve as a practical adjunctive biomarker for preoperative risk stratification and risk awareness, rather than a sole determinant of clinical decision-making. Further prospective multicenter studies with larger sample sizes are needed to validate these findings and explore the potential benefits of integrating IPI into clinical decision-making protocols.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the University of Health Sciences Türkiye, Bursa City Hospital Scientific Research Ethics Committee (approval number: 2025-2/6, date: 22.01.2025). The study was performed in accordance with the ethical principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Acknowledgments

We would like to thank Beytullah Kınabaş for his technical support.

Footnotes

Authorship Contributions

Concept: H.G., D.Ç.; Design: H.G., D.Ç.; Data Collection or Processing: H.G., D.Ç.; Analysis or Interpretation: H.G., D.Ç.; Literature Search: H.G., D.Ç.; Writing: H.G., D.Ç.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Bonati LH, Jansen O, de Borst GJ, Brown MM. Management of atherosclerotic extracranial carotid artery stenosis. Lancet Neurol. 2022;21:273-83. doi: 10.1016/S1474-4422(21)00359-8.
2. Howard DPJ, Gaziano L, Rothwell PM; Oxford Vascular Study. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. Lancet Neurol. 2021;20:193-202. doi: 10.1016/S1474-4422(20)30484-1. Erratum in: Lancet Neurol. 2021;20:e4. doi: 10.1016/S1474-4422(21)00076-4.
3. Rerkasem K, Rothwell PM. Systematic review of the operative risks of carotid endarterectomy for recently symptomatic stenosis in relation to the timing of surgery. Stroke. 2009;40:e564-72. doi: 10.1161/STROKEAHA.109.558528.
4. AbuRahma AF, Avgerinos ED, Chang RW, Darling RC, Duncan AA, Forbes TL, et al. Society for Vascular Surgery clinical practice guidelines for management of extracranial cerebrovascular disease. J Vasc Surg. 2022;75:4S-22S. doi: 10.1016/j.jvs.2021.04.073.
5. Cybulsky MI, Gimbrone MA Jr. Endothelial expression of a mononuclear leukocyte adhesion molecule during atherogenesis. Science. 1991;251:788-91. doi: 10.1126/science.1990440.
6. King AH, Schmaier AH, Harth KC, Kumins NH, Wong VL, Zidar DA, et al. Elevated neutrophil-lymphocyte ratio predicts mortality following elective endovascular aneurysm repair. J Vasc Surg. 2020;72:129-37. doi: 10.1016/j.jvs.2019.10.058.
7. Pinato DJ, Shiner RJ, Seckl MJ, Stebbing J, Sharma R, Mauri FA. Prognostic performance of inflammation-based prognostic indices in primary operable non-small cell lung cancer. Br J Cancer. 2014;110:1930-5. doi: 10.1038/bjc.2014.145.
8. Yuksel A, Velioglu Y, Korkmaz UTK, Deser SB, Topal D, Badem S, et al. Systemic immune-inflammation index for predicting poor outcome after carotid endarterectomy: a novel hematological marker. Vascular. 2024;32:565-72. doi: 10.1177/17085381221141476.
9. Casanova N, Diaz-Duran C, Nieto L, Llort C, Elosua R, Clara A. Predictive value of complete blood count-derived inflammatory markers for 5-year survival after carotid endarterectomy: implications for practice. Angiology. 2022;73:675-81. doi: 10.1177/00033197211067581.
10. Dirican N, Dirican A, Anar C, Atalay S, Ozturk O, Bircan A, et al. A new inflammatory prognostic index, based on C-reactive protein, the neutrophil to lymphocyte ratio and serum albumin is useful for predicting prognosis in non-small cell lung cancer cases. Asian Pac J Cancer Prev. 2016;17:5101-6. doi: 10.22034/APJCP.2016.17.12.5101.
11. Badem S, Pekcolaklar A. Inflammatory prognostic index predicts new-onset atrial fibrillation and mortality after on-pump coronary artery bypass grafting. Rev Assoc Med Bras (1992). 2023;69:e20230226. doi: 10.1590/1806-9282.20230226.

12. Badem S, Atasoy MS. Inflammatory prognostic index is a new predictive marker for perioperative mortality in patients undergoing type A aortic dissection surgery. Turk J Vasc Surg. 2025;34:25-32. DOI: 10.9739/tjvs.2024.12.060

13. North American Symptomatic Carotid Endarterectomy Trial Collaborators; Barnett HJM, Taylor DW, Haynes RB, Sackett DL, Peerless SJ, et al. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med. 1991;325:445-53. doi: 10.1056/NEJM199108153250701.

14. AbuRahma AF, Avgerinos ED, Chang RW, Darling RC, Duncan AA, Forbes TL, et al. The Society for Vascular Surgery implementation document for management of extracranial cerebrovascular disease. J Vasc Surg. 2022;75:26S-98S. doi: 10.1016/j.jvs.2021.04.074.

15. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005;352:1685-95. doi: 10.1056/NEJMra04343.

16. Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chan WL, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. Eur J Clin Invest. 2020;50:e13230. doi: 10.1111/eci.13230.

17. Niculescu R, Russu E, Arbănași EM, Kaller R, Arbănași EM, Melinte RM, et al. Carotid Plaque features and inflammatory biomarkers as predictors of restenosis and mortality following carotid endarterectomy. Int J Environ Res Public Health. 2022;19:13934. doi: 10.3390/ijerph192113934.

18. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation. 2002;105:1135-43. doi: 10.1161/hc0902.104353.

19. Zhou H, Wang A, Meng X, Lin J, Jiang Y, Jing J, et al. Low serum albumin levels predict poor outcome in patients with acute ischaemic stroke or transient ischaemic attack. Stroke Vasc Neurol. 2021;6:458-66. doi: 10.1136/svn-2020-000676.

20. Cai Z, He W, Zhuang FJ, Chen Y. The role of high high-sensitivity C-reactive protein levels at admission on poor prognosis after acute ischemic stroke. Int J Neurosci. 2019;129:423-9. doi: 10.1080/00207454.2018.1538139.

ORIGINAL ARTICLE

DOI: 10.4274/e-cvsi.2025.1926
Cardiovasc Surg Int 2026;13(1):20-26

CARDIOVASCULAR SURGERY AND INTERVENTIONS

Comparative evaluation of clinical, hematological, and echocardiographic parameters in NSTE-MI patients undergoing CABG versus PCI

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Received: September 09, 2025 **Accepted:** October 25, 2025 **Epub:** January 19, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Objectives: Non-ST segment elevation myocardial infarction (NSTE-MI) patients may be managed with either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). This study compares clinical, hematological, and echocardiographic characteristics between these two groups.

Patients and methods: We conducted a retrospective analysis of 120 NSTE-MI patients, with 60 undergoing CABG and 60 undergoing PCI. Demographic features, laboratory values, echocardiographic measurements, and angiographic SYNTAX scores were collected. Correlation analyses were performed using Spearman's method.

Results: The mean age was higher in the CABG group (64.9±11.1 *vs.* 62.2±11.5 years, p=0.254). Mean platelet volume (MPV), was 8.90±1.75 in the CABG group and 8.57±1.23 in the PCI group (p=0.347). Platelet count was slightly higher in the CABG group (232,583±74.3 *vs.* 225,816±54.5, p=0.927). Baseline ejection fraction (EF) was significantly higher in PCI patients (60.3±5.4 *vs.* 55.3±8.8, p=0.002), and the change in EF during hospitalization (ΔEF) was more pronounced in the CABG group (5.0 [3.0-9.5] *vs.* 1.0 [0.0-4.0], p<0.001). Peak troponin levels were higher in the CABG group (6418.8±11103.3 *vs.* 6135.3±9647.2, p=0.983). SYNTAX score was significantly greater in the CABG group (39.7±7.0 *vs.* 30.1±3.9, p<0.001). C-reactive protein levels were higher in CABG patients (19.5±3.9 *vs.* 16.5±2.4, p=0.937). Median neutrophil-to-lymphocyte (N/L) ratio was 2.5 *vs.* 2.2 (p=0.675). WBC counts were similar between groups (9.0×10^3 *vs.* 9.02×10^3, p=0.971). According to Spearman correlation analysis, MPV was positively correlated with ΔEF (r=0.259, p=0.005), while SYNTAX score was negatively correlated with baseline EF (r=-0.288, p=0.002). A positive correlation was observed between peak troponin and ΔEF (r=0.553, p<0.001), as well as between SYNTAX score and ΔEF (r=0.542, p<0.001). Additionally, N/L ratio was positively correlated with ΔEF (r=0.228, p=0.013).

Conclusion: CABG-treated NSTE-MI patients showed higher anatomical complexity and greater EF decline. Several correlations between hematological and functional parameters were identified.

Keywords: NSTE-MI, CABG, PCI, SYNTAX score, ejection fraction.

Non-ST-segment elevation myocardial infarction (NSTE-MI) represents a clinically significant form of acute coronary syndrome (ACS), encompassing a heterogeneous group of patients with varying degrees of myocardial ischemia and injury.[1] Unlike ST-segment elevation myocardial infarction (STEMI), NSTE-MI is not characterized by persistent ST-segment elevation on the electrocardiogram, but is nonetheless associated with elevated cardiac biomarkers indicative of myocardial necrosis.[2] It often reflects subtotal coronary artery obstruction or severe stenosis, and carries a considerable risk of short- and long-term adverse cardiovascular outcomes, especially in patients with extensive atherosclerosis, diabetes, or left ventricular dysfunction.[3]

Optimal management of NSTE-MI hinges on timely risk stratification and appropriate selection of a revascularization strategy. Both the European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend an early invasive approach for high-risk patients.[2,3] The choice between percutaneous coronary intervention (PCI) and coronary artery bypass

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Cite this article as: Aydın S, Ziaeitorbati M. Comparative evaluation of clinical, hematological, and echocardiographic parameters in NSTE-MI patients undergoing CABG versus PCI. Cardiovasc Surg Int. 2026;13(1):20-26

grafting (CABG), however, must be tailored to individual anatomical and clinical characteristics. PCI is typically favored due to its minimally invasive nature, faster recovery, and lower immediate procedural risk. Conversely, CABG is generally preferred in cases involving multivessel disease, left main involvement, or high SYNTAX scores, as it offers more comprehensive and durable revascularization.[4]

Although CABG is often reserved for patients with greater coronary complexity and worse baseline clinical status, several studies suggest that it may provide superior improvement in myocardial perfusion and left ventricular function compared to PCI, particularly in the presence of viable but ischemic myocardium. However, data comparing early changes in cardiac function following CABG versus PCI in NSTE-MI patients remain limited.[5]

Ejection fraction (EF) is a central measure of left ventricular systolic performance and a key prognostic marker in myocardial infarction. It is not a static parameter, and may improve after effective revascularization, especially in patients with hibernating or stunned myocardium. Therefore, evaluating not only the baseline EF but also its change during hospitalization (ΔEF) may provide valuable insights into myocardial recovery and the impact of the chosen revascularization strategy.[6]

In addition to imaging-based assessments, several hematological and inflammatory markers have emerged as potential indicators of disease severity and prognosis in ACSs. Parameters such as mean platelet volume (MPV), neutrophil-to-lymphocyte (N/L) ratio, white blood cell count (WBC), and high-sensitive C-reactive protein (CRP) are easily accessible through routine blood tests and may reflect both the thrombotic and inflammatory burden. These markers could offer supplementary prognostic value, particularly when interpreted alongside anatomical and functional data.[7-9]

In this context, the present study aimed to provide a comparative evaluation of NSTE-MI patients undergoing CABG or PCI by analyzing their clinical characteristics, hematological parameters, echocardiographic measurements, and angiographic complexity as assessed by the SYNTAX score. Particular attention was given to changes in EF during hospitalization and the potential relationships between laboratory markers and functional recovery. This integrated approach may contribute to a more nuanced understanding of how different revascularization strategies influence short-term cardiac outcomes in this diverse and high-risk patient population.

PATIENTS AND METHODS

Study Design and Setting

This was a retrospective, observational, single-center study conducted at a tertiary care academic hospital specializing in cardiovascular care. The study was designed to compare clinical, hematological, and echocardiographic outcomes in patients diagnosed with NSTE-MI who underwent either PCI or CABG during the same hospitalization period. Ethical approval for the study protocol was obtained from the Institutional Review Board of Bakırçay University Çiğli Training and Research Hospital (date: 23.09.2025, document number: KU.FR.09 no:1/1) and the research was conducted in accordance with the Declaration of Helsinki principles.

Study Population

A total of 120 patients with a confirmed diagnosis of NSTE-MI were included in the analysis. Patients were consecutively selected from electronic hospital records between January 2022 and December 2024. The diagnosis of NSTE-MI was established based on clinical symptoms (typically chest pain lasting >20 minutes), electrocardiographic findings (absence of persistent ST-segment elevation), and elevated cardiac biomarkers (specifically high-sensitivity troponin I levels exceeding the 99th percentile upper reference limit).

Patients were divided into two equal groups based on the revascularization strategy applied. The PCI group included those who underwent coronary angiography followed by PCI with stent implantation. In contrast, the CABG group consisted of patients who were evaluated by the heart team and referred for surgical revascularization due to anatomical complexity, multivessel disease, or other clinical considerations.

Inclusion and Exclusion Criteria

Patients aged 18 years or older with a confirmed diagnosis of NSTE-MI who underwent revascularization via either PCI or CABG during the index hospitalization were included in the study. Eligibility also required the availability of complete laboratory, echocardiographic, and angiographic data.

Patients were excluded if they had ST-segment elevation myocardial infarction (STEMI), presented with cardiogenic shock, had a history of prior CABG surgery, or were affected by active infection, systemic inflammatory disease, known hematologic disorders, or malignancy. Incomplete clinical records or missing echocardiographic data also constituted exclusion criteria.

Data Collection and Variables

All data were retrospectively collected from institutional digital medical records. The recorded and analyzed variables included demographic and clinical parameters such as age, sex, cardiovascular risk factors (including hypertension, diabetes mellitus, hyperlipidemia, and smoking), past medical history (prior myocardial infarction, heart failure, atrial fibrillation, and stroke), as well as presenting symptoms and the time interval from symptom onset to hospital admission.

Hematological and Inflammatory Parameters

Laboratory data were obtained from blood samples drawn within the first 6 hours of hospital admission, prior to revascularization, and included measurements of (MPV, fL), platelet count ($\times 10^9$/L), WBC count ($\times 10^3$/μL), N/L ratio, high-sensitivity C-reactive protein (hsCRP, mg/L), and peak high-sensitivity cardiac troponin I (ng/L).

Echocardiographic Evaluation

Transthoracic echocardiography (TTE) was performed for all patients upon admission and repeated prior to discharge using standard parasternal and apical views in accordance with American Society of Echocardiography guidelines. Left ventricular EF was calculated using the biplane Simpson's method.[10] The following variables were extracted: Baseline EF (%), EF at discharge (%), change in EF (ΔEF = discharge EF - baseline EF). All transthoracic echocardiographic examinations were performed using a GE Vivid E9 echocardiography system (GE Healthcare, Horten, Norway) by experienced cardiologists.

Coronary Angiography and SYNTAX Score

Selective coronary angiography was performed via the femoral approach using the Judkins technique and a General Electric Innova 3100 angiographic system (Buc Cedex, France). Multiple angiographic views were obtained to ensure optimal visualization of the coronary anatomy, including at least four projections for the left anterior descending and left circumflex arteries, and at least two projections for the right coronary artery. All angiographic recordings were stored in DICOM format on compact discs. Coronary angiograms and SYNTAX scores were independently assessed by two experienced interventional cardiologists who were blinded to the patients' clinical data; any discrepancies in scoring were resolved by consensus. In patients assigned to the PCI group, PCIs were performed by experienced operators. In the CABG group, surgical strategy and graft selection were determined based on the detailed angiographic findings. Coronary lesion complexity was evaluated using the SYNTAX scoring algorithm, which incorporates factors such as lesion location, bifurcation involvement, thrombus burden, calcification, and total occlusions. Treatment allocation was influenced by the SYNTAX score, with patients having a score of 33 or higher generally being directed toward CABG due to the greater anatomical complexity.[4]

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Kolmogorov-Smirnov test. Normally distributed continuous variables were presented as mean ± standard deviation (SD), while non-normally distributed variables were presented as median (interquartile range). Categorical variables were expressed as frequencies and percentages. Between-group comparisons were performed using appropriate statistical tests based on data distribution and type. The independent samples t-test was used for normally distributed continuous variables, while the Mann-Whitney U test was applied for non-normally distributed continuous variables. Categorical variables were compared using either the chi-square test or Fisher's exact test, as appropriate. To assess the relationships between selected hematological, echocardiographic, and angiographic parameters, Spearman's rank correlation coefficient (r) was employed. A two-tailed p-value of less than 0.05 was considered indicative of statistical significance in all analyses.

RESULTS

A total of 120 patients diagnosed with NSTE-MI were included in the study, comprising two equal groups: 60 patients underwent PCI, while the remaining 60 patients underwent CABG operation. The mean age of the entire cohort was 63.6±11.3 years, with the CABG group being slightly older (64.9±11.1 years) than the PCI group (62.2±11.5 years), although this difference did not reach statistical significance (p=0.254). Both groups were comparable in terms of sex distribution and cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, smoking status, and history of prior myocardial infarction, indicating that the baseline clinical profiles were relatively balanced.

Regarding hematological parameters, the MPV, a marker often associated with platelet reactivity and inflammation, was marginally higher in the CABG group (8.90±1.75 fL) compared to the PCI group (8.57±1.23 fL), but this difference was not statistically significant (p=0.347). Platelet counts were also slightly elevated in the CABG group (232.5±74.3×10^3/µL *vs.* 225.8±54.5×10^3/µL), yet without statistical significance (p=0.927). Similarly, CRP levels, a non-specific indicator of systemic inflammation, were higher in the CABG group (19.5±3.9 mg/L) than in the PCI group (16.5±2.4 mg/L), but this difference too was not significant (p=0.937). WBC counts were nearly identical in both groups (9.0×10^3/µL *vs.* 9.02×10^3/µL; p=0.971). Median neutrophil-to-lymphocyte (N/L) ratio, another emerging inflammatory marker, was slightly higher in the CABG group (2.5 *vs.* 2.2), although this did not differ significantly between interventions (p=0.675). These findings suggest that the systemic inflammatory and hematologic profiles at baseline were largely similar between patients selected for either revascularization strategy.

In contrast, significant differences emerged when angiographic complexity and echocardiographic findings were evaluated. The SYNTAX score, which quantifies the anatomical complexity and severity of coronary artery disease (CAD), was substantially higher in the CABG group (39.7±7.0) compared to the PCI group (30.1±3.9), with the difference being highly statistically significant (p<0.001). This confirms that patients selected for CABG had more diffuse, multivessel, and anatomically challenging disease. Interestingly, this anatomical severity translated into functional impairment: baseline left ventricular EF was significantly lower in the CABG group (55.3±8.8%) than in the PCI group (60.3±5.4%) (p=0.002), suggesting a greater degree of myocardial dysfunction at presentation among patients undergoing surgical revascularization. ROC curve analysis was performed to evaluate the predictive value of the SYNTAX score for guiding treatment strategy in patients with non-ST-elevation myocardial infarction (NSTEMI). As demonstrated in Figure 1, the SYNTAX score showed a significant ability to discriminate patients who underwent CABG operation. The optimal cut-off value was identified at 32.75, yielding a sensitivity of 88.3% and a specificity of 83.3%.

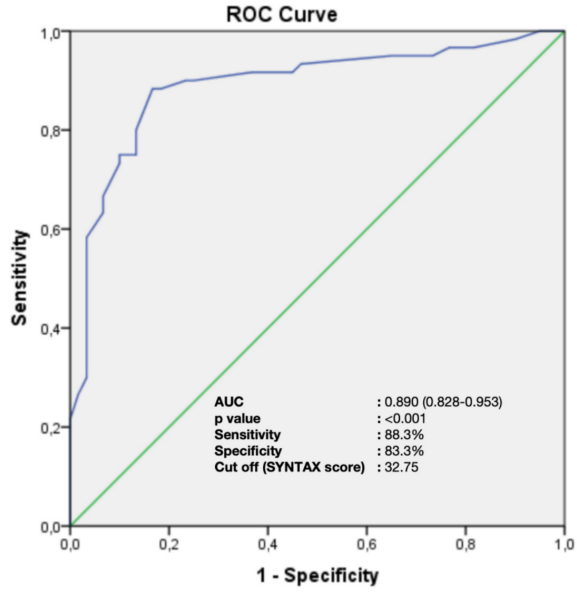

Figure 1. ROC curve analysis of SYNTAX score for predicting CABG selection in NSTEMI patients.
ROC: Receiver operating characteristic; CABG: Coronary artery bypass grafting; NSTEMI: Non–ST-elevation myocardial infarction; AUC: Area under the curve.

Despite this initial disadvantage in baseline EF, the CABG group demonstrated a notably greater improvement in EF during the course of hospitalization. The median (25^{th}-75^{th}) change in EF (ΔEF) was significantly higher in the CABG group (5.0 [3.0-9.5]) than in the PCI group (1.0 [0.0-4.0]) (p<0.001) (Figure 2). This finding indicates that patients who underwent CABG experienced a more robust functional recovery, likely attributable to more complete and anatomically comprehensive revascularization achieved via surgical grafting. These observations support the hypothesis that even in patients with lower baseline systolic function, surgical intervention may yield substantial gains in myocardial performance when the anatomical burden of disease is high. Table 1 presents the clinical and laboratory findings of patients with NSTEMI according to the applied treatment management.

Additional analysis revealed important correlations among the study parameters. A negative correlation was found between SYNTAX score and baseline EF (Spearman's r=-0.288, p=0.002), implying that patients with more complex coronary lesions tend to have more impaired ventricular function at the time of presentation. In contrast, SYNTAX score was strongly and positively correlated with ΔEF (r=0.542, p<0.001),

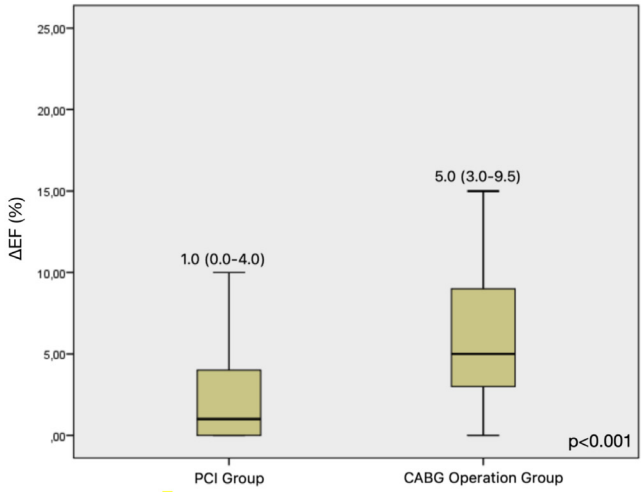

Figure 2. Comparison of ΔEF between PCI and CABG groups.
ΔEF: Change in ejection fraction; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; Statistical data were presented as median (25^{th}-75^{th}), and a p-value <0.05 was considered statistically significant.

suggesting that patients with greater anatomical disease burden derived greater benefit in terms of left ventricular function improvement after revascularization - an effect particularly pronounced in the CABG group.

Furthermore, peak troponin levels, while not significantly different between the groups (CABG: 6418.8±11,103.3 ng/L *vs.* PCI: 6135.3±9647.2 ng/L; p=0.983), demonstrated a robust positive correlation with ΔEF (r=0.553, p<0.001). This indicates that higher troponin release-typically associated with greater myocardial injury-was paradoxically linked to greater improvement in EF, possibly reflecting the recovery of stunned or hibernating myocardium after successful reperfusion.

Among hematological markers, MPV showed a significant positive correlation with ΔEF (r=0.259, p=0.005), suggesting a potential role for platelet activity in modulating myocardial recovery. Although high MPV values have been traditionally linked to worse cardiovascular outcomes, in this study, higher MPV may represent a physiological response to myocardial injury and repair processes rather than an exclusively prothrombotic state. Likewise, the N/L ratio, despite not differing significantly between groups, exhibited a statistically significant positive correlation with ΔEF (r=0.228, p=0.013), reinforcing the notion that systemic inflammatory activation during acute coronary events might be related to post-revascularization myocardial remodeling and recovery.

Collectively, these findings emphasize that patients selected for CABG, although presenting with more severe coronary disease and reduced baseline systolic function, benefited from more pronounced improvement in left ventricular performance following intervention. The data also suggest that beyond anatomical complexity, simple laboratory markers such as MPV and N/L ratio may carry independent prognostic information related to myocardial recovery. The consistent and significant correlations between SYNTAX score, troponin, MPV, and ΔEF strengthen the potential utility of combining clinical, anatomical, biochemical, and hematological data to guide therapeutic decision-making in NSTE-MI.

In the multivariate logistic regression analysis performed to identify independent predictors of undergoing CABG surgery, ΔEF (%) and SYNTAX score were found to be significant determinants. An increase in ΔEF was independently associated with higher odds of CABG (odds ratio [OR]: 1.908, 95% confidence interval [CI]: 1.354-2.689, p<0.001). Similarly, a higher SYNTAX score significantly predicted CABG referral (OR: 1.388, 95% CI: 1.197-1.610, p<0.001) (Table 2).

Table 1. Baseline characteristics according to treatment management in patients with non–ST-elevation myocardial infarction

Treatment group	PCI group, n=60	CABG group, n=60	p-value
Age	62.17±11.50	64.87±11.11	0.254
Gender (male,%)	70.0	71.7	0.841
SYNTAX score	30.17±3.88	39.72±7.03	**p<0.001***
Δ-EF (%)	2.27±2.39	6.58±4.88	**p<0.001***
CRP (mg/dL)	16.52±24.88	19.46±38.93	0.937
MPV (fL)	8.57±1.24	8.91±1.76	0.347
Neu/L ratio	4.27±5.83	3.68±3.15	0.675
Platelet count (×10^3/μL)	225.82±54.48	232.58±74.34	0.927
Troponin level (ng/L)	6135.32±9647.26	6418.77±11103.32	0.983

PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; CRP: C-reactive protein; MPV: Mean platelet volume; Neu/L: Neutrophil-to-lymphocyte ratio.

Table 2. Multivariate logistic regression analysis for predictors of CABG operation

	p-value	OR	95% CI
Gender (male)	0.408	1.865	0.426-8.166
Troponin level	0.001	1.000	1.000-1.000
Baseline EF (%)	0.258	1.075	0.948-1.219
ΔEF (%)	<0.001	1.908	1.354-2.689
Age	0.113	1.051	0.988-1.119
SYNTAX score	<0.001	1.388	1.197-1.610

ΔEF: Change in ejection fraction; CABG: Coronary artery bypass grafting; CI: Confidence interval; OR: Odds ratio.

DISCUSSION

This study provides a comparative analysis of NSTE-MI patients who underwent either PCI or CABG operation, focusing on hematological markers, angiographic complexity, and echocardiographic outcomes. Our findings reveal that although patients treated with CABG had a significantly higher anatomical disease burden and lower baseline EF, they exhibited greater improvement in EF (ΔEF) during hospitalization. These results underscore the functional benefits of surgical revascularization in patients with more extensive CAD, and highlight the prognostic value of integrating hematological and anatomical indices into clinical decision-making.

Our data showed that the SYNTAX score, a validated index of coronary complexity was significantly higher in the CABG group, suggesting that patients selected for surgery had more anatomically diffuse or multivessel disease. This finding aligns with the current ESC and ACC/AHA guidelines, which recommend CABG in patients with high SYNTAX scores and diabetes, or in those with complex multivessel disease, as it is associated with lower long-term mortality and major adverse cardiovascular events compared to PCI.[2-4]

Despite having significantly lower baseline EF, CABG patients demonstrated a more pronounced improvement in EF during hospitalization. This observation may partly reflect the selection of patients with viable or hibernating myocardium who are more likely to recover function once adequate perfusion is restored, rather than the surgical technique itself. The more complete revascularization typically achieved with CABG - especially in cases involving chronic total occlusions or diffuse atherosclerosis-could also contribute to this finding. Similar trends have been noted in previous studies, where postoperative EF gains were associated with myocardial viability and restoration of blood flow rather than a direct effect of the revascularization modality itself.[11-13] One of the key innovations of our study is the assessment of hematological markers specifically MPV and N/L ratio in relation to functional cardiac recovery. MPV, a well-established surrogate marker for platelet activation and systemic inflammation, was found to be positively associated with changes in ΔEF. This finding appears to contrast with the majority of existing literature, in which elevated MPV levels have been consistently associated with adverse cardiovascular outcomes, including increased risk of myocardial infarction, heart failure, and mortality.[14-16] However, emerging evidence suggests that, particularly in the setting of ACSs, transient elevations in MPV may not solely reflect a prothrombotic state but could also indicate dynamic hematological changes secondary to reperfusion, inflammatory resolution, or hemodilution post-CABG.[17] Therefore, rather than implying a causal relationship, our observation may reflect a context-dependent response associated with perioperative physiological adaptation and recovery. Similarly, the N/L ratio—an easily obtainable marker of systemic inflammation and stress—was also found to correlate with ΔEF in our study. This association should be interpreted cautiously, as fluctuations in N/L ratio may represent not only inflammatory activation but also subsequent resolution or normalization of immune balance after revascularization.[18] These observations align with reports suggesting that temporal changes in N/L ratio can provide insight into both the extent of injury and the trajectory of recovery in ACSs.[19] In contrast to previous studies where elevated MPV and N/L ratio were linked to adverse outcomes, our findings suggest a context-dependent association between these hematological markers and functional cardiac recovery (ΔEF) after revascularization. While Khan et al.[11] demonstrated that CABG offers superior long-term outcomes compared to PCI in patients with left ventricular systolic dysfunction, their analysis did not specifically address short-term improvements in EF. Conversely, Soetisna et al.[12] reported a significant postoperative increase in EF among patients with baseline EF <35%, attributing this improvement to recovery of hibernating myocardium following complete revascularization. Taken together, our study complements these findings by introducing an additional dimension suggesting that perioperative hematological and inflammatory dynamics may serve as surrogate indicators of myocardial repair and adaptive recovery after CABG.

The inverse correlation between SYNTAX score and baseline EF suggests that more complex coronary disease is associated with reduced left ventricular function at presentation.[20] This is biologically plausible, as greater atherosclerotic burden leads to more ischemic myocardium and impaired systolic performance. However, the strong positive correlation between SYNTAX score and ΔEF may seem contradictory. A potential explanation is that patients with low baseline EF and extensive disease may have more viable myocardium that can recover once complete revascularization is achieved, particularly through CABG. The correlation between peak troponin levels and ΔEF further supports this interpretation in our study. Higher troponin levels, while typically associated with more severe myocardial necrosis, may also indicate a larger area of reversible ischemia, particularly in non-transmural infarctions. In such scenarios, prompt and complete revascularization could salvage myocardium and improve contractile function.[21]

Our results suggest that CABG may offer superior short-term functional outcomes in selected NSTE-MI patients, especially those with high SYNTAX scores and impaired baseline EF. Moreover, simple hematological markers such as MPV and N/L ratio may help identify patients who are more likely to experience meaningful improvement in myocardial function after revascularization. These parameters are inexpensive, routinely available, and could be incorporated into clinical risk models.

This study has several limitations. First, it was conducted in a single-center with a retrospective design, which may introduce selection bias and precludes causal inferences. Second, the study was non-randomized, and potential confounding factors could not be fully controlled. Third, long-term follow-up data were not available; therefore, we could not evaluate outcomes such as survival, rehospitalization, or recurrent ischemia. In particular, the absence of extended follow-up limits our ability to determine whether the observed improvement in ΔEF is independently associated with mortality or hospital readmission.

Fourth, ΔEF was measured only during hospitalization and may not accurately represent sustained functional recovery. Fifth, advanced imaging modalities such as myocardial strain analysis or viability studies were not performed, which could have provided additional mechanistic insights into myocardial recovery. Despite these limitations, our study offers a multidimensional perspective on the interplay between anatomical complexity, hematological markers, and cardiac function, thereby contributing to the growing body of evidence supporting individualized revascularization strategies in NSTE-MI.

In NSTE-MI, CABG patients exhibit greater angiographic disease burden but benefit from significant improvement in cardiac function. Integration of MPV, N/L ratio, and SYNTAX score into clinical practice may refine risk stratification and inform revascularization decisions. Further prospective studies are warranted to validate these associations.

Ethics

Ethics Committee Approval: Ethical approval for the study protocol was obtained from the Institutional Review Board of Bakırçay University Çiğli Training and Research Hospital (date: 23.09.2025, document number: KU.FR.09 no:1/1) and the research was conducted in accordance with the Declaration of Helsinki principles.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: S.A.; Design: S.A.; Data Collection or Processing: S.A., M.Z.; Analysis or Interpretation: S.A., M.Z.; Literature Search: S.A.; Writing: S.A., M.Z.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Mitsis A, Gragnano F. Myocardial infarction with and without ST-segment elevation: a contemporary reappraisal of similarities and differences. Curr Cardiol Rev. 2021;17:e230421189013. doi: 10.2174/1573403X16999201210195702.
2. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023;44:3720-826. doi: 10.1093/eurheartj/ehad191. Erratum in: Eur Heart J. 2024;45:1145. doi: 10.1093/eurheartj/ehad870.
3. Rao SV, O'Donoghue ML, Ruel M, Rab T, Tamis-Holland JE, Alexander JH, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2025;151:e771-862. doi: 10.1161/CIR.0000000000001309. Erratum in: Circulation. 2025;151:e865. doi: 10.1161/CIR.0000000000001328. Erratum in: Circulation. 2025;151:e1098. doi: 10.1161/CIR.0000000000001346. Erratum in: Circulation. 2025;152:e402. doi: 10.1161/CIR.0000000000001397.
4. Yang H, Zhang L, Xu CH. Use of the SYNTAX score II to predict mortality in interventional cardiology: a systematic review and meta-analysis. Medicine (Baltimore). 2019;98:e14043. doi: 10.1097/MD.0000000000014043.
5. Arjomandi Rad A, Tserioti E, Magouliotis DE, Vardanyan R, Samiotis IV, Skoularigis J, et al. Assessment of myocardial viability in ischemic cardiomyopathy with reduced left ventricular function undergoing coronary artery bypass grafting. Clin Cardiol. 2024;47:e24307. doi: 10.1002/clc.24307.
6. Katsi V, Georgiopoulos G, Laina A, Koutli E, Parissis J, Tsioufis C, et al. Left ventricular ejection fraction as therapeutic target: is it the ideal marker? Heart Fail Rev. 2017;22:641-55. doi: 10.1007/s10741-017-9624-5.
7. Ekici B, Erkan AF, Alhan A, Sayın I, Aylı M, Töre HF. Is mean platelet volume associated with the angiographic severity of coronary artery disease? Kardiol Pol. 2013;71:832-8. doi: 10.5603/KP.2013.0195.
8. Tanındı A, Erkan AF, Ekici B, Alhan A, Töre HF. Neutrophil to lymphocyte ratio is associated with more extensive, severe and complex coronary artery disease and impaired myocardial perfusion. Turk Kardiyol Dern Ars. 2014;42:125-30. doi: 10.5543/tkda.2014.18949.
9. Bouzidi N, Messaoud MB, Maatouk F, Gamra H, Ferchichi S. Relationship between high sensitivity C-reactive protein and angiographic severity of coronary artery disease. J Geriatr Cardiol. 2020;17:256-63. doi: 10.11909/j.issn.1671-5411.2020.05.003.
10. Cheitlin MD, Armstrong WF, Aurigemma GP, Beller GA, Bierman FZ, Davis JL, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: summary article. a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). J Am Soc Echocardiogr. 2003;16:1091-110. doi: 10.1016/S0894-7317(03)00685-0.
11. Khan MR, Kayani WT, Pelton J, Ansari A, Paniagua D, Khalid U, et al. Coronary artery bypass grafting versus percutaneous coronary intervention in patients with left ventricular systolic dysfunction. Cardiovasc Drugs Ther. 2021;35:575-85. doi: 10.1007/s10557-020-07063-0.
12. Soetisna TW, Nugraha WA, Rokim FS, Namretta L, Pradana MBR, Utama D. Complete revascularization showed a better cardiac function improvement in patients with low ejection fraction. Heart Surg Forum. 2022;25:E425-8. doi: 10.1532/hsf.4123.
13. Machiraju VR. Complete surgical myocardial revascularization: shift of paradigm of the gold standard in the current era. Vessel Plus. 2019;3:25. http://dx.doi.org/10.20517/2574-1209.2019.008
14. Yazici HU, Poyraz F, Sen N, Tavil Y, Turfan M, Tulmaç M, et al. Relationship between mean platelet volume and left ventricular systolic function in patients with metabolic syndrome and ST-elevation myocardial infarction. Clin Invest Med. 2011;34:E330. doi: 10.25011/cim.v34i6.15892.
15. Kandis H, Ozhan H, Ordu S, Erden I, Caglar O, Basar C, et al. The prognostic value of mean platelet volume in decompensated heart failure. Emerg Med J. 2011;28:575-8. doi: 10.1136/emj.2009.088401.

16. Hendra TJ, Oswald GA, Yudkin JS. Increased mean platelet volume after acute myocardial infarction relates to diabetes and to cardiac failure. Diabetes Res Clin Pract. 1988;5:63-9. doi: 10.1016/s0168-8227(88)80080-9.

17. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des. 2011;17:47-58. doi: 10.2174/138161211795049804.

18. Chuang SY, Hsu YC, Chou KW, Chang KS, Wong CH, Hsu YH, et al. RETRACTED: neutrophil-lymphocyte ratio as a predictor of cerebral small vessel disease in a geriatric community: the I-lan longitudinal aging study. Brain Sci. 2023;13:1087. doi: 10.3390/brainsci13071087. Retraction in: Brain Sci. 2025;15:1246. doi: 10.3390/brainsci15111246.

19. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol. 2008;102:653-7. doi: 10.1016/j.amjcard.2008.05.006.

20. Węgiel M, Dziewierz A, Jarosz P, Bartuś S, Surdacki A, Rakowski T. SYNTAX score as a predictor of left ventricular function in patients after myocardial infarction. Kardiol Pol. 2025;83:891-3. doi: 10.33963/v.phj.105652.

21. White HD. Pathobiology of troponin elevations: do elevations occur with myocardial ischemia as well as necrosis? J Am Coll Cardiol. 2011;57:2406-8. doi: 10.1016/j.jacc.2011.01.029. Erratum in: J Am Coll Cardiol. 2011;58:2356.

ORIGINAL ARTICLE

DOI: 10.4274/e-cvsi.2025.2060
Cardiovasc Surg Int 2026;13(1):27-30

CARDIOVASCULAR SURGERY AND INTERVENTIONS

Contrast-induced nephropathy after endovascular interventions in peripheral artery disease: Predictive value of the Mehran score

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Received: September 12, 2025 **Accepted:** September 20, 2025 **Epub:** February 24, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Objectives: To evaluate the predictive value of the Mehran score for contrast-induced nephropathy (CIN) following peripheral transcatheter angioplasty (PTA) in patients with peripheral artery disease (PAD).

Patients and methods: We retrospectively analyzed 103 patients who underwent PTA at our center between January 2020 and July 2024. The Mehran score was calculated for all patients meeting inclusion criteria. CIN was defined as an absolute increase in serum creatinine ≥0.5 mg/dL or a relative increase ≥25% within 48-72 hours post-procedure. Receiver operating characteristic analysis was used to assess the predictive value of the Mehran score. Multivariate logistic regression identified independent risk factors for CIN.

Results: CIN occurred in 19 patients (18.4%). Patients who developed CIN received significantly higher contrast volumes ($p<0.05$). The optimal Mehran score cut-off for predicting CIN was 11.2, with an area under the curve of 0.712 (95% confidence interval: 0.612-0.826; sensitivity 69%, specificity 73%). Independent predictors of CIN included advanced age, diabetes mellitus, higher contrast volume, baseline glomerular filtration rate, and the Mehran score. Patients with CIN had longer hospital stays (3.9±1.7 *vs.* 1.9±0.7 days, $p=0.002$) and higher amputation rates (10.6% *vs.* 2.9%, $p=0.004$).

Conclusion: The Mehran score is a valuable tool for predicting CIN after PTA in PAD patients. Risk stratification using the Mehran score may guide preventive strategies, although PAD-specific models incorporating additional parameters are warranted.

Keywords: Peripheral artery disease, percutaneous transcatheter angioplasty, Mehran score, contrast-induced nephropathy.

Peripheral artery disease (PAD) is a prevalent vascular disorder associated with increased morbidity and mortality, with higher prevalence in older populations.[1,2] Untreated PAD carries a high risk of complications. Endovascular interventions, such as peripheral transcatheter angioplasty (PTA), have become preferred treatment options due to lower complication rates compared with medical therapy or surgical revascularization.[3]

However, contrast media used during these procedures may precipitate contrast-induced nephropathy (CIN), defined as an increase in serum creatinine ≥0.5 mg/dL or ≥25% within 48-72 hours post-procedure. CIN occurs more frequently in elderly or comorbid patients.[4-7]

Risk factors for CIN include advanced age, pre-existing renal impairment, diabetes mellitus (DM), anemia, heart failure, hemodynamic instability, and high contrast volume. The Mehran score, developed to predict post-coronary intervention CIN, incorporates both clinical and procedural parameters, including hypotension, intra-aortic balloon pump requirement, congestive heart failure, chronic kidney disease, diabetes, age >75 years, anemia, and contrast volume.[7,8]

The predictive value of the Mehran score in PAD patients undergoing PTA has not been extensively evaluated. This study aimed to assess the utility of the Mehran score for predicting CIN after PTA in this population.

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Cite this article as: Gürses E. Contrast-induced nephropathy after endovascular interventions in peripheral artery disease: predictive value of the Mehran score. Cardiovasc Surg Int. 2026;13(1):27-30

PATIENTS AND METHODS

Study Design and Population

This retrospective, single-center cohort study was conducted with Local Ethics Committee of İzmir Bakırçay University (decision no: 1839, approval no: 2487, date: 07.11.2024) approval in accordance with the Declaration of Helsinki. Patients ≥18 years old who underwent PTA for PAD between January 2020 and July 2024 were included. Due to the retrospective design of the study, the requirement for written informed consent was waived.

Inclusion Criteria

Documented serum creatinine within 7 days prior to PTA and at least one post-procedure creatinine measurement within 48-72 hours.

Exclusion Criteria

End-stage renal disease on dialysis, acute kidney injury (AKI) at baseline, regular use of nephrotoxic medications (e.g., non-steroidal anti-inflammatory drugs), or incomplete clinical/laboratory data.

Demographic, clinical, and procedural data—including age, sex, body mass index, comorbidities (DM, hypertension, congestive heart failure, anemia, chronic kidney disease), procedure type, contrast type and volume, procedure duration, and hemodynamic parameters—were obtained from electronic medical records.

Mehran Score Calculation

The Mehran score was calculated using pre- and intra-procedural clinical and procedural variables. Patients were categorized into low (0-5), moderate (6-10), high (11-15), and very high (≥16) risk groups.

Definition of CIN

CIN was defined as an increase in serum creatinine ≥0.5 mg/dL or ≥25% within 48-72 hours post-PTA. For sensitivity analysis, KDIGO-AKI criteria were also applied.

Endpoints

The primary endpoint was CIN development. Secondary endpoints included hospital length of stay, acute dialysis requirement, and 30-day and 1-year all-cause mortality.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median (interquartile range) and compared using Student's t-test or Mann-Whitney U test. Categorical variables were expressed as frequencies (%) and compared using the chi-square test. Receiver operating characteristic (ROC) analysis determined the predictive value of the Mehran score for CIN. Variables with $p<0.10$ in univariate analysis or clinical relevance were included in multivariate logistic regression to identify independent CIN predictors. Statistical significance was set at $p<0.05$.

RESULTS

A total of 103 patients were included (mean age 62.6±10.1 years; 71% male). Comorbidities included smoking (74.7%), DM (55.3%), hypertension (52.4%), and chronic kidney disease (14.6%). The incidence of CIN was 18.4% (n=19), with a mean Mehran score of 8.9±2.1 (Table 1).

Mean procedure duration was 41.3±17.7 minutes, mean contrast volume was 141.7±41.3 mL, and mean hospital stay was 2.1±0.8 days.

Patients who developed CIN had longer hospital stays (3.9±1.7 *vs.* 1.9±0.7 days, p=0.002) and higher amputation rates (10.6% *vs.* 2.9%, p=0.004). Baseline glomerular filtration rate (GFR) was significantly lower in the CIN group (p=0.026). ROC analysis showed an area under the curve (AUC) of 0.712 (95% confidence interval [CI]: 0.612-0.826; sensitivity 69%, specificity 73%), with an optimal Mehran score cut-off of 11.2. Multivariate analysis identified anemia, high contrast volume, DM, baseline GFR, baseline creatinine, and Mehran score as independent predictors of CIN (Table 2). ROC curve analysis demonstrated that the Mehran score had good predictive accuracy for CIN (AUC: 0.712), as shown in Figure 1.

Table 1. General characteristics of the study population

	CIN (n=19)	NKF (n=84)	p-value
Age,years	64.5±9.9	62.2±10.7	0.568
Male gender, %	13 (68.4%)	61 (72.6%)	0.212
Systolic BP, mmHg	128.8±17.4	129.6±18.3	0.656
Diastolic BP, mmHg	74.7±13.5	81.4±19.9	0.046*
Diabetes mellitus, %	14 (73.6%)	43 (51.1%)	0.012*
Hypertension, %	13 (68.4%)	41 (48.8%)	0.008*
CAD, %	9 (47.3%)	27 (32.1%)	0.032*
CKD, %	5 (26.3%)	10 (11.9%)	0.062
Iliac-femoral, %	2 (10.5%)	11 (13.1%)	0.468
SFA,%	11 (57.8%)	53 (63.1%)	0.282
BTK, %	5 (26.3%)	20 (23.8%)	0.404
LVEF, %	52.5±8.8	56.2±9.2	0.108
Creatinine (baseline), mg/dL	1.29±0.28	1.12±0.24	0.044*
GFR, mg/dL/1.73 m^2	57±10.2	68±13.1	0.002*
Mehran score	11.5±3.5	9.8±2.8	0.001*
Hemoglobin conf, mg/dL	11.7±2.7	12.6±2.4	0.033*
Contrast volume, mL	204±48	174±33	<0.001*
In-hospital stay, days	3.9±1.7	1.8±0.9	<0.001*
Mortality, 1 year	2 (10.5%)	4 (4.7%)	0.256
BARC >2 bleeding, %	2 (10.5%)	6 (7.1%)	0.542

*: p<0.05 was considered statistically significant; BARC: Bleeding academic research consortium; BP: Blood pressure; BTK: Below the knee; CAD: Coronary artery disease; CIN: Contrast induced nephropathy; GFR: Glomerular filtration rate; LVEF: Left ventricle ejection fraction; NKF: Normal kidney function; SFA: Superficial femoral artery.

Table 2. Univariate and multivariate analysis of contrast induced nephropathy predictors

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Age	1.2 (0.4-1.6)	0.042	ns	ns
Contrast volume	3.3 (1.6-6.1)	<0.001	2.2 (1.2-3.5)	<0.001*
GFR	4.2 (2.0-6.9)	<0.001	2.5 (1.7-3.6)	<0.001*
Baseline creatinine	2.1 (1.1-3.8)	0.004	1.5 (0.9-2.9)	0.030*
Mehran score	2.7 (1.4-4.9)	<0.001	1.8 (1.1-3.2)	0.007*
DM	1.8 (0.9-3.3)	0.014	1.2 (0.6-2.2)	0.049*
Anemia	1.9 (0.7-3.7)	0.008	1.2 (0.8-2.0)	0.041*
LVEF	1.1 (0.3-1.8)	0.048	ns	ns

*: p<0.05 was considered statistically significant; CI: Confidence interval; DM: Diabetes mellitus; GFR: Glomerular filtration rate; LVEF: Left ventricle ejection fraction.

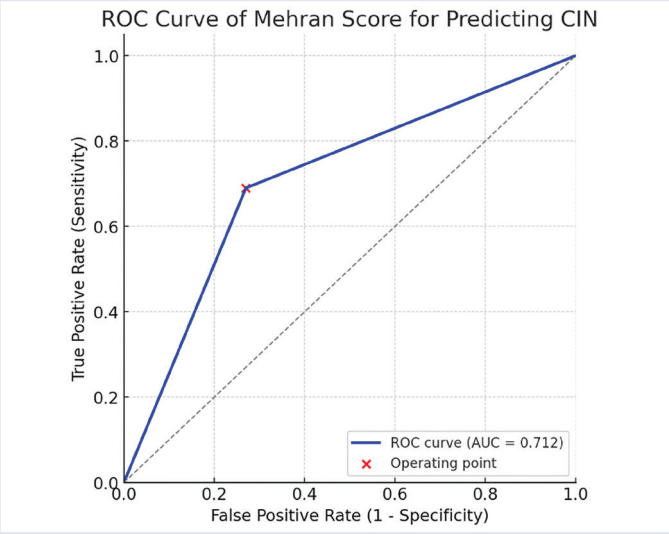

Figure 1. The ROC curve of the Mehran score predicting the development of contrast-induced nephropathy. (AUC; 0.712, sensitivity 69%; specificity 73%)

AUC: Area under the curve; ROC: Receiver operating characteristic; CIN: Contrast-induced nephropathy.

DISCUSSION

In this cohort of PAD patients undergoing PTA, CIN incidence was 18.4%, consistent with previously reported rates of 10-30%. The Mehran score demonstrated significant predictive value, with a cut-off of 11.2 (AUC 0.712), aligning with prior studies in coronary interventions and TAVI procedures.[8-10]

CIN is primarily attributed to contrast-induced renal toxicity and ischemia, with patient-related factors (age, DM, heart failure, impaired renal function) and procedural factors (contrast volume, hemodynamic instability) contributing to risk. In our study, CIN patients had higher prevalence of DM, reduced left ventricle ejection fraction (LVEF), and lower baseline renal function. PAD patients often have high rates of DM, smoking, and concomitant renal and coronary disease, potentially explaining increased heart failure prevalence and poorer outcomes.[8,10-13]

Higher contrast volume was associated with CIN, while procedure-related hypotension or blood loss was not significantly associated. Lower hemoglobin levels were observed in the CIN group. CIN remains a leading cause of hospital-acquired renal failure.[14-16] Post-procedural renal dysfunction has been linked to increased morbidity and mortality, although one-year mortality was not statistically different in our cohort. Amputation rates were higher in the CIN group, likely reflecting higher comorbidity burden.

In this study, the incidence of CIN was 18.4%, and affected patients experienced prolonged hospitalization, higher amputation rates, and worse baseline renal function. ROC analysis identified a Mehran score cut-off of 11.2 with good predictive accuracy, while multivariate analysis confirmed anemia, high contrast volume, DM, baseline GFR, creatinine, and Mehran score as independent predictors of CIN. These findings are consistent with previous reports highlighting the prognostic impact of mo difiable risk factors and validated risk scores in predicting CIN after cardiac and transcatheter interventions.[7,17-19] Early identification of high-risk patients and optimization of preventable risk factors remain crucial to improve outcomes.

Consistent with previous studies, Karakişi et al.[20] reported that the incidence of AKI following coronary artery bypass grafting was 7.6%, with previous myocardial infarction and postoperative creatinine increase as independent predictors of AKI. Similarly, Yurdam et al.[21] demonstrated that in patients undergoing PCI for chronic total occlusion, higher contrast volume, elevated blood glucose levels, reduced baseline renal function, and lower left ventricular ejection fraction were independent predictors of CIN. These findings underscore the importance of careful pre-procedural risk assessment and optimization of modifiable factors to minimize CIN incidence.

The Mehran score is a validated tool for predicting CIN and future adverse outcomes after percutaneous interventions. In our study, anemia, DM, baseline GFR, baseline creatinine, contrast volume, and Mehran score independently predicted CIN. These findings support its utility in risk stratification for PAD patients undergoing PTA. Preventive strategies—including contrast minimization and pre-procedural intravenous hydration—should be considered in high-risk patients.

Given the high prevalence of diabetes, smoking, and chronic kidney disease in PAD patients, the application of established coronary risk models such as the Mehran score may require recalibration or modification for peripheral interventions. Future multicenter studies with larger cohorts are needed to develop PAD-specific CIN risk models incorporating procedural complexity and lesion characteristics.

This study is limited by its retrospective, single-center design, small sample size, variability in hydration protocols, heterogeneity in contrast type and volume, and incomplete long-term renal follow-up. The Mehran score is a valuable tool for predicting CIN in PAD patients undergoing endovascular interventions. While it can guide risk stratification and preventive strategies, PAD-specific risk models incorporating additional parameters are warranted.

Ethics

Ethics Committee Approval: This retrospective, single-center cohort study was conducted with Local Ethics Committee of İzmir Bakırçay University (decision no: 1839, approval no: 2487, date: 07.11.2024) approval in accordance with the Declaration of Helsinki.

Informed Consent: Due to the retrospective design of the study, the requirement for written informed consent was waived.

Footnotes

Financial Disclosure: The author declared that this study received no financial support.

REFERENCES

1. Dua A, Lee CJ. Epidemiology of peripheral arterial disease and critical limb ischemia. Tech Vasc Interv Radiol. 2016;19:91-5. doi: 10.1053/j.tvir.2016.04.001.
2. Morley RL, Sharma A, Horsch AD, Hinchliffe RJ. Peripheral artery disease. BMJ. 2018;360:j5842. doi: 10.1136/bmj.j5842.
3. Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, et al. Global vascular guidelines on the management of chronic limbthreatening ischemia. Eur J Vasc Endovasc Surg. 2019;58:S1-109.e33. doi: 10.1016/j.ejvs.2019.05.006. Erratum in: Eur J Vasc Endovasc Surg. 2020;59:492-3. doi: 10.1016/j.ejvs.2019.11.025. Erratum in: Eur J Vasc Endovasc Surg. 2020;60:158-9. doi: 10.1016/j.ejvs.2020.04.033.
4. Liu KD, Yang J, Tan TC, Glidden DV, Zheng S, Pravoverov L, et al. Risk factors for recurrent acute kidney injury in a large population-based cohort. Am J Kidney Dis. 2019;73:163-73. doi: 10.1053/j.ajkd.2018.08.008.
5. Saratzis A, Harrison S, Barratt J, Sayers RD, Sarafidis PA, Bown MJ. Intervention associated acute kidney injury and long-term cardiovascular outcomes. Am J Nephrol. 2015;42:285-94. doi: 10.1159/000440986.
6. Sigterman TA, Krasznai AG, Snoeijs MG, Heijboer R, Schurink GW, Bouwman LH. Contrast induced nephropathy and long-term renal decline after percutaneous transluminal angioplasty for symptomatic peripheral arterial disease. Eur J Vasc Endovasc Surg. 2016;51:386-93. doi: 10.1016/j.ejvs.2015.08.023.
7. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int Suppl. 2006;S11-5. doi: 10.1038/sj.ki.5000368.
8. Dangas G, Iakovou I, Nikolsky E, Aymong ED, Mintz GS, Kipshidze NN, et al. Contrast-induced nephropathy after percutaneous coronary interventions in relation to chronic kidney disease and hemodynamic variables. Am J Cardiol. 2005;95:13-9. doi: 10.1016/j.amjcard.2004.08.056.
9. Zungur M, Gul I, Tastan A, Damar E, Tavli T. Predictive value of the Mehran score for contrast-induced nephropathy after transcatheter aortic valve implantation in patients with aortic stenosis. Cardiorenal Med. 2016;6:279-88. doi: 10.1159/000443936.
10. Gul I, Zungur M, Tastan A, Okur FF, Damar E, Uyar S, et al. The importance of contrast volume/glomerular filtration rate ratio in contrast-induced nephropathy patients after transcatheter aortic valve implantation. Cardiorenal Med. 2015;5:31-9. doi: 10.1159/000369943.
11. Hayashida K, Bouvier E, Lefèvre T, Hovasse T, Morice MC, Chevalier B, et al. Impact of CT-guided valve sizing on post-procedural aortic regurgitation in transcatheter aortic valve implantation. EuroIntervention. 2012;8:546-55. doi: 10.4244/EIJV8I5A85.
12. Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med. 1998;104:343-8. doi: 10.1016/s0002-9343(98)00058-8.
13. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130:461-70. doi: 10.7326/0003-4819-130-6-199903160-00002.
14. Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol. 2004;44:1393-9. doi: 10.1016/j.jacc.2004.06.068.
15. Wi J, Ko YG, Shin DH, Kim JS, Kim BK, Choi D, et al. Prediction of contrast-induced nephropathy with persistent renal dysfunction and adverse long-term outcomes in patients with acute myocardial infarction using the Mehran risk score. Clin Cardiol. 2013;36:46-53. doi: 10.1002/clc.22060.
16. Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis. 2002;39:930-6. doi: 10.1053/ajkd.2002.32766.
17. Karkouti K, Wijeysundera DN, Yau TM, Callum JL, Cheng DC, Crowther M, et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. Circulation. 2009;119:495-502. doi: 10.1161/CIRCULATIONAHA.108.786913.
18. Elhmidi Y, Bleiziffer S, Piazza N, Hutter A, Opitz A, Hettich I, et al. Incidence and predictors of acute kidney injury in patients undergoing transcatheter aortic valve implantation. Am Heart J. 2011;161:735-9. doi: 10.1016/j.ahj.2011.01.009.
19. Bagur R, Webb JG, Nietlispach F, Dumont E, De Larochellière R, Doyle D, et al. Acute kidney injury following transcatheter aortic valve implantation: predictive factors, prognostic value, and comparison with surgical aortic valve replacement. Eur Heart J. 2010;31:865-74. doi: 10.1093/eurheartj/ehp552.
20. Karakişi SO, Ergene Ş, Hemşinli D, Küçüker ŞA. Our early and mid-term results for endovascular repair of abdominal aortic aneurysms. Turk Gogus Kalp Damar Cerrahisi Derg. 2019;27:29-34. doi: 10.5606/tgkdc.dergisi.2019.16328.
21. Yurdam FS, Demir Y, Bakır EO, Başkurt AA. Predictors of contrast nephropathy after percutaneous intervention of chronic total occlusion in patients with chronic coronary syndrome: a single-center study. Cardiovasc Surg Int. 2025;12:97-102. DOI: 10.5606/e-cvsi.2023.1527.

ORIGINAL ARTICLE

DOI: 10.4274/e-cvsi.2025.2049
Cardiovasc Surg Int 2026;13(1):31-35

CARDIOVASCULAR SURGERY AND INTERVENTIONS

Electro-mechanical atrial and diastolic dysfunction in hypertensive patterns

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Received: September 09, 2025 **Accepted:** September 28, 2025 **Epub:** January 07, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Objectives: Diastolic dysfunction (DD) remains a diagnostic challenge, particularly in hypertensive patients with non-dipping blood pressure profiles. Emerging evidence suggests that left atrial reservoir strain (LASr) and P-wave dispersion (Pd) may serve as sensitive, non-invasive markers for subclinical atrial dysfunction.

Patients and methods: This single-center, retrospective observational study included 176 individuals: 76 non-dipper hypertensive, 65 dipper hypertensive, and 35 normotensive controls. All subjects underwent transthoracic echocardiography and 12-lead electrocardiogram (ECG). LASr was measured via speckle-tracking echocardiography, and Pd was manually calculated from standard ECGs.

Results: Non-dipper patients exhibited significantly reduced LASr (19.27±5.1%) and increased Pd (50.57±8.1 ms) compared to dippers and controls ($p<0.001$). A strong inverse correlation between LASr and Pd was observed. DD prevalence was highest among non-dippers (92.0%). Receiver operating characteristic analysis identified a Pd cut-off of 40.5 ms with 83% sensitivity, 80% specificity, and area under the curve 0.84 (95% confidence interval: 0.78-0.90) for detecting DD.

Conclusion: LASr and Pd provide complementary insights into atrial mechanical and electrical remodeling in hypertensive patients. Pd, as a simple and cost-effective ECG marker, may serve as a valuable tool for identifying DD, especially when advanced imaging is unavailable. These findings support integrating Pd into routine hypertensive patient evaluation.

Keywords: P-wave dispersion, left atrial reservoir strain, diastolic dysfunction, non-dipper hypertension, hypertension, ambulatory blood pressure monitoring.

Diastolic dysfunction (DD) remains a challenging clinical condition to diagnose, particularly in early stages and in the presence of chronic hemodynamic stressors such as hypertension.[1] The development of left ventricular hypertrophy and increased myocardial stiffness impairs ventricular relaxation and raises filling pressures. Over time, this leads to volume overload and structural remodeling of the left atrium, including progressive atrial fibrosis.[2] These histopathological changes disrupt both intra- and interatrial conduction continuity, ultimately resulting in atrial electromechanical discordance.[2-4] In recent years, the use of advanced imaging parameters—such as left atrial reservoir strain (LASr) measured via speckle-tracking echocardiography—has gained attention for non-invasive assessment of this complex process.[5,6]

In parallel, P-wave dispersion (Pd), a simple and widely accessible electrocardiogram (ECG) parameter, has emerged as a potential surrogate marker of atrial conduction heterogeneity.[7] In our study, we stratified hypertensive individuals into dipper and non-dipper groups and observed that the non-dipper blood pressure profile was associated with more pronounced DD. The significant and strong inverse correlation identified between LASr and Pd highlights the potential of Pd as a practical, low-cost marker that may reflect underlying atrial electromechanical imbalance. These findings suggest that Pd may serve as a complementary tool in the early detection and monitoring of DD, particularly in the hypertensive population.

PATIENTS AND METHODS

This single-center, retrospective observational study was conducted at the Department of Cardiology, Gazi University Faculty of Medicine, following approval by the University's Ethics Committee (approval no:

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Cite this article as: Seçkin Ö, Candemir M, Ünlü S. Electro-mechanical atrial and diastolic dysfunction in hypertensive patterns. Cardiovasc Surg Int. 2026;13(1):31-35

2025-1408, date: 04.08.2025). All procedures adhered to the ethical standards of the Declaration of Helsinki, and required institutional permissions were obtained prior to data access.

Patient Selection

A total of 176 individuals who underwent both transthoracic echocardiography and 12-lead electrocardiography between January 2022 and June 2025 were evaluated retrospectively. Based on 24-hour ambulatory blood pressure monitoring, patients with hypertension were classified into dipper (n=65) and non-dipper (n=76) groups, while a normotensive group was included as the control cohort (n=35). The dipping pattern was defined according to current hypertension guidelines, with a nocturnal systolic blood pressure decline of ≥10% accepted as dipper status.[8,9]

Inclusion criteria encompassed adults aged 18 or older with a diagnosis of essential hypertension for the patient groups, presence of normal sinus rhythm, and complete clinical, echocardiographic, and electrocardiographic records of acceptable quality. Patients were excluded if they had a history of atrial arrhythmias, moderate or severe valvular heart disease, reduced left ventricular systolic function (LVEF <50%), congenital heart disease, prior cardiac surgery, or suboptimal imaging quality.

Echocardiographic Evaluation

All echocardiographic assessments were conducted by experienced cardiologists using standard imaging protocols and a commercially available ultrasound machine (GE Vivid E95). The evaluation was carried out according to the 2016 guidelines from the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[10,11] DD was diagnosed when at least three of the following four parameters were abnormal: septal e' velocity <7 cm/s or lateral e' <10 cm/s, E/e' ratio >14, left atrial volume index (LAVI) >34 mL/m², or peak tricuspid regurgitation velocity (TR V_{max}) >2.8 m/s.[12]

Left Atrial Strain Analysis

LASr was assessed offline using two-dimensional speckle-tracking echocardiography. Apical four-chamber views were acquired at a frame rate between 60-90 fps, and endocardial borders were manually traced at end-systole using dedicated software (EchoPAC v206, GE Healthcare). LASr was defined as the peak positive longitudinal strain of the left atrium during ventricular systole. Measurements were performed by two independent observers blinded to clinical and ECG data.

Electrocardiographic Assessment

Standard 12-lead ECGs were recorded with a paper speed of 25 mm/s and calibration of 10 mm/mV, which corresponds to routine clinical practice. The ECGs were manually analyzed using handheld calipers and magnifying lenses by two experienced cardiologists blinded to the echocardiographic findings. P-wave duration was measured in all leads, from the onset of the P-wave (initial deflection from the isoelectric line) to the end (return to baseline). The maximum and minimum P-wave durations were identified, and Pd was calculated as their difference.[13] All measurements were repeated by both observers, and average values were used. A random sample of 30 ECGs was reanalyzed to assess intra- and inter-observer reproducibility. Agreement was quantified using the intraclass correlation coefficient (ICC), which demonstrated excellent reproducibility for Pd measurements (intra-observer ICC =0.93, inter-observer ICC =0.91).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 26.0. The Shapiro-Wilk test was used to determine data distribution. Continuous variables were presented as mean ± standard deviation or median with interquartile ranges, and analyzed using independent-samples t-test or Mann-Whitney U test where appropriate. Categorical data were expressed as frequencies and compared using the chi-square test. Correlations between Pd and LASr, as well as other echocardiographic parameters, were evaluated using Spearman or Pearson coefficients. Receiver operating characteristic (ROC) analysis was conducted to determine the optimal Pd cut-off for predicting DD. Statistical significance was set at a p-value <0.05.

RESULTS

A total of 176 individuals were included in the study, comprising 35 normotensive controls, 65 dipper hypertensive patients, and 76 non-dipper hypertensive patients. The three groups were similar in terms of age and sex distribution. Left ventricular ejection fraction was preserved in all groups, with no statistically significant difference observed (p=0.074). However, the left ventricular mass index progressively increased from the control group to the non-dipper group (88.5±9.3 *vs.* 101.4±10.6 *vs.* 112.8±12.2 g/m²; p<0.001) (Table 1).

Daytime and nighttime systolic blood pressures were significantly higher in both hypertensive groups compared to controls, with the highest values observed in the non-dipper group (daytime SBP: 145.5±10.1 mmHg; nighttime SBP: 139.2±9.3 mmHg; both p<0.001). Estimated glomerular filtration rate showed a modest but statistically significant decline in the non-dipper group compared to controls (76.1±12.4 *vs.* 84.2±10.7 mL/min/1.73 m²; p=0.022).

Diastolic function parameters revealed significant deterioration in the non-dipper group. E/A ratio, E velocity, and E/e' values were significantly elevated in this group (E/e': 20.71±3.1; p=0.004), while e' velocities were reduced (5.58±1.1 cm/s; p=0.021). Similarly, the LAVI and peak TR V_{max} were significantly higher in the non-dipper group (LAVI: 45.8±5.4 mL/m²; TR V_{max}: 3.50±0.27 m/s).

Left atrial strain analysis revealed a marked reduction in LASr among non-dippers (19.27±5.1%) compared to dippers (26.72±4.8%) and controls (32.22±4.5%), with a statistically significant difference (p=0.002). In parallel, Pd was significantly prolonged in the non-dipper group (50.57±8.1 ms), compared to both dipper patients (42.15±7.0 ms) and controls (35.70±6.6 ms) (p<0.001). DD was identified in 64.0% of dipper patients and 92.0% of non-dipper patients, while none of the control subjects met the diagnostic criteria (p=0.001) (Table 2).

A significant inverse correlation was observed between Pd and LASr, while positive correlations were noted between Pd and E/e', LAVI, and TR V_{max} (Table 3).

ROC analysis indicated that a Pd cut-off value of 40.5 ms predicted the presence of DD with 83% sensitivity and 80% specificity, yielding an area under the curve (AUC) of 0.84 (95% confidence interval: 0.78-0.90) (Figure 1).

Table 1. Baseline clinical and imaging characteristics of study participants

Parameter	Control (n=35)	Dipper (n=65)	Non-dipper (n=76)	p-value
Age (years), mean	58.9	58.9	61.9	0.065
Female, n (%)	16 (45.7%)	32 (49.2%)	40 (52.6%)	0.62
EF (%)	63.2±3.1	62.5±3.4	61.8±3.8	0.074
LVMI (g/m^2)	88.5±9.3	101.4±10.6	112.8±12.2	<0.001
Daytime SBP (mmHg)	121.6±7.4	138.9±8.6	145.5±10.1	<0.001
Nighttime SBP (mmHg)	111.4±6.5	121.8±6.9	139.2±9.3	<0.001
eGFR (mL/min/1.73 m^2)	84.2±10.7	79.5±11.1	76.1±12.4	0.022
E/A ratio	0.70±0.09	1.18±0.25	2.21±0.41	0.003
E (cm/s)	45.7±6.1	77.0±8.4	111.3±10.2	0.012
e' (cm/s)	8.07±1.0	6.33±1.2	5.58±1.1	0.021
E/e' ratio	5.78±1.1	12.62±2.3	20.71±3.1	0.004
LAVI (mL/m^2)	27.8±3.6	37.9±4.8	45.8±5.4	0.018
TR V_{max} (m/s)	2.43±0.22	3.00±0.24	3.50±0.27	0.047
LASr (%)	32.22±4.5	26.72±4.8	19.27±5.1	0.002
P-wave dispersion (ms)	35.70±6.6	42.15±7.0	50.57±8.1	<0.001
Diastolic dysfunction, n (%)	0 (0%)	42 (64%)	70 (92%)	0.001

Values are presented as mean ± standard deviation or number (percentage). P-values indicate comparisons among the three groups (control, dipper, and non-dipper) using One-Way ANOVA or chi-square test, as appropriate.
EF: Ejection fraction; LVMI: Left ventricular mass index; SBP: Systolic blood pressure; eGFR: Estimated glomerular filtration rate; E/A: Ratio of early (E) to late (A) mitral inflow velocity; e': Early diastolic mitral annular velocity; E/e': Ratio of mitral inflow velocity to mitral annular early diastolic velocity; LAVI: Left atrial volume index; TR V_{max}: Tricuspid regurgitation maximum velocity; LASr: Left atrial reservoir strain.

Table 2. Comparison of independent parameters according to the presence of diastolic dysfunction

Parameter	DD present (n=78)	DD absent (n=98)	p-value
P-wave dispersion (ms)	46.36±6.33	35.70±6.59	<0.001
LASr (%)	22.99±4.95	32.22±4.53	<0.001

Values are expressed as mean ± standard deviation. P-values indicate comparisons between patients with and without diastolic dysfunction. DD: Diastolic dysfunction; LASr: Left atrial reservoir strain.

Table 3. Correlation analysis between P-wave dispersion and echocardiographic parameters

Parameter	Spearman correlation	p-value
LASr (%)	-0.72	<0.001
E/e'	0.65	<0.001
LAVI (mL/m^2)	0.60	<0.001
TR V_{max} (m/s)	0.58	<0.001

Correlation coefficients were calculated using Spearman's rank correlation test.
LASr: Left atrial reservoir strain; E/e': Ratio of mitral inflow velocity to mitral annular early diastolic velocity; LAVI: Left atrial volume index; TR V_{max}: Tricuspid regurgitation maximum velocity.

Intra- and inter-observer reproducibility for Pd measurements was excellent, with ICC values of 0.93 and 0.91, respectively.

DISCUSSION

LASr and Pd have increasingly gained attention as sensitive and accessible markers for the detection of DD.[14] In our study, we demonstrated that patients with a non-dipping hypertension pattern exhibit significant alterations not only in hemodynamic parameters but also in atrial mechanical and electrophysiological properties, particularly reflected by reduced LASr and increased Pd values.

LASr, derived from speckle-tracking echocardiography, has emerged as a reliable non-invasive index of left atrial compliance and reservoir function. In a 2022 study by Miljković et al.,[1] a LASr cut-off of 24.27% was reported to predict DD with a sensitivity of 78.9% and specificity of 84.6%. In our cohort, non-dipper patients demonstrated a substantially lower average LASr value (19.27%, p=0.002), clearly indicating a greater impairment in atrial functional reserve compared to dipper and control groups. This supports the notion that LASr is not only a marker of DD itself, but also a sensitive indicator of the deleterious impact of altered circadian blood pressure rhythms on atrial performance.

Similarly, Pd—a measure of atrial conduction heterogeneity—was found to be significantly elevated in the non-dipper group and was positively correlated with the presence of DD. While Pd has traditionally been associated with arrhythmia risk, our findings suggest that it may also reflect the burden of diastolic pressure and atrial structural remodeling.[15] The mean Pd in non-dippers was 50.57 ms, a value approaching thresholds considered to be arrhythmogenic in prior

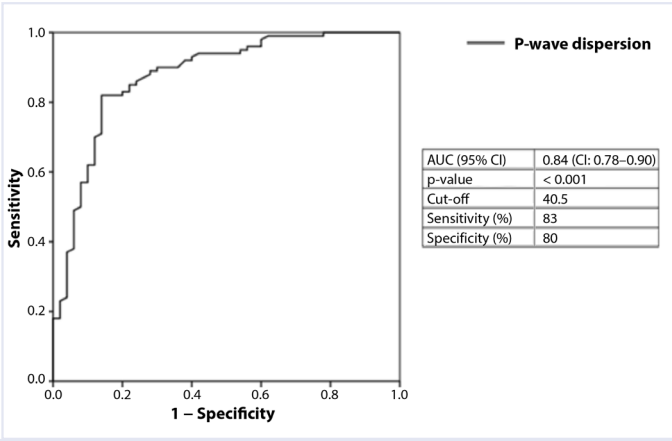

Figure 1. Receiver operating characteristic (ROC) curve of P-wave dispersion for predicting diastolic dysfunction.

ROC curve of P-wave dispersion for predicting diastolic dysfunction. The ROC analysis demonstrated the discriminatory performance of P-wave dispersion in identifying diastolic dysfunction. The area under the curve (AUC) was 0.84 (95% confidence interval [CI]: 0.78-0.90, p<0.001). A cut-off value of 40.5 ms yielded a sensitivity of 83% and a specificity of 80%.

studies. Importantly, we identified a Pd cut-off value of 40.5 ms, which demonstrated 83% sensitivity and 80% specificity in predicting DD, with an AUC of 0.84. This level of diagnostic performance supports the potential of Pd as a simple yet clinically valuable tool in the early identification of DD.

In our cohort, non-dipper hypertensive individuals tended to demonstrate lower LASr values, suggesting a potentially higher cardiovascular risk. Moreover, the inverse relationship observed between LASr and Pd may reflect underlying atrial electromechanical disintegration, a mechanism that could link elevated diastolic load to impaired atrial conduction.

In summary, this study emphasizes the diagnostic value of LASr and Pd as non-invasive, accessible, and complementary parameters for detecting subclinical DD.[16,17] The concurrent presence of reduced LASr and elevated Pd appears to reflect both mechanical and electrical atrial impairment, providing a more comprehensive assessment of atrial involvement in patients with disturbed circadian blood pressure profiles.[14] These findings not only highlight the importance of evaluating atrial function in hypertensive patients, but also suggest that Pd may serve as a valuable screening tool in clinical practice when echocardiographic modalities are limited or unavailable.

This study has several limitations that should be acknowledged. First, its retrospective and single-center design may limit the generalizability of the findings. Second, although Pd measurements were carefully performed using manual calipers on standard 12-lead ECGs, the potential for inter-observer variability remains, despite internal validation. Third, although Pd is traditionally associated with arrhythmic risk, our study did not evaluate arrhythmic outcomes such as atrial fibrillation or other supraventricular arrhythmias; this limitation should be addressed in future prospective studies. Finally, prospective, multi-center studies with larger sample sizes and long-term follow-up are needed to further validate these results.

In conclusion, our study demonstrates that both Pd and LASr are strongly associated with DD, particularly in patients with a non-dipping hypertensive profile. The identification of a Pd cut-off value of 40.5 ms with high diagnostic accuracy supports its potential as a simple, cost-effective screening parameter. When combined with LASr, Pd may offer a more comprehensive, non-invasive approach to assessing atrial function and subclinical DD in clinical practice. These findings contribute to the growing body of evidence supporting atrial-focused assessment in the evaluation of hypertensive patients at risk for diastolic impairment.

Ethics

Ethics Committee Approval: This single-center, retrospective observational study was conducted at the Department of Cardiology, Gazi University Faculty of Medicine, following approval by the University's Ethics Committee (approval no: 2025-1408, date: 04.08.2025).

Informed Consent: Due to the retrospective nature of the study, written informed consent was waived by the local ethics committee.

Footnotes

Authorship Contributions

Surgical Medical Practices: Ö.S.; Concept: Ö.S., M.C.; Design: Ö.S., M.C.; Data Collection or Processing: Ö.S., S.Ü.; Analysis or Interpretation: Ö.S., M.C.; Literature Search: Ö.S.; Writing: Ö.S.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Miljković T, Ilić A, Milovančev A, Bjelobrk M, Stefanović M, Stojšić-Milosavljević A, et al. Left atrial strain as a predictor of left ventricular diastolic dysfunction in patients with arterial hypertension. Medicina. 2022;58:156. doi: 10.3390/medicina58020156.
2. Ottosen CI, Nadruz W, Inciardi RM, Johansen ND, Fudim M, Biering-Sørensen T. Diastolic dysfunction in hypertension: a comprehensive review of pathophysiology, diagnosis, and treatment. Eur Heart J Cardiovasc Imaging. 2024;25:1525-36. doi: 10.1093/ehjci/jeae178.
3. Smiseth OA, Baron T, Marino PN, Marwick TH, Flachskampf FA. Imaging of the left atrium: pathophysiology insights and clinical utility. Eur Heart J Cardiovasc Imaging. 2021;23:2-13. doi: 10.1093/ehjci/jeab191.
4. Kockskaemper J, Pluteanu F. Left atrial myocardium in arterial hypertension. Cells. 2022;11:3157. doi: 10.3390/cells11193157.
5. Kupczyńska K, Mandoli GE, Cameli M, Kasprzak JD. Left atrial strain - a current clinical perspective. Kardiol Pol. 2021;79:955-64. doi: 10.33963/KP.a2021.0105.
6. Pathan F, D'Elia N, Nolan MT, Marwick TH, Negishi K. Normal ranges of left atrial strain by speckle-tracking echocardiography: a systematic review and meta-analysis. J Am Soc Echocardiogr. 2017;30:59-70.e8. doi: 10.1016/j.echo.2016.09.007.
7. Centurión OA, García LB, Marecos A, Tolares J, Scavenius K, Mino L, et al. P-wave morphology, amplitude, duration and dispersion in atrial arrhythmias. Journal of Cardiology and Therapeutics. 2018;6:1-6.

8. Aydin M, Ozeren A, Bilge M, Dursun A, Cam F, Elbey MA. Effects of dipper and non-dipper status of essential hypertension on left atrial mechanical functions. Int J Cardiol. 2004;96:419-24. doi: 10.1016/j.ijcard.2003.08.017.

9. Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, et al. The Japanese Society of hypertension guidelines for the management of hypertension (JSH 2019). Hypertens Res. 2019;42:1235-481. doi: 10.1038/s41440-019-0284-9.

10. Nauta JF, Hummel YM, van der Meer P, Lam CS, Voors AA, van Melle JP. Correlation with invasive left ventricular filling pressures and prognostic relevance of the echocardiographic diastolic parameters used in the 2016 ESC heart failure guidelines and in the 2016 ASE/EACVI recommendations: a systematic review in patients with heart failure with preserved ejection fraction. Eur J Heart Fail. 2018;20:1303-11. doi: 10.1002/ejhf.1220.

11. Almeida JG, Fontes-Carvalho R, Sampaio F, Ribeiro J, Bettencourt P, Flachskampf FA, et al. Impact of the 2016 ASE/EACVI recommendations on the prevalence of diastolic dysfunction in the general population. Eur Heart J Cardiovasc Imaging. 2018;19:380-6. doi: 10.1093/ehjci/jex252.

12. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2016;17:1321-60. doi: 10.1093/ehjci/jew082.

13. Okutucu S, Aytemir K, Oto A. P-wave dispersion: what we know till now? JRSM Cardiovasc Dis. 2016;5:2048004016639443. doi: 10.1177/2048004016639443.

14. Gunduz H, Binak E, Arinc H, Akdemir R, Ozhan H, Tamer A, et al. The relationship between P wave dispersion and diastolic dysfunction. Tex Heart Inst J. 2005;32:163.

15. Dilaveris PE, Gialafos JE. P-wave dispersion: a novel predictor of paroxysmal atrial fibrillation. Ann Noninvasive Electrocardiol. 2001;6:159-65. doi: 10.1111/j.1542-474x.2001.tb00101.x.

16. Carluccio E, Biagioli P, Mengoni A, Francesca Cerasa M, Lauciello R, Zuchi C, et al. Left atrial reservoir function and outcome in heart failure with reduced ejection fraction. Circ Cardiovasc Imaging. 2018;11:e007696. doi: 10.1161/CIRCIMAGING.118.007696.

17. Pérez-Riera AR, de Abreu LC, Barbosa-Barros R, Grindler J, Fernandes-Cardoso A, Baranchuk A. P-wave dispersion: an update. Indian Pacing Electrophysiol J. 2016;16:126-33. doi: 10.1016/j.ipej.2016.10.002.

ORIGINAL ARTICLE

CARDIOVASCULAR SURGERY AND INTERVENTIONS

DOI: 10.4274/e-cvsi.2025.2051
Cardiovasc Surg Int 2026;13(1):36-43

Prognostic value of the Naples prognostic score for predicting major adverse cardiac events and long-term outcomes in patients with NSTEMI

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Received: September 09, 2025 **Accepted:** October 25, 2025 **Epub:** January 14, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Objectives: The Naples prognostic score (NPS) is determined using four parameters: Serum albumin, total cholesterol, the neutrophil-to-lymphocyte ratio, and the lymphocyte-to-monocyte ratio. Since both inflammation and nutritional status have a critical impact on the onset and advancement of cardiovascular diseases, this score has been suggested as a beneficial prognostic tool. In this research, we sought to assess the predictive value of NPS, measured at the time of hospital admission, for major adverse cardiac events (MACE) and long-term outcomes in patients with non-ST-segment elevation myocardial infarction (NSTEMI).

Patients and methods: A cohort of 125 individuals with NSTEMI, identified between January 1 and June 1, 2019, was retrospectively evaluated. According to their NPS values, the cohort was stratified into two groups: Low NPS (0-2 points; n=73) and high NPS (3,4 points; n=52). Over an average follow-up period of 60 months, the manifestation of MACE and overall mortality was systematically documented.

Results: MACE was observed in 31 patients, with a markedly greater frequency in the high-NPS group (n=22; p<0.001). Long-term mortality occurred in 18 individuals, of whom 15 belonged to the high-NPS category (p<0.001). ROC curve analysis determined an optimal NPS threshold of 2.5 for predicting both MACE and overall mortality. Survival analysis using the Kaplan-Meier method revealed a considerable decrease in survival among patients with elevated NPS (p<0.001).

Conclusion: The NPS, which incorporates inflammatory and nutritional components, functions as a prognostic determinant of MACE and long-term mortality in NSTEMI cases.

Keywords: Naples prognostic score, non-ST-segment elevation myocardial infarction, major adverse cardiac events, risk stratification, mortality.

Acute myocardial infarction (AMI) continues to be a leading cause of death across the globe and represents a substantial public health burden. From a clinical perspective, AMI is categorized into two principal subtypes based on electrocardiographic results: ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI).[1] While both entities share similar pathophysiological mechanisms, they differ in clinical presentation, management strategies, and long-term prognosis. From a physiological standpoint, AMI occurs due to an abrupt disruption of coronary blood flow, which may present as complete occlusion—as typically seen in STEMI and occasionally in NSTEMI—or as partial obstruction, more frequently observed in NSTEMI.[2] This condition typically results from erosion or disruption of atherosclerotic plaques within the coronary arteries.[3] In recent years, the prevalence of NSTEMI has risen, primarily

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Cite this article as: Evsen A, Aktan A, Kılıç R, Güzel T, İldırımlı K, Özbek M, et al. Prognostic value of the Naples prognostic score for predicting major adverse cardiac events and long-term outcomes in patients with NSTEMI. Cardiovasc Surg Int. 2026;13(1):36-43

as a consequence of the extensive implementation of high-sensitivity troponin tests in patients with acute chest pain.[4] Risk stratification in individuals with NSTEMI may facilitate the detection of those at higher risk for adverse cardiac occurrences. Early recognition of high-risk patients enables the application of tailored interventions that may contribute to improved clinical outcomes. The Naples prognostic score (NPS), originally designed to estimate postoperative mortality within the cohort of colorectal cancer cases undergoing surgery,[5] integrates serum albumin concentration (Alb), total cholesterol (TC), neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR), thereby enabling a combined evaluation of malnutrition and inflammation. Given the critical role of inflammation and malnutrition in the pathophysiology of certain cardiovascular diseases, the prognostic potential of the NPS in these patient populations warrants further investigation.[6] Previous studies have assessed the predictive significance of the NPS in STEMI patients treated with primary percutaneous coronary intervention (PCI). Several studies have demonstrated that, in this patient population, the NPS is a an indicator of mortality risk during hospitalization and in long-term follow-up.[7,8] It is well established that, compared to STEMI patients, those with NSTEMI are generally older, have a greater burden of comorbidities, and exhibit a higher propensity for inflammation.[9] Studies investigating the NPS in this patient population remain limited in the literature.[10]

Aim: The objective of this research was to explore the prognostic utility of the NPS, obtained at admission, in forecasting major adverse cardiac events (MACE) and extended overall mortality in individuals with NSTEMI.

PATIENTS AND METHODS

Study Design and Population

In this retrospective, single-center observational study, 125 patients diagnosed with NSTEMI and treated with coronary angiography and/or PCI between January 1 and June 1, 2019, were included. Retrospective follow-up was conducted, with a mean duration of 60 months. Clinical data—including baseline characteristics, laboratory results, imaging parameters, and follow-up outcomes— were obtained from digital health records and patient charts of the hospital.

Exclusion Criteria

Patients with neoplastic diseases, those receiving chemotherapy, individuals with evidence of any acute or chronic inflammatory condition, active infection, recent (within the past 3 months) glucocorticoid therapy, or use of immunosuppressive agents were removed from the study cohort. Additional exclusion criteria included severe hepatic dysfunction (e.g., cirrhosis, chronic hepatitis), marked kidney impairment (described as glomerular filtration rate <30 mL/min/1.73 m² or chronic hemodialysis), severe anemia (hemoglobin <8 g/dL), cardiogenic shock requiring inotropic support or resulting in in-hospital mortality, severe valvular heart disease, and incomplete or missing data. A total of 62 patients meeting one or more of these criteria were excluded from the final analysis (Figure 1).

NPS Calculation and Risk Grouping

The NPS was determined using laboratory parameters measured following hospital admission. Scoring was performed according to previously established components and cut-off values reported in earlier studies:[5,7,8]

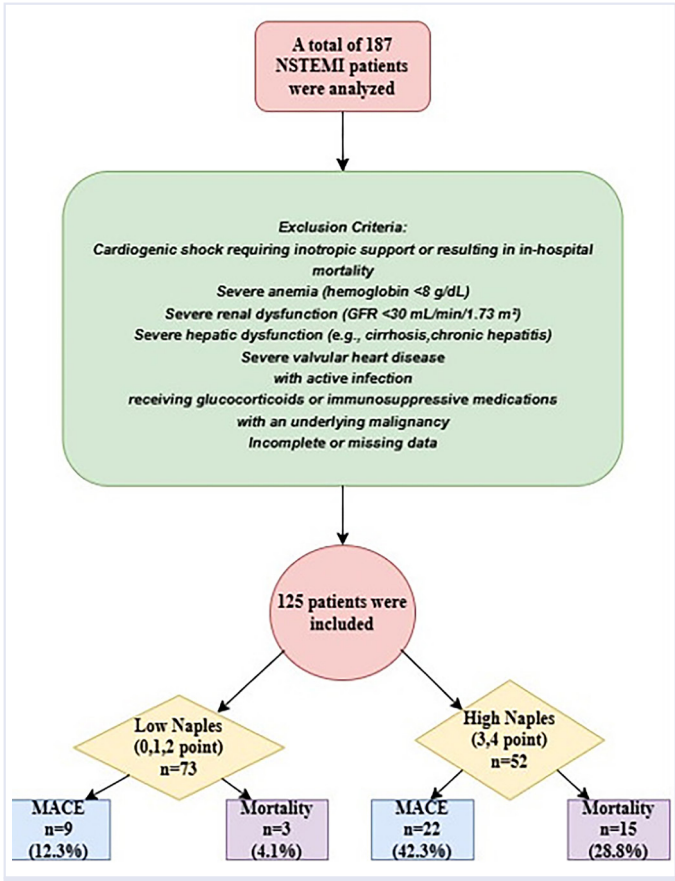

Figure 1. Study design flowchart.
MACE: Major adverse cardiac events; GFR: Glomerular filtration rate; NSTEMI: Non-ST-segment elevation myocardial infarction.

1) TC ≤180 mg/dL

2) Alb <4 g/dL

3) NLR >2.96

4) LMR ≤4.44.

One point was assigned to patients for each parameter meeting the specified thresholds (score range: 0-4). According to their total NPS, patients were classified into two groups: Low NPS (0, 1, or 2 points) and high NPS (3 or 4 points).

Study Endpoints

During the follow-up period, patients were evaluated based on the occurrence of MACE and overall long-term mortality. MACE was described as the combined of cardiovascular death, non-fatal myocardial infarction (MI), and non-fatal cerebrovascular events. Mortality information was retrieved from hospital archives and the national social security registry. Patients who experienced death during follow-up were classified according to their respective risk groups.

Ethical Consideration

The investigation was authorized by the Institutional Ethics Committee of Mardin Artuklu University (approval no: 2025/4-37, April 22, 2025), and the research was executed out in line with the principles of the Declaration of Helsinki (2024).

Statistical Analysis

Statistical analyses were executed using SPSS software, version 26.0 (Chicago, IL, USA). Descriptive statistics were applied to summarize baseline demographic and clinical variables. Normality of data distribution was evaluated using histograms and analytical tests. For group comparisons, continuous variables were examined with the autonomous samples t-test when normally distributed, and with the Mann-Whitney U test when distributional assumptions were not met. Categorical variables were examined using either the chi-square test or Fisher's exact test, as suitable. Data are demonstrated as mean ± standard deviation for normally distributed continuous variables, median (interquartile range) for non-normally distributed data, and percentages for categorical variables. The prognostic performance of the NPS in relation to MACE and long-term mortality was investigated using receiver operating characteristic (ROC) curve analysis. Cox proportional hazards regression, both univariate and multivariate, was applied to determine independent determinants of long-term outcomes. Survival probabilities were illustrated by Kaplan-Meier curves, and between-group differences were evaluated using the log-rank test. Statistical importance was set at a two-sided p-value <0.05.

RESULTS

After exclusions, the final study cohort consisted of 125 patients (Figure 1). Of these, 79 patients (63.2%) were male. Based on their NPS scores, Patients were grouped into two categories: Low NPS (0, 1, or 2 points; n=73) and High NPS (3 or 4 points; n=52). Demographic, laboratory, imaging, and procedural characteristics of the individuals are demonstrated in Table 1. There were no notable differences detected between the two groups regarding demographic, imaging, and procedural parameters. Among the laboratory variables, lymphocyte value (p<0.001) and Alb (p=0.005) were lower in the high NPS group, whereas neutrophil value (p<0.001) was higher (Table 1).

During the follow-up period, MACE was observed in 31 patients, 22 of whom belonged to the high NPS group (p<0.001). Additionally, overall death was observed in 18 patients, 15 of whom were in the high NPS group (p<0.001) (Table 1).

Cox regression analyses, both univariate and multivariate, were conducted to determine autonomous predictors of long-term mortality. The univariate evaluation demonstrated that ejection fraction (EF) (p=0.011) and Naples score (p=0.002) were markedly related to mortality. In the subsequent multivariate analysis, conducted to determine the most robust predictor among them, the Naples score remained independently and importantly related with long-term mortality (hazard ratio: 6.762; 95% confidence interval [CI]: 1.937-23.602; p=0.003) (Table 2).

The diagnostic accuracy of the Naples score in forecasting overall death and MACE was evaluated using ROC curve analyses. For all-cause mortality, the area under the curve (AUC) was 0.763 (95% CI: 0.639-0.888; p<0.001). A cut-off value of 2.5 for the Naples score demonstrated 83% sensitivity and 66% specificity in predicting long-term mortality (Figure 2A). For MACE prediction, the AUC was 0.730 (95% CI: 0.622-0.837; p<0.001), and a Naples score cut-off value of 2.5 yielded 71% sensitivity and 69% specificity (Figure 2B).

According to Kaplan-Meier estimates, individuals with higher Naples scores showed a markedly greater risk of long-term mortality throughout the 60-month follow-up period (Log-rank =14.382, p<0.001) (Figure 3A). Additionally, Kaplan-Meier analysis revealed a markedly higher incidence of MACE among patients with high Naples scores during the same follow-up period (Log-rank =14.216, p<0.001) (Figure 3B).

Mean Naples scores in patients with and without all-cause mortality were compared using a bar chart. The mean Naples score was 3.16 in the mortality group and 2.13 in the non-mortality group, with a statistically meaningful discrepancy between the two (p<0.001) (Figure 4).

DISCUSSION

This research was designed to investigate the prognostic utility of the NPS among NSTEMI patients, and the main findings are as follows:

1) Higher NPS values are positively linked to an elevated risk of MACE.

2) Higher NPS values are connected with an elevated risk of long-term overall death.

3) Following its use in cancer patients and certain cardiovascular disease populations, the NPS also offers a novel perspective in the risk classification of patients with NSTEMI.

The significance of the NPS lies in its components: It incorporates NLR and LMR as markers of inflammation, along with serum albumin and TC serving as markers of malnutrition, thereby enabling simultaneous assessment of both inflammatory status and nutritional condition.[5] The coexistence of inflammation and malnutrition may exacerbate adverse clinical outcomes and exert a synergistic effect on prognosis. Inflammation is a crucial factor in the initiation and progression of coronary artery disease (CAD). Contributing to the formation, progression, and rupture of atherosclerotic plaques, as well as promoting the activation of procoagulant pathways.[11] Neutrophils contribute significantly to atherosclerotic plaque instability. They are key regulators of the inflammatory response following MI, and elevated neutrophil counts have been connected with an elevated risk of cardiovascular mortality.[12] In contrast to neutrophils, lymphocytes play a regulatory role in inflammation and are therefore considered to have an anti-atherosclerotic effect. While anemia and thrombosis tend to exacerbate inflammation, lymphocytes may help attenuate its severity.[13] Thus, NLR has been identified as a biomarker of systemic inflammation and considered a possible predictor of both risk and prognosis in CAD.[14,15] NLR has been studied in many heart diseases before, and important findings have been discovered.[16,17]

As essential immune cells participating in the development of inflammation and atherosclerosis, lymphocytes and monocytes additionally affect the prognosis of MI patients. Low lymphocyte values and elevated monocyte values have been connected with adverse cardiovascular outcomes in patients with CAD.[18,19] Monocytes exhibit procoagulant properties in the setting of inflammation and MI, primarily through the formation of thrombotic monocyte-platelet aggregates.[20] Considering all these factors, it has been suggested that a composite inflammatory marker reflecting the balance between lymphocytes and monocytes may yield further value in cardiovascular risk analysis. Accordingly, the LMR has been regarded as a indicator of systemic inflammation. Numerous studies have revealed that the LMR is connected with the severity of cardiovascular disease and mortality.[21,22]

Table 1. Basic demographic and laboratory characteristics of the patients

Variables	Low Naples (n=73)	High Naples (n=52)	p-value
Gender (female), n (%)	29 (39.7)	17 (32.7)	0.422
Age, (years)	60.3±11.1	62.2±11.0	0.333
TIMI -1, n (%) -2, n (%) -3, n (%)	 20 (27.4) 38 (52.1) 15 (20.5)	 9 (17.3) 27 (51.9) 16 (30.8)	0.271
GRACE	1.97±0.72	2.03±0.62	0.598
Culprit artery, n (%) -LAD -Cx -RCA	 33 (45.2) 24 (32.9) 16 (21.9)	 23 (44.2) 15 (28.8) 14 (26.9)	0.786
HT, n (%)	50 (68.5)	38 (73.1)	0.580
DM, n (%)	19 (26.0)	10 (19.2)	0.375
Dyslipidemia, n (%)	20 (27.4)	18 (34.6)	0.387
CKD, n (%)	5 (6.8)	4 (7.7)	0.857
Smoking, n (%)	23 (31.5)	22 (42.3)	0.215
Previous MI, n (%)	11 (15.1)	7 (13.5)	0.801
Previous PCI, n (%)	13 (17.8)	5 (9.6)	0.198
Percutaneous coronary intervention, n (%)	50 (68.5)	42 (80.8)	0.125
LVEF, (%)	60 (55-60)	60 (53-60)	0.207
WBC, ($x10^3$/uL)	9.2 (8.1-10.8)	10.5 (8.3-12.5)	0.069
Lymphocyte, ($x10^3$/uL)	2.67±1.04	1.89±0.65	**<0.001**
Neutrophil, ($x10^3$/uL)	5.94±2.51	7.99±3.35	**<0.001**
Monocyte, ($x10^3$/uL)	0.68±0.29	0.72±0.23	0.387
Hemoglobin, (gr/L)	13.7±1.8	13.9±1.8	0.406
Platelet (10^3/uL)	259.3±57.0	260.2±87.0	0.948
Glucose, (mg/dL)	112 (101-210)	112 (99-136)	0.679
BUN, (mg/dL)	37.2±13.6	38.0±8.7	0.739
Creatinine, (mg/dL)	0.99±0.26	0.97±0.19	0.703
Albumin, (gr/dL)	3.76±0.48	3.54±0.40	**0.005**
CRP, (mg/dL)	6.4 (4.0-12.0)	8.2 (5.2-14.3)	0.137
Total cholesterol, (mg/dL)	175.8±34.4	189.2±41.1	0.065
HDL-C, (mg/dL)	36.1±7.1	36.4±6.5	0.844
LDL-C, (mg/dL)	108.3±27.2	117.4±36.6	0.143
Triglyceride, (mg/dL)	156.5±64.7	177.5±58.0	0.059
MACE, n (%)	9 (12.3)	22 (42.3)	**<0.001**
Mortality, n (%)	3 (4.1)	15 (28.8)	**<0.001**

TIMI: Thrombolysis in myocardial infarction; GRACE: The global registry of acute coronary events; LAD: Left anterior descending; Cx: Circumflex; RCA: Right coronary artery; HT: Hypertension; DM: Diabetes mellitus; CKD: Chronic kidney disease; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; LVEF: Left ventricular ejection fraction; WBC: White blood cells (10^6/L), BUN: Blood urea nitrogen; CRP: C-reactive protein; HDL-C: High-density lipoprotein cholesterol (mg/dL); LDL-C: Low-density lipoprotein cholesterol (mg/dL); MACE: Major adverse cardiac events. Data are presented as mean ± standard deviation or n (%). Statistical significance is considered at a p-value of less than 0.05.

In NSTEMI patients, nutritional status plays a crucial role in clinical outcomes; malnutrition is commonly observed and linked to higher rates of morbidity and mortality.[23] Malnutrition reflects not only inflammation but also frailty, a condition characterized by increased vulnerability and dysfunction across multiple physiological systems. Serum albumin levels can be used as a marker for assessing nutritional status. Hypoalbuminemia is not only a marker of malnutrition but also an indicator of systemic inflammation, resulting from the pro-inflammatory effects of different cytokines that suppress Albs.[24] Serum albumin levels reflect protein and calorie intake and indicate the degree of inflammation and disease severity during acute illness.[25] In addition, albumin plays critical roles in maintaining oncotic pressure, transporting various molecules, scavenging free radicals, and inhibiting platelet aggregation.[26] Hypoalbuminemia causes impaired endothelial function and increased blood viscosity.[27]

Table 2. Independent predictors of 5-year mortality in univariate and multivariate Cox regression analysis models

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	p	HR	95% CI	p
Age	1.038	0.996-1.083	0.080			
Gender	1.063	0.412-2.742	0.900			
DM	1.312	0.468-3.680	0.606			
HT	3.561	0.819-15.488	0.090			
LVEF	0.934	0.886-0.984	**0.011**	0.952	0.903-1.003	0.067
CRP	3.318	0.959-11.483	0.058			
Naples group	7.415	2.146-25.614	**0.002**	6.762	1.937-23.602	**0.003**

DM: Diabetes mellitus; HT: Hypertension; LVEF: Left ventricular ejection fraction; CRP: C-reactive protein; CI: Confidence interval; HR: Hazard ratio. Statistical significance is considered at a p-value of less than 0.05.

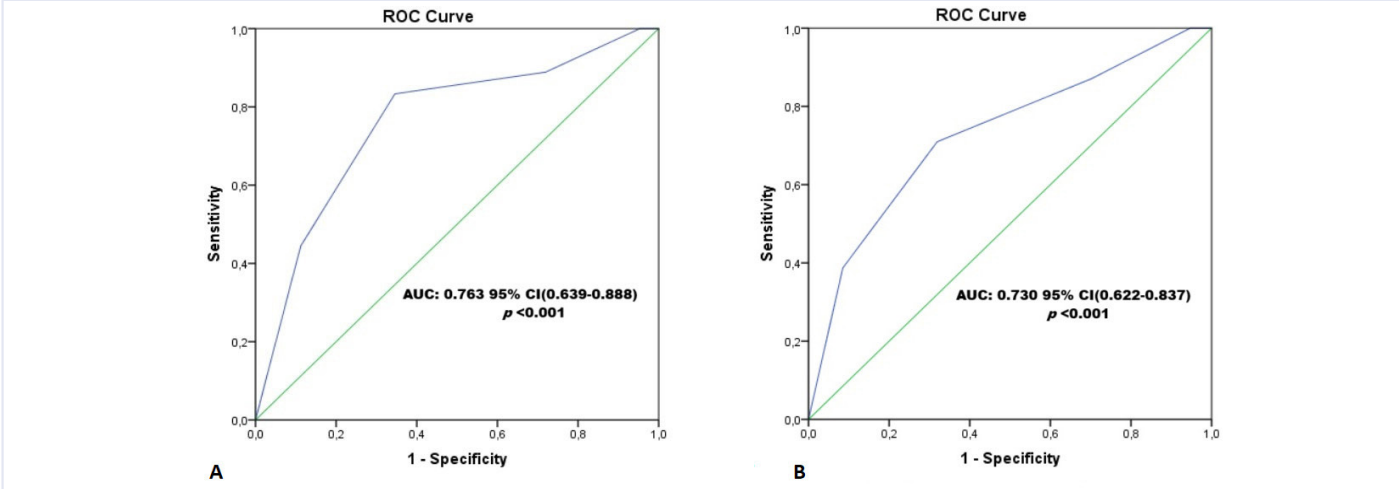

Figure 2. A. The ROC curve analysis of the Naples score, which predicts long-term mortality based on all causes, shows a cut-off value of 2.5, sensitivity of 83%, and specificity of 66%. **B.** The ROC curve analysis of the Naples score predicting MACE development, cut-off value 2.5, sensitivity 71%, and specificity 69%.

ROC: Receiver operating characteristic; AUC: Area under the curve; CI: Confidence interval; MACE: Major adverse cardiac events.

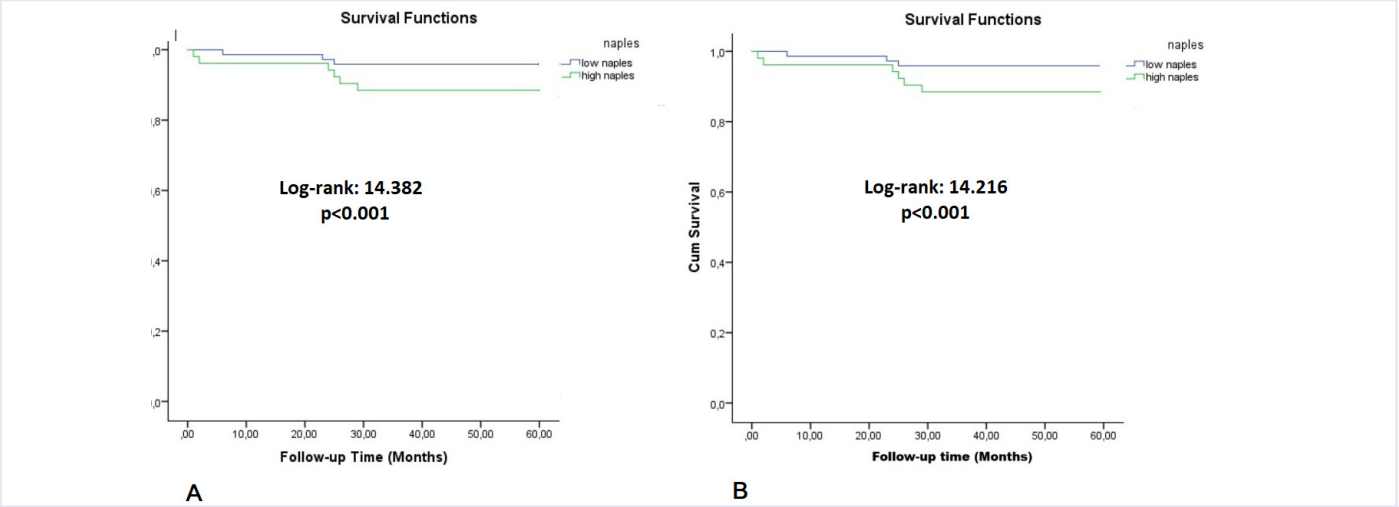

Figure 3. A. Kaplan-Meier survival curves comparing long-term mortality from all causes between groups with low and high Naples scores (log-rank test: 14.382, p<0.001) **B.** Kaplan-Meier survival curves showing MACE development between groups with low and high Naples scores (log-rank test: 14.216, p<0.001).

MACE: Major adverse cardiac events.

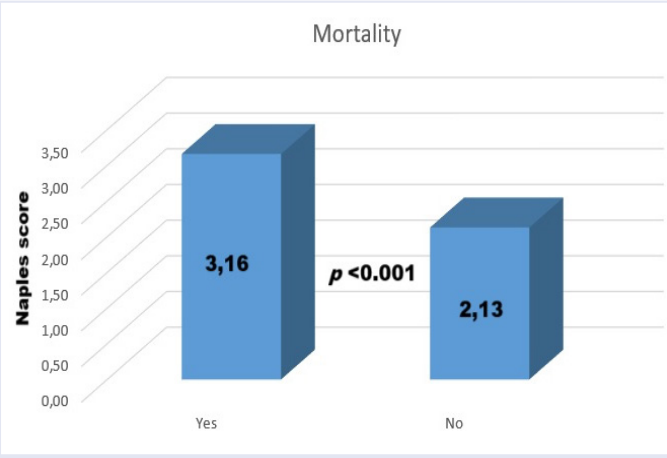

Figure 4. Naples score/mortality relationship: Bar chart showing average Naples scores in those with and without mortality.

It also contributes to poor survival rates by reflecting both systemic inflammation and malnutrition.[28] Indeed, a study by Bicciré et al.[29] demonstrated that low serum albumin values were connected to elevated death in patients with STEMI. Although hypercholesterolemia is a recognized major risk factor for CAD,[30] hypocholesterolemia—one of the components of the NPS—has been shown to be linked to elevated all-cause mortality in patients with CAD.[31] Although the underlying mechanism of this paradox remains unclear, several studies have showed an inverse correlation between TC values and mortality.[32,33]

Composed of lymphocyte count, serum albumin concentration, and TC values, the controlling nutritional status (CONUT) score has proven to be an effective means of determining nutritional status in hospitalized populations. The geriatric nutritional risk index (GNRI) is a practical and widely used scoring system for analyzing nutritional status and forecasting the risk of morbidity and mortality in older adults individuals. Both scores include the albumin parameter and are biomarkers specifically developed to assess nutritional status. Malnutrition, as evaluated by indices such as CONUT and GNRI, has been shown to be linked to higher rates of cardiovascular events and overall mortality.[34,35]

Validated risk assessment scores such as TIMI, GRACE, and CRUSADE have been developed to guide the handling of patients suffering from NSTEMI and the selection of optimal treatment strategies. While the TIMI and GRACE scores primarily emphasize myocardial ischemic injury and mortality, the CRUSADE score focuses on bleeding risk assessment. These prognostic tools have been validated in different populations and are widely recognized as valuable instruments for clinical practice. They provide essential guidance in estimating prognosis and shaping treatment strategies for patients presenting with NSTEMI.[36,37] Nonetheless, these scoring systems have limitations, as they do not incorporate critical factors such as inflammation and nutritional status, both of which substantially affect cardiovascular outcomes. As a composite marker of both inflammation and malnutrition, the NPS may offer a prognostic advantage over isolated biomarkers of either condition in patients with NSTEMI. This positions the NPS as a potentially more comprehensive indicator of long-term outcomes in this patient population.

In recent years, the NPS has been the subject of numerous studies as a prognostic indicator in cardiovascular diseases. Erdogan et al.[7] found that, in individuals with STEMI, the NPS was linked to both in-hospital and follow-up outcomes, concluding that it was an autonomous indicator of overall mortality and MACE. In line with these findings, Şaylık et al.[8] reported that the NPS may serve as a useful risk classification tool for evaluating long-term mortality in STEMI patients undergoing primary PCI. Birdal et al.[38] demonstrated that the NPS was markedly inversely related with EF and may aid in identifying high-risk patients with STEMI. These results indicate that the NPS could act as a valuable biomarker for risk classification and prognosis in STEMI patients. Furthermore, Aydın et al.[39] reported that the NPS is a promising separate marker of long-term mortality in individuals with heart failure. Moreover, studies on patients undergoing transcatheter aortic valve implantation for severe aortic stenosis have shown that the NPS is a valuable tool for predicting mortality and MACE.[40] These results suggest that the NPS may also be beneficial in patients with structural heart disease.

As evident from the literature, the prognostic value of the NPS has been showed in several cardiovascular diseases; however, its role in the context of NSTEMI remains particularly intriguing. In a study by Gitmez et al.,[10] the NPS was identified as a useful and autonomous indicator of one-year death in NSTEMI patients undergoing elective PCI. In this study, we sought to address the gap in the literature by examining the association of the NPS with both MACE and long-term all-cause mortality among NSTEMI patients. Our results indicate that the NPS could function as a practical risk marker for forecasting MACE and long-term mortality in this patient cohort.

The single-center and retrospective design of our study stands out as the main limitations. A further limitation of this study is the modest number of participants and clinical events, which may raise concerns regarding statistical power and model overfitting. This was due to the inclusion of consecutive patients within a specific time frame to minimize potential bias, along with the application of strict exclusion criteria to reduce the influence of confounding factors. Furthermore, the NPS was derived from laboratory data collected at hospital admission, without accounting for subsequent dynamic variations over time. Future wide-ranging, multi-institutional prospective research are needed to further clarify the predictive significance of the NPS in NSTEMI patients.

The NPS serves as an important and independent prognostic marker for both MACE and long-term overall mortality in NSTEMI patients. By integrating markers of both inflammation and malnutrition, the NPS enables a comprehensive approach to risk assessment. This makes it a more valuable tool compared to other biomarkers. Our findings support the potential utility of the NPS as an affordable and readily applicable tool to improve risk classification and support therapeutic management strategy in patients with NSTEMI.

Ethics

Ethics Committee Approval: The investigation was authorized by the Institutional Ethics Committee of Mardin Artuklu University (approval no: 2025/4-37, April 22, 2025), and the research was executed out in line with the principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: A.E., A.A., R.K., T.G., K.İ., M.Ö., M.Z.K.; Design: A.E., A.A., R.K., T.G., K.İ., M.Ö., M.Z.K.; Data Collection or Processing: A.E., A.A., R.K., T.G., K.İ., M.Ö., M.Z.K.; Analysis or Interpretation: A.E., A.A., R.K., T.G., K.İ., M.Ö., M.Z.K.; Literature Search: A.E., A.A., R.K., T.G., K.İ., M.Ö., M.Z.K.; Writing: A.E., A.A., R.K., T.G., K.İ., M.Ö., M.Z.K.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC guidelines for the management of acute coronary syndromes. Eur Heart J. 2023;44:3720-826. doi: 10.1093/eurheartj/ehad191. Erratum in: Eur Heart J. 2024;45:1145. doi: 10.1093/eurheartj/ehad870.
2. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Ganiats TG, Holmes DR, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64:e139-228. doi: 10.1016/j.jacc.2014.09.017. Erratum in: J Am Coll Cardiol. 2014;64:2713-4. Dosage error in article text.
3. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37:267-315. doi: 10.1093/eurheartj/ehv320.
4. Tziakas D, Chalikias G, Al-Lamee R, Kaski JC. Total coronary occlusion in non ST elevation myocardial infarction: time to change our practice? Int J Cardiol. 2021;329:1-8. doi: 10.1016/j.ijcard.2020.12.082.
5. Galizia G, Lieto E, Auricchio A, Cardella F, Mabilia A, Podzemny V, et al. Naples prognostic score, based on nutritional and inflammatory status, is an independent predictor of long-term outcome in patients undergoing surgery for colorectal cancer. Dis Colon Rectum. 2017;60:1273-84. doi: 10.1097/DCR.0000000000000961.
6. Liu J, Huang Z, Huang H, He Y, Yu Y, Chen G, et al. Malnutrition in patients with coronary artery disease: prevalence and mortality in a 46,485 Chinese cohort study. Nutr Metab Cardiovasc Dis. 2022;32:1186-94. doi: 10.1016/j.numecd.2021.12.023.
7. Erdogan A, Genc O, Ozkan E, Goksu MM, Ibisoglu E, Bilen MN, et al. Impact of Naples prognostic score at admission on in-hospital and follow-up outcomes among patients with ST-segment elevation myocardial infarction. Angiology. 2023;74:970-80. doi: 10.1177/00033197231151559.
8. Şaylık F, Çınar T, Selçuk M, Akbulut T, Hayıroğlu Mİ, Tanboğa İH. Evaluation of Naples score for long-term mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Angiology. 2024;75:725-33. doi: 10.1177/00033197231170982.
9. Mandelzweig L, Battler A, Boyko V, Bueno H, Danchin N, Filippatos G, et al. The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. Eur Heart J. 2006;27:2285-93. doi: 10.1093/eurheartj/ehl196.
10. Gitmez M, Ekingen E, Zaman S. Predictive value of the Naples prognostic score for one-year mortality in NSTEMI patients undergoing selective PCI. Diagnostics (Basel). 2025;15:640. doi: 10.3390/diagnostics15050640.
11. Libby P, Okamoto Y, Rocha VZ, Folco E. Inflammation in atherosclerosis: transition from theory to practice. Circ J. 2010;74:213-20. doi: 10.1253/circj.cj-09-0706.
12. Shah AD, Denaxas S, Nicholas O, Hingorani AD, Hemingway H. Neutrophil counts and initial presentation of 12 cardiovascular diseases: a CALIBER cohort study. J Am Coll Cardiol. 2017;69:1160-9. doi: 10.1016/j.jacc.2016.12.022. Erratum in: J Am Coll Cardiol. 2017;69:3125-6. doi: 10.1016/j.jacc.2017.05.026.
13. Barlas RS, Honney K, Loke YK, McCall SJ, Bettencourt-Silva JH, Clark AB, et al. Impact of hemoglobin levels and anemia on mortality in acute stroke: analysis of UK regional registry data, systematic review, and meta-analysis. J Am Heart Assoc. 2016;5:e003019. doi: 10.1161/JAHA.115.003019.
14. Venkatraghavan L, Tan TP, Mehta J, Arekapudi A, Govindarajulu A, Siu E. Neutrophil lymphocyte ratio as a predictor of systemic inflammation - a cross-sectional study in a pre-admission setting. F1000Res. 2015;4:123. doi: 10.12688/f1000research.6474.1.
15. Kim S, Eliot M, Koestler DC, Wu WC, Kelsey KT. Association of neutrophil-to-lymphocyte ratio with mortality and cardiovascular disease in the Jackson heart study and modification by the duffy antigen variant. JAMA Cardiol. 2018;3:455-62. doi: 10.1001/jamacardio.2018.1042.
16. Chen C, Cong BL, Wang M, Abdullah M, Wang XL, Zhang YH, et al. Neutrophil to lymphocyte ratio as a predictor of myocardial damage and cardiac dysfunction in acute coronary syndrome patients. Integr Med Res. 2018;7:192-9. doi: 10.1016/j.imr.2018.02.006.
17. Balta S, Celik T, Mikhailidis DP, Ozturk C, Demirkol S, Aparci M, et al. The relation between atherosclerosis and the neutrophil-lymphocyte ratio. Clin Appl Thromb Hemost. 2016;22:405-11. doi: 10.1177/1076029615569568.
18. Núñez J, Miñana G, Bodí V, Núñez E, Sanchis J, Husser O, et al. Low lymphocyte count and cardiovascular diseases. Curr Med Chem. 2011;18:3226-33. doi: 10.2174/092986711796391633.
19. Greene SJ, Harinstein ME, Vaduganathan M, Suba□ius H, Konstam MA, Zannad F, et al. Prognostic value of monocyte count in patients hospitalized for heart failure with reduced ejection fraction (from the EVEREST Trial). Am J Cardiol. 2012;110:1657-62. doi: 10.1016/j.amjcard.2012.07.035.
20. Shantsila E, Lip GY. The role of monocytes in thrombotic disorders. Insights from tissue factor, monocyte-platelet aggregates and novel mechanisms. Thromb Haemost. 2009;102:916-24. doi: 10.1160/TH09-01-0023.
21. Quan XQ, Wang RC, Zhang Q, Zhang CT, Sun L. The predictive value of lymphocyte-to-monocyte ratio in the prognosis of acute coronary syndrome patients: a systematic review and meta-analysis. BMC Cardiovasc Disord. 2020;20:338. doi: 10.1186/s12872-020-01614-x.
22. Si Y, Liu J, Shan W, Zhang Y, Han C, Wang R, et al. Association of lymphocyte-to-monocyte ratio with total coronary plaque burden in patients with coronary artery disease. Coron Artery Dis. 2020;31:650-5. doi: 10.1097/MCA.0000000000000857.
23. Kose N, Akin F, Yildirim T, Ergun G, Altun I. The association between the lymphocyte-to-monocyte ratio and coronary artery disease severity in patients with stable coronary artery disease. Eur Rev Med Pharmacol Sci. 2019;23:2570-5. doi: 10.26355/eurrev_201903_17406.
24. Gong S, Gao X, Xu F, Shang Z, Li S, Chen W, et al. Association of lymphocyte to monocyte ratio with severity of coronary artery disease. Medicine (Baltimore). 2018;97:e12813. doi: 10.1097/MD.0000000000012813.
25. Yu Y, Wang S, Wang P, Xu Q, Zhang Y, Xiao J, et al. Predictive value of lymphocyte-to-monocyte ratio in critically Ill patients with atrial fibrillation: a propensity score matching analysis. J Clin Lab Anal. 2022;36:e24217. doi: 10.1002/jcla.24217.
26. Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. Semin Dial. 2004;17:432-7. doi: 10.1111/j.0894-0959.2004.17603.x.
27. Joles JA, Willekes-Koolschijn N, Koomans HA. Hypoalbuminemia causes high blood viscosity by increasing red cell lysophosphatidylcholine. Kidney Int. 1997;52:761-70. doi: 10.1038/ki.1997.393.

28. Polat N, Oylumlu M, Işik MA, Arslan B, Özbek M, Demir M, et al. Prognostic significance of serum albumin in patients with acute coronary syndrome. Angiology. 2020;71:903-8. doi: 10.1177/0003319720941747.

29. Bicciré FG, Pastori D, Tanzilli A, Pignatelli P, Viceconte N, Barillà F, et al. Low serum albumin levels and in-hospital outcomes in patients with ST segment elevation myocardial infarction. Nutr Metab Cardiovasc Dis. 2021;31:2904-11. doi: 10.1016/j.numecd.2021.06.003.

30. Stamler J, Wentworth D, Neaton JD. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the multiple risk factor intervention trial (MRFIT). JAMA. 1986;256:2823-8.

31. Ndrepepa G, Holdenrieder S, Cassese S, Xhepa E, Fusaro M, Kastrati A. Hypocholesterolaemia and mortality in patients with coronary artery disease. Eur J Clin Invest. 2020;50:e13194. doi: 10.1111/eci.13194.

32. Iribarren C, Reed DM, Chen R, Yano K, Dwyer JH. Low serum cholesterol and mortality. Which is the cause and which is the effect? Circulation. 1995;92:2396-403. doi: 10.1161/01.cir.92.9.2396.

33. Jeong SM, Choi S, Kim K, Kim SM, Lee G, Son JS, et al. Association of change in total cholesterol level with mortality: A population-based study. PLoS One. 2018;13:e0196030. doi: 10.1371/journal.pone.0196030. Erratum in: PLoS One. 2019;14:e0215934. doi: 10.1371/journal.pone.0215934.

34. Wada H, Dohi T, Miyauchi K, Doi S, Konishi H, Naito R, et al. Prognostic impact of nutritional status assessed by the Controlling Nutritional Status score in patients with stable coronary artery disease undergoing percutaneous coronary intervention. Clin Res Cardiol. 2017;106:875-83. doi:10.1007/s00392-017-1132-z.

35. Kuang M, Qiu J, Yang R, Wang C, Huang X, Xie G, et al. Prognostic value of geriatric nutritional risk index in patients with stable coronary artery disease undergoing percutaneous coronary intervention. BMC Cardiovasc Disord. 2024;24:264. doi: 10.1186/s12872-024-03940-w.

36. Hammami R, Jdidi J, Mroua F, Kallel R, Hentati M, Abid L, et al. Accuracy of the TIMI and GRACE scores in predicting coronary disease in patients with non-ST-elevation acute coronary syndrome. Rev Port Cardiol. (Engl. Ed.) 2018;37:41-9. doi:10.1016/j.repc.2017.05.012.

37. Cordero A, Rodriguez-Manero M, García-Acuña JM, López-Palop R, Cid B, Carrillo P, et al. Additive value of the CRUSADE score to the GRACE score for mortality risk prediction in patients with acute coronary syndromes. Int J Cardiol. 2017;245:1-5. doi: 10.1016/j.ijcard.2017.07.095.

38. Birdal O, Pay L, Aksakal E, Yumurtaş AÇ, Çinier G, Yücel E, et al. Naples prognostic score and prediction of left ventricular ejection fraction in STEMI patients. Angiology. 2024;75:36-43. doi: 10.1177/00033197231161903.

39. Aydın SŞ, Aydemir S, Özmen M, Aksakal E, Saraç İ, Aydınyılmaz F, et al. The importance of Naples prognostic score in predicting long-term mortality in heart failure patients. Ann Med. 2024;57:2442536. doi: 10.1080/07853890.2024.2442536.

40. Gitmez M, Güzel T, Kis M, Coskun F, İsik MA, Aktan A, et al. The performance of the NAPLES prognostic score in predicting one-year mortality and major adverse cardiovascular events (MACEs) after transcatheter aortic valve implantation in patients with severe aortic stenosis. Kardiol Pol. 2025;83:287-94. doi: 10.33963/v.phj.103230.

INVITED REVIEW

CARDIOVASCULAR SURGERY AND INTERVENTIONS

DOI: 10.4274/e-cvsi.2026.2026-1-1
Cardiovasc Surg Int 2026;13(1):44-48

In pursuit of the heart: A comparative analysis of Medieval Western and Islamic medical approaches to cardiac diseases

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Received: January 08, 2026 **Accepted:** February 17, 2026 **Epub:** February 25, 2026 **Publication Date:** March 02, 2026

ABSTRACT

This study examines how cardiac diseases were understood, defined, and treated in medieval Western Europe and the Eastern Islamic world, and explores the historical transformation of cardiac knowledge within its intellectual and cultural context. This study adopted a historical–comparative qualitative approach. Medieval medical texts and scholarly traditions were analyzed by situating knowledge of the heart at the intersection of belief, morality, and medical practice. The study focuses on conceptual definitions of cardiac disease, the impact of Islamic medical knowledge on Western perceptions of the heart, and the therapeutic approaches used in cardiac treatment. The findings indicate that medieval knowledge of the heart and cardiovascular diseases emerged within a dynamic intellectual milieu shaped by continuous interaction between East and West. Cardiac anatomy and physiology were addressed with a notable degree of conceptual depth for the period, while therapeutic approaches largely reflected dietetic and humoral principles. The transmission of Islamic medical scholarship played a key role in the development of institutional medical learning in medieval Europe. Medieval cardiac medicine reflects a complex and multifaceted process of knowledge exchange rather than a simple East-West divide. This period constitutes a formative stage in the historical development of cardiovascular thought and represents an important intellectual foundation for the emergence of modern cardiology.

Keywords: Medieval medicine, cardiac diseases, humoral theory, Islamic medicine, Western medicine.

Modern historiography of medicine has long characterized the Middle Ages as a "dark age," interpreting the period as one dominated by scientific stagnation and scholastic dogmatism. A significant part of the misconception that portrays the Middle Ages as a period devoid of scientific progress stems from an insufficient awareness of the intellectual accumulation and scientific developments that took place during the Late Middle Ages.[1] However, since the late twentieth century, the comprehensive transformation that has taken place in historiographical approaches to the Middle Ages has led to a profound reassessment of this conventional perception. In this context, the Middle Ages is no longer portrayed in the scholarly literature as a uniformly "dark" period.[2] This approach has gradually been replaced by historiographical reinterpretations which emphasize that the intellectual world of the Middle Ages possessed its own internal logic and a specific form of rationality. Although the intellectual production of the period was largely shaped by religious references, it is evident that processes of observation, experience, and transmission in the production of knowledge were carried out within a certain framework of intellectual coherence. At the core of this intellectual framework, the "heart" occupies a significant symbolic and physiological position. In Medieval thought, the heart was not only regarded as a physiological organ, but also as the centre of the soul and faith, and as the point at which human existence came into contact with divine order. Accordingly, heart diseases in this period were perceived not only as bodily disorders,

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Cite this article as: Çeken M, Gül Ö. In pursuit of the heart: a comparative analysis of Medieval Western and Islamic medical approaches to cardiac diseases. Cardiovasc Surg Int. 2026;13(1):44-48

but also as manifestations of moral and spiritual disruption.[1] From this historiographical perspective, it becomes evident that knowledge production in the Middle Ages was not confined to abstract intellectual speculation.

In practice-oriented disciplines such as medicine, knowledge developed within a particular order and internal coherence, and a continuity was established between theoretical approaches and practical experience. Reflections on the human body in this period were shaped within an intellectual milieu in which religious and moral assumptions intersected with observation-based medical practice.

PATIENTS AND METHODS

This study examines how heart diseases were understood, defined, and treated in medieval Europe and in the Islamic world, with careful attention to their historical contexts. Using a historical-comparative qualitative approach, it frames knowledge of the heart not only as a medical topic but also as part of wider processes of knowledge production shaped by belief and moral thought. Accordingly, rather than establishing a direct continuity between medieval medicine and modern cardiology, the study seeks to reveal the historical transformation of the concept of the heart.

Within his framework, the research focuses on the following questions:

• How were heart diseases defined in medieval Western Europe and Islamic world of the East?

• In what ways did the transmission of medical knowledge from the Islamic world contribute to the transformation of European conceptions of the heart?

• What were the principal methods employed in the treatment of heart diseases in the Middle Ages?

The Heart in Medieval Thought: Symbolic and Medical Perceptions

It is generally stated that knowledge concerning the anatomy of the cardiovascular system (CVS) can be traced back to around 3500 BCE, to the civilization of ancient Egypt. The body of knowledge concerning the heart —which was defined as a major organ that carried air, urine, blood, and the vital spirit through a series of channels— was further developed over the course of history in parallel with advances in this field, particularly through the Hippocratic Corpus, eventually giving rise to the recognition of the heart as "the central organ of the CVS".[3] In the 4th century BCE, Aristotle attributed a philosophical meaning to the heart, conceiving it as the seat of the mind or the soul.[4] By the 2nd century CE, Galen approached the subject from a more medical perspective and, in the context of cardiac function, advanced the theory that the arteries contained blood rather than air.[3] Galen's theories on medicine —and particularly on the heart— nourished and informed not only the intellectual world of his own time, but also the knowledge of medieval European society on these matters for many centuries.[4] By synthesizing the teachings of Hippocrates and Aristotle, Galen attributed to the heart not only a physiological role but also a philosophical meaning, defining it —together with the brain and the liver— as one of the principal organs of the soul. At the same time, he regarded the heart as the center of vitality and emotions.[5] In particular, the humoral —that is, "four-fluid"— theory proposed by Galen in Antiquity, which became the theoretical foundation for the anatomy and physiology of the CVS throughout Medieval medicine, was endorsed by the Catholic Church and, for a long period, enjoyed considerable authority in Medieval Europe.[1,4] However, although Galen's humoral theory was accepted for many centuries, he misinterpreted the circulation of blood within the body and, under the erroneous assumption that there were perforations in the interventricular septum, maintained that blood was consumed as it passed through the organs and tissues.[6] For this reason, his views not only delayed a proper understanding of physiology, but also led to the misinterpretation of anatomy. Nevertheless, Galen ultimately provided subsequent generations with a scientific groundwork upon which more detailed and accurate analyses of the CVS could later be developed.[7]

"...أَلاَ وَإِنَّ فِي الْجَسَدِ مُضْغَةً إِذَا صَلَحَتْ صَلَحَ الْجَسَدُ كُلُّهُ، وَإِذَا فَسَدَتْ فَسَدَ الْجَسَدُ كُلُّهُ، أَلاَ وَهِيَ الْقَلْبُ."

"...Verily, in the body there is a piece of flesh; if it is sound, the whole body is sound, and if it is corrupted, the whole body is corrupted. Indeed, that (piece of flesh) is the heart".[8]

As noted above, this hadith transmitted by al-Bukhārī and included in the *Kutub al-Sitta* —the canonical collection regarded as comprising sound (ṣaḥīḥ) traditions— demonstrates that in Islamic thought the heart occupies a central position for both bodily and spiritual well-being. The studies carried out by Muslim physicians on the heart and the circulatory system in the Middle Ages indicate that the significance attributed to the heart in this hadith also found a counterpart within the medical literature. Drawing upon the theoretical legacy of Greco-Roman physicians such as Hippocrates, Aristotle, and Galen —and at times criticizing, developing, or even surpassing this tradition— Muslim physicians including al-Rāzī, ʿAlī b. al-ʿAbbās, Ibn Sīnā, al-Akhawaynī al-Bukhārī, and Ibn al-Nafīs made significant contributions through their medical works, shaping not only the intellectual horizon of their own age but also they medical knowledge of subsequent periods. In the Medieval Western world as well, the meanings attributed to the heart were shaped through a holistic perspective comparable to that found in the Islamic world. In this period as well, the treatment of the heart not merely as a physiological organ but in conjunction with moral and spiritual dimensions indirectly —yet distinctly— influenced the medical thought of the time; this perspective also played a role in shaping diagnostic and therapeutic practices. Within the Christian intellectual tradition, the conception of the heart articulated by Augustine in his "confessiones" provides a crucial framework for understanding the mental and spiritual background of medieval Latin medicine. Augustine, by emphasizing that God knows the depths of the heart (cor) —which was regarded as the centre of human identity and bodily existence— located faith, conscience, and moral order within the heart.[9] This perspective provided an intellectual framework in the medieval Western world that enabled physicians, when addressing heart diseases, to interpret such conditions not only in terms of physiological causes, but also in relation to spiritual, emotional, and moral imbalances.

Hildegard von Bingen (1098-1179), a German Benedictine nun and one of the most influential female intellectuals of twelfth-century Western Europe, is also known as the "Sybil of the Rhine".[10] In "Physica", Hildegard von Bingen offers noteworthy observations concerning the diagnosis and treatment of cardiac disorders within the framework of herbal therapeutic practices.[11] In this context, she states that the

plant known as galingale (galangal),[12], which continues to be used in traditional medicine in some Asian countries even today, has a healing effect on individuals who experience cardiac pain or whose hearts are weakened. Hildegard expresses this situation in the following words: "*One with pain in his heart, or with a weak heart, will soon be better if he eats enough galingale.*" In the same work, Hildegard describes yellow gentian as an herbal remedy that alleviates cardiac pain and restores the vital force of the heart through its warming quality, stating: "*Yellow gentian (gentiana) is fairly hot. One who suffers heart pain, as if his heart is just barely alive, should pulverize yellow gentian and eat that powder in broth, and it will strengthen his heart*".[11]

In the sections devoted to gemstones in "Selected Writings of Hildegard of Bingen", Hildegard von Bingen identifies heart pain as a clear medical symptom and, particularly through her discussion of the onyx stone, proposes a heat-based therapeutic approach. The practice of heating the stone with body warmth and using it together with wine is presented as a treatment that can be interpreted within the prevailing Galenic framework, in which excess heat was understood as a sign of imbalance requiring therapeutic correction. The statement in the same work, "*Also for anyone suffering pains in the heart: make the sign of the cross over their heart with the hyacinth and say the aforesaid words, and they will feel better*", clearly illustrates that, medical elements are closely intertwined with symbolic and religious components. The act of holding the hyacinth stone over the heart and performing the sign of the cross while reciting a prayer constitutes a significant example of the principle of body-soul unity that shaped the medical understanding of medieval Europe. Therefore, the practice in question represents not so much a medical prescription in the modern sense as a conception of healing in which humoral balance and religious symbolism are interwoven.[13]

However, this mystical–medical approach did not constitute a singularly dominant orientation within the medical world of Medieval Europe; rather, it continued to exist alongside the medical tradition that developed in the Mediterranean basin during the same period, which was grounded in written texts and the systematic production of knowledge. In this context, the Salerno Medical School played a significant role in the institutionalization of European medicine. "The Regimen Sanitatis Salernitanum",[14] one of the most widespread and influential dietetic texts of Medieval European medicine, was composed in the twelfth century within the intellectual milieu of the Salerno Medical School. Although the author of the work is unknown, it is generally accepted that it represents the collective intellectual contribution of physicians belonging to the Salernitan tradition. Its composition in "Leonine" verse facilitated its memorization and circulation among wide audiences; in this respect, the work was used for centuries not only within scholarly circles, but also as a practical health guide. Working within the established Galenic model, the Regimen articulated cardiac health through dietary moderation and emotional regulation, assuming that equilibrium of qualities was essential to bodily stability. The dietetic and lifestyle practices recommended in "the Regimen Sanitatis" aim to preserve the balance among these humors; excessive eating, intense emotional states, and irregular modes of living are presented as among the primary causes of illness. In particular, emotions such as anger, sorrow, and excessive joy may have adverse effects on the body, and consequently on the heart.[15]

In the *"Regimen Sanitatis*", the following statements concerning the heart are included: "*Take saffron if your heart make glad you will, but not too much, for that the heart may kill*,' which may be rendered as, "*If you wish to cheer your heart, take saffron — but do not exceed the proper measure, for excess may harm the heart*".[14] As previously noted, this statement is significant in that it reflects the perception, within Medieval medical thought, of the heart as the center of vital heat and emotional equilibrium. Furthermore, the warning that excessive use of saffron may be fatal for the heart highlights the importance of the concept of moderation (temperantia), which constituted a fundamental principle in the preservation of health. In the "Regimen Sanitatis Salernitanum," cardiac health is approached within a regimen of life that simultaneously takes into account the balance of body and soul. The work treats a proper diet, mental tranquility, and the maintenance of a cheerful and unburdened heart as primary elements in the preservation of health. While the adverse effects of excessive anxiety and anger on the human body are emphasized, it is stated that balanced nutrition, regular physical activity, and consistent sleep habits have a soothing effect on the whole body, including the heart.[14] This approach demonstrates that, in Medieval medicine, the heart was also perceived as a center directly associated with emotional states.

In the Middle Ages, the body of knowledge concerning heart diseases in Western Europe was largely based on the medical tradition of Ancient Greece and Rome. However, this heritage circulated in a relatively limited manner in the West throughout the early Middle Ages, and the texts of authorities such as Galen and Hippocrates were transmitted largely without substantial commentary. From the eleventh century onwards, however, this classical corpus gained a new sphere of circulation through the political, commercial, and intellectual contacts that intensified across the Mediterranean basin".[1,3,7] In this process, the translation activities carried out particularly within the milieu of the Salerno Medical School not only enabled the rediscovery of Ancient Medical knowledge, but also facilitated its transmission to the West together with original contributions that had been developed within different intellectual traditions. At this point, Constantinus Africanus played a decisive role in broadening the intellectual horizon of the Salerno Medical School during the second half of the eleventh century. Having also taught at the school for a period, Africanus became closely acquainted with the Islamic medical tradition during his extended travels in the Islamic world. By translating medical texts written in Arabic into Latin, he facilitated the transmission to Western Europe of classical works by Islamic physicians, particularly those concerning the diagnosis and classification of diseases. Constantine's translation activity provided an important intellectual foundation for the development, in the twelfth century, of a systematic and text-based medical education at the Salerno Medical School. In this context, Johannitius's "Isagoge" and the "Ars Parva" attributed to Galen, both translated into Latin by Africanus, were among the core texts incorporated into the Salernitan curriculum.[15] At this point, one aspect requires particular emphasis: the translation activities carried out through the agency of Constantinus Africanus should not be regarded as a simple transmission of Ancient and Islamic medical heritage to the West; rather, they should be understood as an original form of intellectual production shaped by personal experience, observation, and critical evaluation.

At precisely this juncture, the studies conducted in the Islamic world on the heart and the CVS provided, for Western Europe, an indirect yet decisive framework of reference. The cardiac theories of the Greek and Roman periods were not only preserved by Islamic physicians but were also re-examined through methods grounded in observation. In works

such as "*al-Ḥāwī fī al-Ṭibb*" by al-Rāzī (d. 925)", "*al-Kitāb al-Malikī*" by ʿAlī b. ʿAbbās al-Majūsī (d. 994), "*Hidāyat al-Mutaʿallimīn fī al-Ṭibb*" by al-Akhawaynī al-Bukhārī (d. 983), and "*al-Qānūn fī al-Ṭibb*" by Ibn Sīnā (d. 1037), the heart is treated not merely as a theoretical center, but as an anatomical, physiological, and clinical organ. When transmitted to the Latin world, the approaches developed in these works played a significant role in the transformation of Western conceptions of the heart. In this framework, al-Rāzī's rejection of Galen's view that a bony structure existed at the base of the heart constitutes an early example of the critique of authority-based knowledge. Meanwhile, the morphological descriptions provided by ʿAlī b. ʿAbbās concerning the aorta, the coronary arteries, and the pulmonary artery contributed to the development of circulatory understanding by drawing attention to the functional relationships among these vessels. Al-Akhawaynī al-Bukhārī's explanations concerning pulmonary circulation and his restriction of the heart's primary function to the pumping of blood indicate a gradual departure from earlier pneuma-centered theories. Although some of his explanations are regarded as inaccurate from the standpoint of modern medicine, the identification of the coronary arteries and the thoracic descending aorta may nonetheless be considered a noteworthy advancement in Medieval cardiovascular anatomy. Moreover, ʿAlī b. ʿAbbās explains the function of the pulmonary artery in a manner that closely corresponds to modern terminology, defining it as the vessel that carries blood to the lungs in order to nourish them and to receive air from them.[3,16]

Ibn Sīnā, one of the leading figures of the Middle Ages in the field of cardiovascular studies and a major source of inspiration for modern research through the theories he proposed, did not disregard the ideas put forward by physicians of the Greek and Roman periods, particularly Galen. While Ibn Sīnā accepted some of these theories, he critically examined others and introduced new approaches to the field. For instance, like Galen, Ibn Sīnā did not regard the heart merely as an organ that functioned as a pump within the body of living beings; rather, he conceived of it as a center of power — a source of life that directed all bodily and emotional functions.[1,17] In relation to the cardiosentric model, Ibn Sīnā, who accepted Aristotle's theory concerning the presence of pores in the interventricular septum, made important observations regarding the origin of the arteries arising from the heart and the veins located in the liver, as well as the differences in the thickness of the ventricular walls. In addition, as the first scholar to identify the difference between atrial and ventricular contractions and to point to the existence of capillary circulation, he made significant advances in the anatomical understanding of the heart.[1]

Ibn Sīnā attached great importance to the subject of the heart, a fact clearly demonstrated by his treatise entitled "*Kitāb al-Adviyāt al-Qalbiyya"* (The Book of Remedies for Cardiac Diseases). In this work, Ibn Sīnā provided information on cardiac diseases and certain psychological disorders that affect the physiology of the cardiovascular organs, and introduced the medicines that were beneficial in their treatment. The effects of some of the medicines mentioned by Ibn Sīnā have been scientifically demonstrated in modern times.[18]

In this work, which examines not only cardiac conditions such as dyspnea, palpitations, and syncope but also the effects of psychological disorders—including depression, stress, and anxiety—on the CVS, Ibn Sīnā focused on the relationship between the patient's temperament and the disorder affecting the heart, and provided significant detail regarding the medicines required for cardiac diseases. The significance attributed to this work is reflected in the fact that it was translated into Latin twice—in the fourteenth and sixteenth centuries—under the title *De Medicines Cordialibus*.[19]

Another prominent Islamic scholar who made significant contributions to the medieval field of cardiovascular studies through his work on the anatomy and physiology of the heart was Ibn al-Nafīs (d. 1288). Ibn al-Nafīs's most important discovery was the idea with on the movement of blood between the heart and the lungs".[20] Ibn al-Nafīs was also the first physician to define the true function of the coronary vessels that supply the heart.[1] Ibn al-Nafīs stated that, after being carried to the right ventricle, the blood is conveyed to the lungs through the pulmonary artery, and from there returns to the heart via the pulmonary veins, before being distributed to the body through the aorta.[3] By rejecting Galen's claim that the pores in the septum allowed the passage of blood and spirit between the two chambers, he opposed Galen's theory concerning the functioning of the heart.

RESULTS

This study demonstrates that knowledge concerning heart and cardiovascular diseases in the Middle Ages did not emerge —contrary to common assumptions— within a stagnant or intellectually regressive medical framework, but was instead shaped within a dynamic intellectual milieu that developed through the continuous exchange between Eastern and Western scholarly traditions and the legacy of the ancient world. The theoretical framework of ancient medicine was reinterpreted in the Islamic world and enriched through original contributions. Consequently, this body of knowledge, transmitted through translation movements and scholarly channels of exchange, became incorporated into the institutionalization of Western European medicine and made a substantial contribution to its development. At the same time, the Western scholarly milieu did not merely receive this heritage passively; rather, it re-interpreted and reconstructed it, further enriching it through its own original intellectual contributions. Accordingly, the history of medieval medicine reflects a multilayered circulation of knowledge that developed not through opposition between East and West, but through processes of continuity and synthesis.

Another significant finding of the study is that investigations concerning the cardiovascular organs and heart diseases were extensively addressed throughout the Middle Ages across different regions and by many of the leading physicians of the period. Observations and explanations concerning the anatomy of the heart and the great vessels —and, to some extent, their physiology— display a noteworthy degree of conceptual depth within the limits of the period's scientific possibilities. A key implication of the present analysis is that medieval approaches to cardiac illness, while commonly grounded in Galenic humoralism and expressed through regimen and materia medica, cannot be read as a linear step toward modern cardiology. Rather, they should be situated within a period-specific epistemology that explained cardiac disorder in terms of balanced qualities, bodily temperaments, and affective states, and that shaped therapy through the medical rationalities of the time.

The pioneering approaches developed by physicians of the Islamic world concerning the heart, the pulse, the vascular system, and cardiac diseases were not only influential within their own scholarly milieu, but were also received with interest by Western medicine and, for centuries, served as authoritative references in both medical education

and therapeutic practice. This reception highlights the cross-cultural mobility of medical knowledge; however, it also suggests that what circulated in Latin Europe was not a transparent transfer but a mediated corpus shaped by translation strategies, institutional and curricular priorities, and the durability of inherited explanatory models—thereby privileging some claims while muting or reconfiguring others. This case underscores that medical knowledge circulated through translation, adaptation, and institutional filtering. Rather than a seamless flow, transmission involved negotiation, selective uptake, and occasional resistance—processes that shaped what was preserved, transformed, or left aside.

In conclusion, the Middle Ages represents a critical period in which the earliest universities emerged —such as the Salerno Medical School— and in which medical thought began to acquire an institutional framework. The diagnostic and therapeutic approaches developed in relation to heart and vascular diseases during this period are not merely matters of historical curiosity; they are also of great significance for understanding the intellectual background of modern medicine. For this reason, the medical heritage of the Middle Ages constitutes a significant scientific legacy that deserves to be re-examined, both for understanding the historical development of heart and vascular diseases and for revealing the intellectual continuity within which modern clinical knowledge was formed.

Footnotes

Authorship Contributions

Concept: M.Ç., Ö.G.; Design: M.Ç., Ö.G.; Analysis or Interpretation: M.Ç., Ö.G.; Literature Search: M.Ç., Ö.G.; Writing: M.Ç., Ö.G.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Ranhel AS, Mesquita ET. The Middle Ages contributions to cular medicine. Braz J Cardiovasc Surg. 2016;31:163-70. doi:10.5935/1678-9741.20160031.
2. Gümüş TT. The history of education in Western Europe from the Middle Ages to the early modern Europe: new approaches. Mersin Univ J Fac Educ. 2010;6:25-40. doi:10.17860/efd.04095.
3. Bestetti RB, Restini CBA, Couto LB. Development of anatomophysiologic knowledge regarding the cardiovascular system: from Egyptians to Harvey. Arq Bras Cardiol. 2014;103:538-45. doi: 10.5935/abc.20140148.
4. Strathern P. A brief history of medicine: from Hippocrates to gene therapy. New York: Carroll & Graf Publishers; 2005.
5. Galenos. Tıp sanatının anayasası, tıp sanatı; Glaukon'a tedavi yöntemi. Nirven N, çevirmen. İstanbul: Pinhan Yayıncılık; 2018.
6. Fullerton JB, Silverman ME. Claudius Galen of Pergamum: authority of medieval medicine. Clin Cardiol. 2009;32:E82-3. doi: 10.1002/clc.20388.
7. Kelly K. The history of medicine: the Middle Ages (500–1450). New York: Infobase Publishing; 2009.
8. Buhârî, el-Câmiʿu's-Sahîh, "Îmân", Hadis no: 39. Available at:https://hadislerleislam.diyanet.gov.tr/sayfa.php?CILT=3&SAYFA=55. Accessed December 11, 2025.
9. Augustine, St. The confessions of St. Augustine. Pilkington JG, translator. Garden City, New York: International Collectors Library.
10. Romaní J, Romaní M. Causes and cures of skin diseases in the work of Hildegard of Bingen. Actas Dermosifiliogr. 2017;108:538-43. English, Spanish. doi: 10.1016/j.ad.2016.09.002.
11. Hildegard of Bingen. Physica: the complete English translation of her classic work on health and healing. Rochester (VT): Healing Arts Press; 1998.
12. Das G, Patra JK, Gonçalves S, Romano A, Gutiérrez-Grijalva EP, Heredia JB, et al. Galangal, the multipotent super spices: a comprehensive review. Trends Food Sci Technol. 2020;101:50-62. doi: 10.1016/j.tifs.2020.04.016.
13. Hildegard of Bingen. Selected writings. London: Penguin Books; 2001.
14. Ordroneaux J, translator. Regimen sanitatis Salernitanum: code of health of the school of Salernum. Philadelphia: J. B. Lippincott & Co.; 1870.
15. Pasca M. The Salerno school of medicine. Am J Nephrol. 1994;14:478-82. doi:10.1159/000168770.
16. Dalfardi B, Mahmoudi Nezhad GS, Mehdizadeh A. How did Haly Abbas look at the cardiovascular system? Int J Cardiol. 2014;172:36-9. doi: 10.1016/j.ijcard.2013.12.171.
17. Avicenna. The Canon of medicine. New York: AMS Press; 1973.
18. Faridi P, Zarshenas MM. Ibn Sina's book on drugs for cardiovascular diseases. Int J Cardiol. 2010;145:223. doi: 10.1016/j.ijcard.2010.04.064.
19. Chamsi-Pasha MAR, Chamsi-Pasha H. Avicenna's contribution to cardiology. Avicenna J Med. 2014;4:10. doi: 10.4103/2231-0770.127415.
20. Mitchell PD. Anatomy and surgery in Europe and the Middle East during the Middle Ages. In: Perdicoyianni-Paleologou H, editor. Anatomy and surgery from antiquity to the Renaissance. Amsterdam: Adolf Hakkert; 2016. p. 1-17.

CASE REPORT

DOI: 10.4274/e-cvsi.2025.1975
Cardiovasc Surg Int 2026;13(1):49-51

CARDIOVASCULAR SURGERY AND INTERVENTIONS

Successful surgical management of hepatic artery injury during cholecystectomy

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Received: July 14, 2025 **Accepted:** October 13, 2025 **Epub:** January 07, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Iatrogenic hepatic artery injury during cholecystectomy is a serious complication, often exacerbated by inflammation and anatomical variations of the vascular structures. In this case report, a 16-year-old patient undergoing laparoscopic cholecystectomy for cholecystitis sustained a hepatic artery injury. The cardiovascular surgery team performed an interposition graft using the saphenous vein to restore arterial flow. Systemic heparinization was administered intravenously at a dose of 100 IU/kg before vascular clamping. Hemostasis was achieved through temporary clamping of the celiac trunk branches. Contrast-enhanced computed tomography angiography on postoperative day 5 confirmed the patency of the graft. In cases where bile duct and hepatic artery injuries occur simultaneously, a multidisciplinary approach is essential to improve patient outcomes and minimize complications.

Keywords: Hepatic artery, cholecystectomy, saphenous vein graft, pediatric vascular injury.

Iatrogenic injury to the hepatic arteries during cholecystectomy is a significant and potentially life-threatening complication. Inflammatory changes in the hepatobiliary region and anatomical variations in vascular structures can complicate surgical dissection and increase the risk of such injuries. The incidence of combined injury to the extrahepatic bile ducts and hepatic afferent vessels has been reported to be approximately 30%, which can severely compromise the patient's overall clinical condition. Bile duct injury during cholecystectomy remains a serious and potentially fatal complication. Over the past two decades, studies have reported that the incidence of complications associated with laparoscopic cholecystectomy ranges from 0.5% to 1.4%.[1] Concomitant injury to hepatic vessels and bile ducts significantly increases patient mortality.[2-4] Clinical studies have reported the incidence of combined extrahepatic bile duct and hepatic artery injuries during cholecystectomy to range from 13.8% to 26%.[3,5] Due to limited experience in some centers, standardized treatment strategies for managing such complex cases have not been fully established. In this study, we present a case of successful surgical management of a hepatic artery injury sustained during cholecystectomy.

CASE REPORT

Informed consent was secured from the patient for the publication of this case and the accompanying images.

A 16-year-old female patient with a known history of symptomatic cholelithiasis presented to the emergency department with nausea, right upper quadrant pain radiating to the shoulder, fever, chills, and generalized fatigue. On admission, the body temperature was 38.5 °C. Laboratory tests showed elevated inflammatory markers: C-reactive protein 98 mg/L; amylase: 44 U/L; lipase: 26 U/L. Abdominal ultrasonography revealed gallbladder wall thickening and multiple stones consistent with acute cholecystitis. The patient was admitted to the pediatric surgery service and scheduled for elective laparoscopic cholecystectomy following stabilization.

During the laparoscopic procedure, significant arterial bleeding was encountered in the hepatobiliary region, which could not be adequately controlled using minimally invasive methods. Due to impaired visualization and the need for vascular repair, the procedure was converted to open cholecystectomy. Intraoperative findings

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Cite this article as: Guseinov Z, Şen Topcu SM, Kocaaslan C, Aydın E. Successful surgical management of hepatic artery injury during cholecystectomy. Cardiovasc Surg Int. 2026;13(1):49-51

prompted an urgent consultation with the cardiovascular surgery team. Hemostasis was initially achieved by temporary vascular clamping of the celiac trunk branches using atraumatic vascular clamps. Further exploration revealed a full-thickness transection of the proper hepatic artery. Systemic anticoagulation was initiated with intravenous heparin at a dose of 100 IU/kg prior to vascular repair.

A saphenous vein graft was harvested from the lower extremity, and an interposition graft was performed to restore arterial continuity (Figure 1). Concurrently, due to the associated bile duct injury, the general surgery team performed a Roux-en-Y hepatojejunostomy for biliary reconstruction. The patient was transferred to the pediatric intensive care unit postoperatively. Recovery was uneventful, and no inotropic support was required.

Liver function tests—aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyl transferase—along with bilirubin levels, gradually returned to normal. To protect the vascular graft, low molecular weight heparin therapy was initiated. On postoperative day 5, contrast-enhanced computed tomography angiography confirmed the patency of the hepatic artery and adequate graft perfusion (Figure 2). The patient was discharged in stable condition after full clinical and biochemical recovery.

DISCUSSION

Hepatic artery injuries during laparoscopic cholecystectomy are rare but potentially life-threatening complications, especially in the presence of inflammation, anatomical variations, or surgical inexperience. In our case, conversion to open surgery was essential for adequate exploration and vascular control. This approach allowed for prompt identification and successful repair of the hepatic artery using a saphenous vein interposition graft.

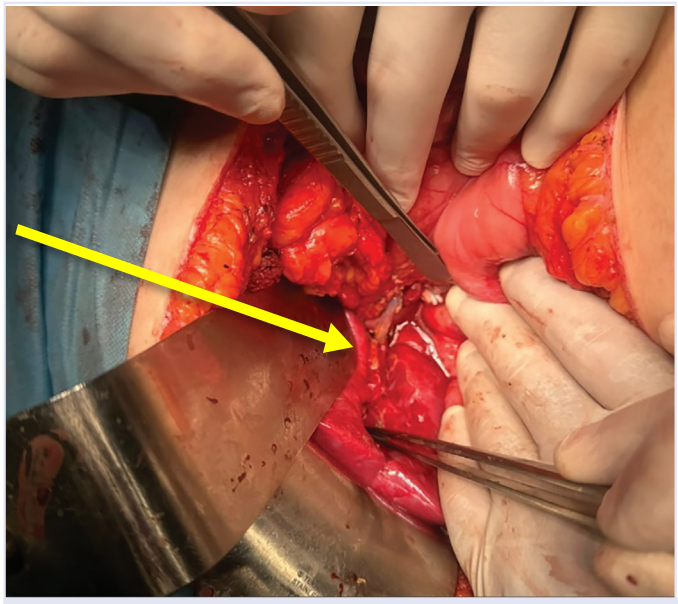

Figure 1. Intraoperative image showing hepatic artery repair with saphenous vein interposition graft. The saphenous vein graft is visible between the proximal and distal hepatic artery segments (yellow arrow).

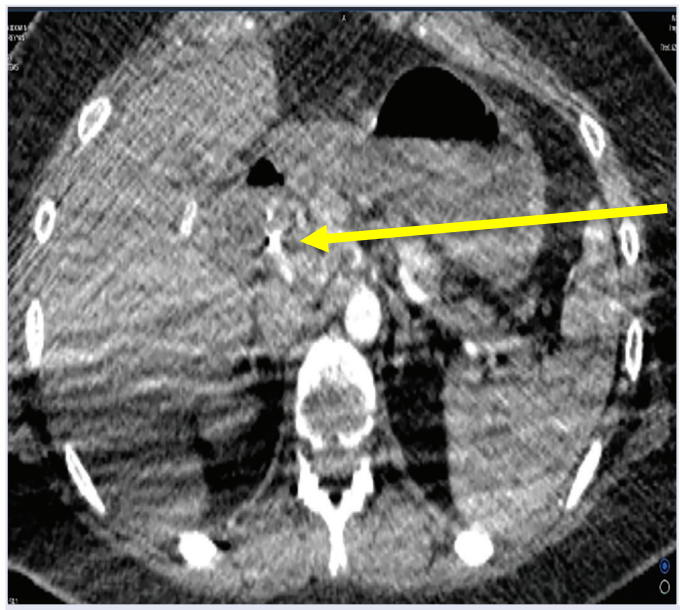

Figure 2. Postoperative CT angiography showing patent saphenous vein graft on postoperative day 5. White arrow indicates the course of the graft and confirms arterial continuity without thrombosis (yellow arrow).
CT: Computed tomography.

Although some studies suggest that isolated hepatic artery injuries may not require revascularization due to intrahepatic collateral flow,[1] this may not apply to pediatric patients, whose collateral networks are often underdeveloped. In such cases, prompt surgical intervention is necessary to prevent ischemia-related liver damage.

This case is particularly notable due to the patient's young age and the successful use of a saphenous vein graft for arterial reconstruction. While most hepatic artery injuries occur in adults, pediatric cases are extremely rare. A recent report by Akış Yıldız et al.[3] described a 6-year-old child with a similar vascular injury during laparoscopic cholecystectomy, underscoring both the rarity and the technical complexity of such cases in children. Ferrada et al.[4] emphasized that combined biliary and vascular injuries may necessitate aggressive interventions such as percutaneous revascularization or staged hepatectomy. However, early recognition and immediate surgical repair can help avoid more extensive hepatic resections.

Although Singla et al.[1] suggested that injuries to the right hepatic artery may not significantly affect mortality due to collateral circulation, this does not hold true for all pediatric patients. Therefore, early revascularization should be prioritized in children. Furthermore, existing literature supports the feasibility and durability of saphenous vein grafts in emergency hepatic artery reconstruction.[2,5] In our case, the uneventful postoperative course and the documented graft patency on imaging support this approach.

In conclusion, hepatic artery injury in pediatric patients, though rare, requires prompt recognition and coordinated management. Saphenous vein interposition grafting can be an effective method to restore arterial continuity when performed early and in conjunction with definitive biliary repair. This case highlights the importance of multidisciplinary collaboration in achieving favorable outcomes in complex hepatobiliary injuries.

Ethics

Informed Consent: Informed consent was secured from the patient for the publication of this case and the accompanying images.

Footnotes

Authorship Contributions

Concept: E.A., C.K., S.M.Ş.T., Z.G.; Design: E.A., C.K., S.M.Ş.T., Z.G.; Data Collection or Processing: E.A., C.K., S.M.Ş.T., Z.G.; Analysis or Interpretation: E.A., C.K., S.M.Ş.T., Z.G.; Literature Search: E.A., C.K., S.M.Ş.T., Z.G.; Writing: E.A., C.K., S.M.Ş.T., Z.G.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Singla S, Singh RK, Kumar S, Prasad U, Mandal M, Kumar S. Cholecystectomy associated vasculobiliary injuries: incidence and impact on surgical repair outcomes. Turk J Surg. 2025;41:24-30. doi: 10.47717/turkjsurg.2025.6577.
2. Felekouras E, Megas T, Michail OP, Papaconstantinou I, Nikiteas N, Dimitroulis D, et al. Emergency liver resection for combined biliary and vascular injury following laparoscopic cholecystectomy: case report and review of the literature. South Med J. 2007;100:317-20. doi: 10.1097/01.smj.0000242793.15923.1a.
3. Akış Yıldız Z, Su ŞM, İlçe Z. Hepatic artery injury in a six-year-old patient after laparoscopic cholecystectomy: a management challenge. J Surg Med. 2024;8:123-7. doi.org/10.28982/josam.7667.
4. Ferrada PISM, Morales HFL, Abarca JAS, Muñoz PIF. Major biliovascular injury associated with cholecystectomy with the need for percutaneous arterial revascularization and staged right hepatectomy: case report. Arq Bras Cir Dig. 2020;33:e1493. doi: 10.1590/0102-672020190001e1493.
5. Khanmoradi K, Defaria W, Moore RE, Guarneri R, Tzakis AG. Gastroduodenal artery as the inflow tract to repair the right hepatic artery in a combined vasculobiliary injury after laparoscopic cholecystectomy. Am Surg. 2007;73:888-9. doi.org/10.1177/000313480707300912.

CASE REPORT

CARDIOVASCULAR SURGERY AND INTERVENTIONS

DOI: 10.4274/e-cvsi.2025.1987
Cardiovasc Surg Int 2026;13(1):52-54

Extracranial internal carotid artery aneurysm: Surgical approach

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Received: August 04, 2025 **Accepted:** November 18, 2025 **Epub:** January 14, 2026 **Publication Date:** March 02, 2026

ABSTRACT

Extracranial internal carotid artery (EICA) aneurysms constitute a significant clinical concern and are exceedingly rare. The most concerning major complications are rupture and thromboembolism. Treatment options for extracranial carotid artery aneurysms include open surgery, endovascular interventions, and non-operative approaches. Although endovascular interventions have gained popularity, surgical treatment: Complete removal of the aneurysm sac and arterial reconstruction still remains relevant. In this article, we will examine a patient with an EICA aneurysm who has been followed up with medical treatment for years. We will discuss the successful interposition of the aneurysm sac with a polytetrafluoroethylene graft following aneurysmectomy.

Keywords: Carotid artery aneurysm, extracranial, internal carotid, surgical reconstruction, endovascular intervention, stent-graft.

Extracranial internal carotid artery (EICA) aneurysms are exceedingly rare, constituting less than 1% of all peripheral artery aneurysms. They are most frequently located near the carotid bifurcation, with the second most common site being the mid-region of the internal carotid artery (ICA).[1] The primary etiological factor is atherosclerosis, particularly in elderly patients. Less common causes include previous carotid surgery, trauma, radiation exposure, fibromuscular dysplasia, and infection.[2] Although EICA aneurysms are often asymptomatic and found incidentally, they can present more symptoms than intracranial aneurysms. Common symptoms include a pulsatile mass, signs of compression on surrounding tissues and cranial nerves, and neurological complications such as transient ischemic attack and stroke. The most concerning complications are rupture and thromboembolism. Although endovascular interventions have gained popularity, surgical treatment: Complete removal of the aneurysm sac and arterial reconstruction still remains relevant. Other treatment modalities include endovascular options and medical management, which encompasses regular follow-up for asymptomatic patients, strategies to prevent aneurysm sac growth, and antithrombotic therapy.

This article examines a case involving an EICA aneurysm in a patient who underwent ICA reconstruction following aneurysmectomy.

In this case report, patient anonymity was preserved and written informed consent was obtained from the patient after informing them about the scientific use and publication of the case details.

CASE REPORT

An 81-year-old woman was admitted to the hospital with a neck mass that has been monitored for 4 years and has exhibited progressive growth. Diagnostic tests indicated a 7x8 cm pulsatile mass in the left cervical region of the carotid artery, which expands during systole (Figure 1).

The patient was diagnosed with an EICA aneurysm and subsequently underwent surgical intervention. Under general anesthesia, a precise incision was made in the skin and subcutaneous tissue at the location of the left carotid artery. The aneurysm sac was meticulously dissected from the surrounding tissues, ensuring the preservation of vascular and nerve structures. The common carotid artery and external carotid artery were explored and secured with tape. Following heparin administration, a clamp was applied to the common carotid artery, and the aneurysm sac was opened, with continuous electroencephalogram (EEG) monitoring in place. The ICA was identified at the distal end of the aneurysm, which was occluded using a carotid shunt, allowing for effective bleeding control. One end of an 8-mm ringed polytetrafluoroethylene (PTFE) graft was anastomosed end-to-end to the distal ICA. The shunt was then removed, and a clamp was placed over the graft. The other end of the graft was subsequently anastomosed end-to-end to the healthy carotid tissue at the bifurcation level (Figure 2). Upon releasing the clamp, the aneurysm sac was wrapped around the graft. There were no EEG changes noted during the procedure, and no complications were

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Cite this article as: Yusifli A, Kale A, Ayık MF, Buket S. Extracranial internal carotid artery aneurysm: surgical approach. Cardiovasc Surg Int. 2026;13(1):52-54

observed. Carotid clamp time was 19 min. The patient was successfully awakened in the operating room and extubated. In the postoperative period, anticoagulant treatment was performed with subcutaneous low molecular weight heparin and antiaggregant treatment with aspirin and clopidogrel. The postoperative period was uneventful and the patient was discharged on the third postoperative day without any neurological complications and with stable parameters.

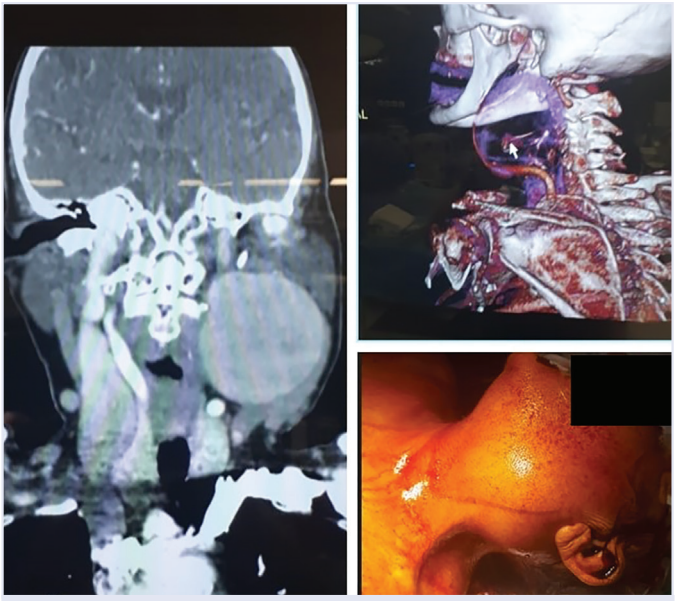

Figure 1. An aneurysmal mass is noted in the left cervical carotid region.

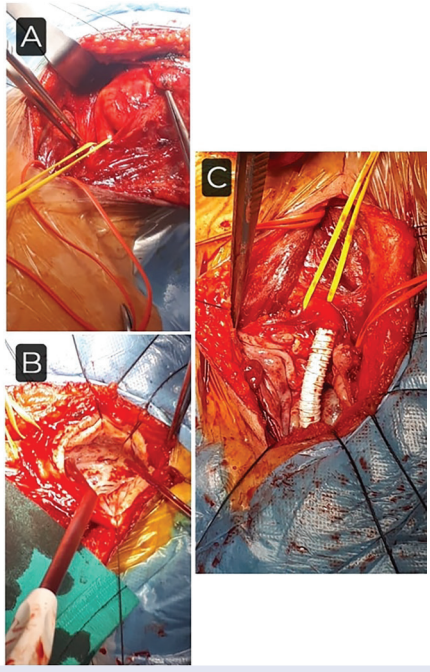

Figure 2. (A) The skin and subcutaneous tissue were incised in the left cervical carotid region, and the aneurysm sac was dissected from the surrounding tissues for thorough exploration; (B) The aneurysm sac was opened, and suspension sutures were applied to the sac wall, revealing the absence of thrombus within the sac; (C) Following the aneurysmectomy, an 8 mm ringed PTFE graft was interposed in the left internal carotid artery.
PTFE: Polytetrafluoroethylene.

DISCUSSION

Carotid artery aneurysms were initially managed with proximal ligation. Subsequently, cases emerged involving end-to-end anastomosis following aneurysmectomy and later, the use of prosthetic grafts. Currently, treatment options for extracranial carotid artery aneurysms encompass open surgery, endovascular interventions, and non-operative methods. Since the advent of open surgical treatment for EICA aneurysms in 1805, surgical techniques have progressed; however, open surgery has consistently been the preferred approach for this condition. Despite advancements in endovascular interventions, open surgery remains the standard of care. The primary objective of surgical intervention is to excise the aneurysm and restore arterial continuity. When reviewing the literature, we see that there are several approaches to the surgical treatment of EICA aneurysms: End-to-end anastomosis after aneurysmectomy, interposition with an autologous saphenous vein graft, or repair of the aneurysm using a saphenous vein patch. For small and elongated EICA aneurysms, an end-to-end anastomosis may be executed post-aneurysmectomy, or interposition may be conducted using either the saphenous vein or synthetic graft materials (PTFE or Dacron). In our case, due to the size and shape of the aneurysm sac, we opted for interposition with a PTFE graft after aneurysmectomy. One study compared five-year patency rates between patients receiving interposition with a synthetic graft versus those with saphenous vein grafts, yielding rates of 88.9% and 66.4%, respectively.[2] Another study indicated a 90% patency rate at 30 months for patients undergoing open surgery.[3] A review of the literature has identified publications demonstrating acceptable mid-term outcomes with endovascular interventions.[4] Additionally, these publications suggest criteria favoring an endovascular approach, including distal cervical ICA aneurysms, prior neck surgery, and previous neck radiation. Another study has shown that endovascular stenting in the treatment of EICAs has acceptable clinical and radiological outcomes, but prospective and larger studies are needed to further confirm the safety and long-term patency of endovascular repair.[5] Non-operative treatment is generally recommended for asymptomatic, small, and stable aneurysms, particularly in patients with significant comorbidities. This approach includes antithrombotic therapy, management of cardiovascular risk factors, and regular ultrasound monitoring.[1]

EICA aneurysms, while rare, represent a serious clinical condition due to their potential to result in severe neurological complications. The gold standard for treatment involves the removal of the aneurysm and restoration of arterial continuity. Open surgery is regarded as the first-line treatment for symptomatic and large aneurysms.

Ethics

Informed Consent: In this case report, patient anonymity was preserved and written informed consent was obtained from the patient after informing them about the scientific use and publication of the case details.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.K., S.B.; Concept: A.Y.; Design: A.Y.; Data Collection or Processing: A.Y., M.F.A.; Analysis or Interpretation: A.Y.; Literature Search: A.Y.; Writing: A.Y.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Fankhauser GT, Stone WM, Fowl RJ, O'Donnell ME, Bower TC, Meyer FB, et al. Surgical and medical management of extracranial carotid artery aneurysms. J Vasc Surg. 2015;61:389-93. doi: 10.1016/j.jvs.2014.07.092.
2. Donas KP, Schulte S, Pitoulias GA, Siebertz S, Horsch S. Surgical outcome of degenerative versus postreconstructive extracranial carotid artery aneurysms. J Vasc Surg. 2009;49:93-8. doi: 10.1016/j.jvs.2008.08.006.
3. Srivastava SD, Eagleton MJ, O'Hara P, Kashyap VS, Sarac T, Clair D. Surgical repair of carotid artery aneurysms: a 10-year, single-center experience. Ann Vasc Surg. 2010;24:100-5. doi: 10.1016/j.avsg.2009.09.006.
4. Li Z, Chang G, Yao C, Guo L, Liu Y, Wang M, et al. Endovascular stenting of extracranial carotid artery aneurysm: a systematic review. Eur J Vasc Endovasc Surg. 2011;42:419-26. doi: 10.1016/j.ejvs.2011.05.008.
5. Giannopoulos S, Trinidad E, Aronow H, Soukas P, Armstrong EJ. Endovascular repair of extracranial carotid artery aneurysms: a systematic review. Vasc Endovascular Surg. 2020;54:254-63. doi: 10.1177/1538574419895383.