

e-ISSN: 2980-1397

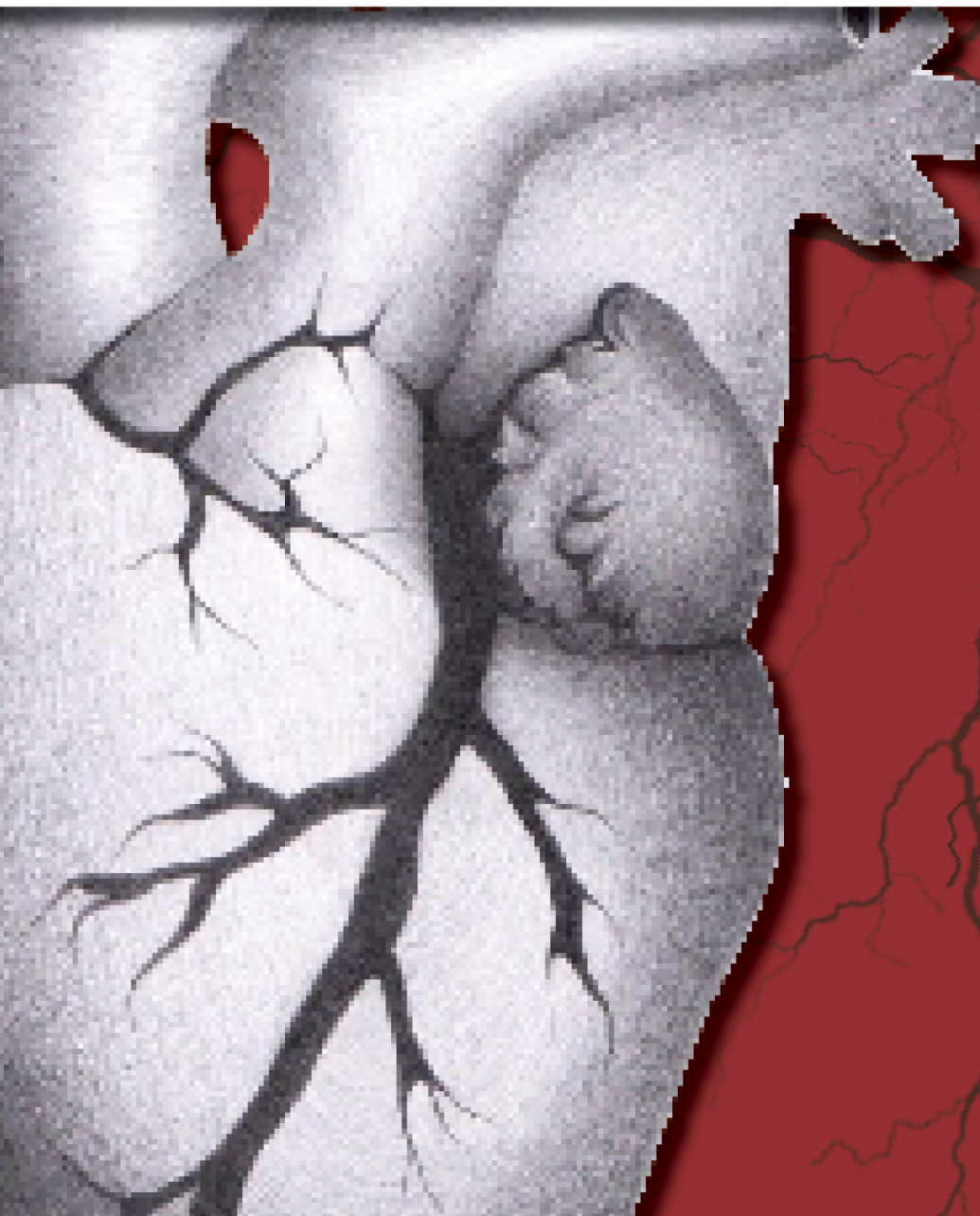
Journal of  
**CARDIOLOGY & CARDIOVASCULAR  
SURGERY**

Volume: 3

Issue: 2

Year: 2025

JCCVS



## EDITOR-IN-CHIEF

### Assoc. Prof. İbrahim Halil İNANÇ

Department of Cardiology, Phoenixville Hospital, Towerhealth, Phoenixville, USA

## ASSOCIATE EDITORS-IN-CHIEF

### Assoc. Prof. Cengiz ŞABANOĞLU

Department of Cardiology, Ümraniye Training and Research Hospital, University of Health Sciences, İstanbul, Türkiye

### Asst. Prof. Esra POLAT

Department of Cardiology, Dr Ersin Arslan Training and Research Hospital, Gaziantep, Türkiye

### Asst. Prof. Hüseyin KANDEMİR

Department of Cardiology, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

### Assoc. Prof. Şaban KELEŞOĞLU

Department of Cardiology, Faculty of Medicine, Erciyes University, Kayseri, Türkiye

### Assoc. Prof. Yücel YILMAZ

Department of Cardiology, Kayseri City Hospital, Kayseri, Türkiye

## EDITORIAL BOARD

### Spec. Anand M. KRISHNAN, MD

Department of Cardiology, University of Vermont Medical Center, Burlington, Vermont, USA

### Asst. Prof. Ajar KOÇAK

Department of Cardiology, Faculty of Medicine, Ufuk University, Ankara, Türkiye

### Prof. Aydın ÇİFCİ

Department of Internal Medicine, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

### Spec. Ayşe HOŞOĞLU, MD

Department of Cardiology, Başkent University Ankara Hospital, Ankara, Türkiye

### Spec. Bilge Nazar ATEŞ, MD

Department of Cardiology, Ankara Bilkent City Hospital, Ankara, Türkiye

### Spec. Deniz MUTLU, MD

Department of Cardiology, Faculty of Medicine, İstanbul University Cerrahpaşa, İstanbul, Türkiye

### Spec. Elca GJINI, MD

Department of Emergency Medicine, Spitali Rajonal Memorial Fier Hospital, Fier, Albania

### Asst. Prof. Enes ALIÇ

Department of Cardiology, VM Medical Park Pendik Hospital. Faculty of Medicine, İstanbul Aydın University, İstanbul, Türkiye

### Spec. Ersin DOĞANÖZÜ, MD

Department of Cardiology, 29 Mayıs State Hospital, Ankara, Türkiye

**Spec. Fulden Akyüz İNANÇ, MD**

*Department of Respiratory Diseases, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye*

**Spec. Haşim TÜNER, MD**

*Department of Cardiology, Memorial Bahçelievler Hospital, İstanbul, Türkiye*

**Spec. Hüseyin DEMİRTAŞ, MD**

*Department of Cardiovascular Surgery, Faculty of Medicine, Gazi University, Ankara, Türkiye*

**Prof. İbrahim ECE, MD**

*Department of Pediatric Cardiology, Ankara Bilkent City Hospital, Ankara, Türkiye*

**Spec. İbrahim Çağrı KAYA, MD**

*Department of Cardiovascular Surgery, Eskişehir City Hospital, Eskişehir, Türkiye*

**Assoc. Prof. İbrahim Etem ÇELİK**

*Department of Cardiology, Ankara Training and Research Hospital, University of Health Sciences, Ankara, Türkiye*

**Prof. Kaan KAYA**

*Department of Cardiovascular Surgery, Ankara Etlik City Hospital, Ankara, Türkiye*

**Prof. Kaan OKYAY**

*Department of Cardiology, Başkent University Ankara Hospital, Faculty of Medicine, Başkent University, Ankara, Türkiye*

**Assoc. Prof. Mehmet KARAHAN**

*Department of Cardiovascular Surgery, Ankara Bilkent City Hospital, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Türkiye*

**Prof. Mehmet Ali KOBAT**

*Department of Cardiology, Faculty of Medicine, Fırat University, Elazığ, Türkiye*

**Spec. Mesut KARATAŞ, MD**

*Department of Cardiology, Koşuyolu Yüksek İhtisas Training and Research Hospital, İstanbul, Türkiye*

**Prof. Murat TULMAÇ**

*Department of Cardiology, Liv Hospital Ankara, Ankara, Türkiye*

**Asst. Prof. Murat Abdulhamit ERCİŞLİ**

*Department of Cardiovascular Surgery, Faculty of Medicine, Adıyaman University, Adıyaman, Türkiye*

**Assoc. Prof. Mustafa ŞAHİN**

*Department of Medical Biochemistry, Çorum Hitit University Erol Olçok Training and Research Hospital, Faculty of Medicine, Hitit University, Çorum, Türkiye*

**Prof. Mustafa DURAN**

*Department of Cardiology, Ankara Training and Research Hospital, University of Health Sciences, Ankara, Türkiye*

**Spec. Mustafa KARAKURT, MD**

*Department of Cardiology, Kırıkkale Yüksek İhtisas Hospital, Kırıkkale, Türkiye*

**Assoc. Prof. Mustafa SABAK**

*Department of Emergency Medicine, Faculty of Medicine, Gaziantep University, Gaziantep, Türkiye*

**Spec. Osman Fehmi BEYAZAL, MD**

*Department of Cardiovascular Surgery, Başakşehir Çam ve Sakura City Hospital, İstanbul, Türkiye*

**Assoc. Prof. Pınar Demir GÜNDOĞMUŞ**

*Department of Sports Medicine, Gülhane Training and Research Hospital, University of Health Sciences, Ankara, Türkiye*

**Assoc. Prof. Selçuk ÖZTÜRK**

*Department of Cardiology, Kırıkkale Yüksek İhtisas Hospital, Kırıkkale, Türkiye*

**Assoc. Prof. Serhat KOCA**

*Department of Pediatric Cardiology, Ankara Bilkent City Hospital, Ankara, Türkiye*

**Asst. Prof. Şevki Mustafa DEMİRÖZ**

*Department of Thoracic Surgery, Faculty of Medicine, Gazi University, Ankara, Türkiye*

**Prof. Tahir DURMAZ**

*Department of Cardiology, Ankara Bilkent City Hospital, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Türkiye*

**Assoc. Prof. Ufuk MÜNGAN**

*Department of Cardiovascular Surgery, Ankara Etlik City Hospital, Ankara, Türkiye*

**Spec. Uğur SAYGISUNAR, MD**

*Department of Cardiology, Medicana International İzmir Hospital, İzmir, Türkiye*

**Asst. Prof. Ünal ÖZTÜRK**

*Department of Cardiology, Faculty of Medicine, Sütçü İmam University, Kahramanmaraş, Türkiye*

**Assoc. Prof. Yıldırım GÜLTEKİN**

*Department of Cardiovascular Surgery, Eskişehir City Hospital, Eskişehir, Türkiye*

**Spec. Yusuf HOŞOĞLU, MD**

*Department of Cardiology, Adıyaman Training and Research Hospital, Adıyaman, Türkiye*

**LANGUAGE EDITOR**

**Assoc. Prof. Esra GÜZEL TANOĞLU**

*Department of Molecular Biology and Genetics, Institute of Health Sciences, University of Health Sciences, İstanbul, Türkiye*

**STATISTICS EDITOR**

**Assoc. Prof. Turgut KÜLTÜR**

*Department of Physical Therapy and Rehabilitation, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye*

**LAYOUT EDITOR**

**Hatice AKYIL**

*Biologist, MediHealth Academy, Ankara, Türkiye*

**Volume: 3      Issue: 2      Year: 2025**

## ORIGINAL ARTICLES

Permanent pacemaker implantation after aortic valve implantation.....21-24

*Arın CB, Karataş M.*

The motivation to quit: smoking cessation rates in ACS versus elective PCI patients..... 25-28

*Arslan GY, Söner S.*

Comparison of Pan-Immune Inflammatory Index in patients dialysed from catheters and fistulas ..... 29-34

*Öztürk H, Felek D, Varlıbaş A, Hacıömeroğlu A, Öztürk ZN, Çifci A.*

Role of Systemic Immune-Inflammation Index in predicting multi-territorial atherosclerotic disease in peripheral arterial disease: a retrospective cohort study ..... 35-39

*Serhatlıoğlu F, Yılmaz Y, Tuğrul C, Yılmaz H, Keleşoğlu Ş.*

## CASE REPORT

Recurrent cardiac papillary fibroelastoma with multiple organ embolism. Is it really benign?: a case report .....40-42

*Beyazal OF, Kandemir Ö, Sapmaz İ, Zorlutuna Y.*



# Permanent pacemaker implantation after aortic valve implantation

 Can Baba Arın<sup>1</sup>,  Mesut Karataş<sup>2</sup>

<sup>1</sup>Department of Cardiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery, Training and Research Hospital, İstanbul, Türkiye

<sup>2</sup>Department of Cardiology, Mogadishu Somali Turkish Recep Tayyip Erdoğan Training and Research Hospital, Mogadishu, Somali

**Cite this article:** Arın CB, Karataş M. Permanent pacemaker implantation after aortic valve implantation. *J Cardiol Cardiovasc Surg.* 2025;3(2):21-24.

**Corresponding Author:** Can Baba Arın, canbabaarin@gmail.com

**Received:** 01/06/2025

**Accepted:** 20/06/2025

**Published:** 27/06/2025

## ABSTRACT

**Aims:** Conduction abnormalities are well-recognized complications following aortic valve replacement, particularly after transcatheter aortic valve implantation (TAVI). The incidence of permanent pacemaker implantation (PPI) post-TAVI remains variable, influenced by patient and procedural factors. To evaluate the incidence, clinical predictors, and outcomes associated with PPI following TAVI, with specific attention to left ventricular ejection fraction (LVEF).

**Methods:** We conducted a retrospective analysis of 60 patients who underwent transfemoral TAVI between 2008 and 2011. Baseline demographic, clinical, procedural, and echocardiographic parameters were compared between patients who required PPI and those who did not. Univariate and bivariate analyses were used to identify potential predictors.

**Results:** PPI was required in 29 of 60 patients (48.3%), with the majority of devices implanted within 72 hours post-procedure. Dual-chamber pacemakers were most commonly utilized, predominantly for complete atrioventricular block or symptomatic bradycardia associated with new-onset left bundle branch block. No statistically significant associations with PPI were found for variables such as age, sex, atrial fibrillation, ischemic heart disease, or baseline LVEF (all  $p > 0.05$ ). Trends suggesting possible associations with atrial fibrillation and mitral regurgitation did not reach statistical significance.

**Conclusion:** PPI remains a frequent yet unpredictable outcome after TAVI, particularly in the era of early-generation valve systems. Our findings underscore the absence of reliable clinical predictors and emphasize the need for prospective studies incorporating procedural, anatomical, and electrophysiologic markers to refine risk stratification and minimize unnecessary device implantation.

**Keywords:** Transcatheter aortic valve implantation, permanent pacemaker, conduction disturbances, aortic stenosis, left ventricular function

## INTRODUCTION

Aortic valve diseases such as stenosis and regurgitation can compromise the cardiac conduction system, often resulting in atrioventricular block (AVB). Surgical aortic valve replacement (SAVR) and more recently, transcatheter aortic valve implantation (TAVI), have been associated with new-onset conduction abnormalities including complete AVB and bundle branch blocks.<sup>1,2</sup> Reports indicate that postoperative AVB requiring pacemaker implantation is not uncommon, with wide variability depending on prosthesis type and procedural factors.<sup>3,4</sup>

Although CoreValve devices are particularly associated with higher permanent pacemaker implantation (PPI) rates due to their self-expanding design and subannular extension, balloon-expandable valves have shown lower incidences.<sup>2</sup> However, results from published studies have been inconclusive in identifying consistent predictors for PPI.<sup>3-5</sup> Conduction disturbances may result from mechanical

injury, calcification-induced stress, or direct trauma to the conduction system during valve deployment.

This study aims to evaluate the incidence and predictors of PPI in a cohort of patients who underwent TAVI, and to assess the effect of PPI on postoperative left ventricular ejection fraction (LVEF).

## METHODS

The study was conducted with the permission of the Ethics Committee of Mogadishu Somalia Türkiye Recep Tayyip Erdoğan Training and Research Hospital (Date: 09.04.2025, Decision No: 1197). This retrospective cohort study included 60 consecutive patients with symptomatic severe aortic stenosis who underwent transfemoral TAVI between September 2008 and March 2011 at a single tertiary care center. All procedures were carried out in accordance

with the ethical rules and the principles of the Declaration of Helsinki. All patients met guideline-based criteria for TAVI, including an aortic valve area  $<1.0 \text{ cm}^2$  and a mean transvalvular gradient  $\geq 40 \text{ mmHg}$ .

PPI was assessed as the primary outcome. Indications for PPI followed institutional protocols and included complete AVB, symptomatic bradycardia, and unresolved high-grade AV block. Pacemaker implantation was performed within 30 days of the TAVI procedure.

Clinical, electrocardiographic (ECG), and echocardiographic data were collected retrospectively from medical records. Baseline parameters included age, sex, comorbidities (e.g., atrial fibrillation, ischemic heart disease), LVEF, and the presence of conduction abnormalities. Post-procedural complications, including valvular regurgitation and new conduction disturbances, were also recorded.

Conduction disturbances were defined using standard WHO/ISFC criteria and included left bundle branch block (LBBB), right bundle branch block (RBBB), and various degrees of AVB.<sup>6</sup> Echocardiographic assessments were conducted by board-certified cardiologists according to the American Society of Echocardiography guidelines, and included evaluation of valvular function, LVEF, and chamber size. The severity of valvular regurgitation and LV dysfunction was graded semi-quantitatively.

ECG data were independently reviewed by two electrophysiologists blinded to clinical outcomes. Clinical endpoints, including PPI, were defined in accordance with the Valve Academic Research Consortium (VARC) criteria to ensure consistency and comparability.<sup>7</sup>

### Statistical Analysis

The data analyses were conducted using SPSS version 19.0 (IBM Corp, Armonk, NY). Continuous variables were expressed as mean  $\pm$  standard deviation and compared using independent samples t-tests. Categorical variables were reported as frequencies and percentages, and analyzed using chi-square or Fisher's exact tests, as appropriate. Univariate and bivariate analyses were performed to identify potential predictors of PPI. A p-value  $<0.05$  was considered statistically significant. Missing data were handled by pairwise deletion, and sensitivity analyses were conducted to validate findings.

## RESULTS

The study cohort comprised 60 patients with symptomatic severe aortic stenosis who underwent transfemoral TAVI between 2008 and 2011. The mean age was  $80.8 \pm 6.5$  years, and 55% were female. Comorbid conditions included atrial fibrillation in 26.7% of patients, ischemic heart disease in 80%, moderate-to-severe mitral regurgitation in 31.7%, and left ventricular dysfunction (LVEF  $<50\%$ ) in 33.3% at baseline.

Following the procedure, PPI was required in 29 patients (48.3%), with the majority (82.8%) receiving pacemakers within the first 72 hours. Dual-chamber pacemakers were most frequently implanted and were primarily indicated for complete AVB or symptomatic bradycardia in the setting of new-onset LBBB.

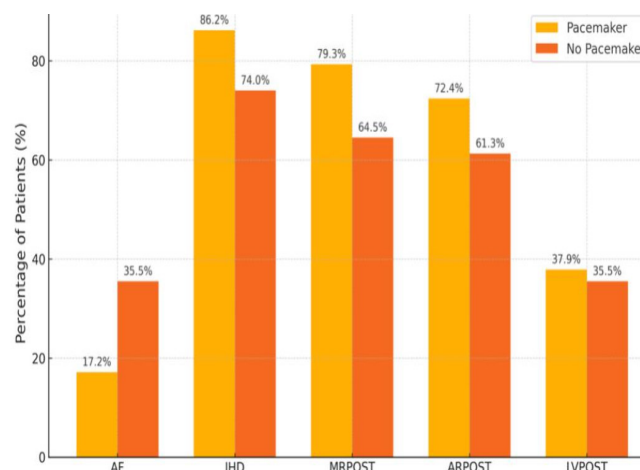
**Table 1** summarizes baseline characteristics of the study population. Comparative analysis between patients who required PPI and those who did not revealed no statistically significant differences in demographic or clinical variables. Specifically, there were no significant differences in age ( $p=0.533$ ), sex distribution ( $p=0.586$ ), presence of atrial fibrillation (17.2% in PPI group vs. 35.5% in non-PPI group;  $p=0.110$ ), ischemic heart disease ( $p=0.245$ ), baseline mitral regurgitation ( $p=0.208$ ), aortic regurgitation ( $p=0.389$ ), or left ventricular dysfunction ( $p=0.850$ ).

**Table 1.** Baseline patient characteristics

Variable	Value
Age	$80.8 \pm 6.5$
Female n (%)	33 (55)
Atrial fibrillation n (%)	16 (26.7)
Ischemic heart disease n (%)	48 (80)
Pacemaker after TAVI n (%)	29 (48.3)
Mitral regurgitaion (pre)	Moderate to severe 19 (31.7)
Mitral regurgitaion (post)	Moderate to severe 18 (30)
Aortic regurgitation (post)	Moderate to severe 10 (16.7)
LV dysfunction pre	Mild to severe 20 (33.3)
LV dysfunction post	Mild to severe 22 (36.7)

TAVI: Transcatheter aortic valve implantation, LV: Left ventricular

**Figure** illustrates the distribution of selected post-procedural complications stratified by pacemaker status. Although not statistically significant, the PPI group showed numerically higher rates of post-TAVI mitral and aortic regurgitation.



**Figure.** Distribution of clinical variables by pacemaker status

Bivariate analysis did not identify any single clinical or echocardiographic variable as a statistically significant predictor of PPI (**Table 2**). These findings suggest that conventional baseline risk factors may have limited value in forecasting the need for PPI following TAVI in this cohort.

## DISCUSSION

In this retrospective analysis of 60 patients undergoing transfemoral TAVI, we found that nearly half (48.3%) required PPI, a rate considerably higher than typically reported in

**Table 2.** Bivariate analysis of groups

Variable	Pacemaker (n=29)	No pacemaker (n=31)	p value
Age (years)	81.4±6.5	80.2±6.5	0.533 <sup>1</sup>
Female n (%)	17 (58.6)	16 (51.6)	0.586 <sup>2</sup>
Atrial fibrillation n (%)	5 (17.2)	11(35.5)	0.110 <sup>2</sup>
Ischemic heart diseases (%)	25 (86.2)	23 (74)	0.245 <sup>2</sup>
LV dysfunction after TAVI n (%)	11 (37.9)	11 (35.5)	0.850 <sup>2</sup>
Mitral regurgitation (psot). %	23 (79.3)	20 (64.5)	0.208 <sup>2</sup>
Aortic regurgitation (psot). %	21 (72.4)	19 (61.3)	0.389 <sup>2</sup>

TAVI: Transcatheter aortic valve implantation, LV: Left ventricular

contemporary series. Despite examining a broad range of clinical and echocardiographic parameters, no statistically significant predictors of PPI were identified. These findings highlight the multifactorial and, in many cases, unpredictable nature of conduction disturbances following TAVI.

Our PPI rate aligns with early experiences using first-generation self-expanding CoreValve devices, which have been consistently associated with higher rates of conduction abnormalities and subsequent pacemaker implantation. Data from the CoreValve U.S. Pivotal trial reported a 30-day PPI rate of approximately 22.3%, which increased with longer follow-up.<sup>8</sup> Similarly, the FRANCE-2 registry showed a 26.7% PPI rate for CoreValve compared to only 6.1% for balloon-expandable Edwards SAPIEN valves.<sup>9</sup> The deeper implantation and subannular extension of self-expanding prostheses are thought to contribute to this elevated risk by exerting mechanical pressure on the atrioventricular conduction axis, particularly the bundle of His.

Despite this well-established anatomical rationale, the identification of consistent clinical predictors remains elusive. In our cohort, variables such as age, sex, atrial fibrillation, left ventricular dysfunction, and valvular regurgitation did not correlate significantly with the need for PPI. This is in agreement with findings from Khawaja et al.,<sup>3</sup> who showed that baseline clinical variables had limited predictive value for post-TAVI PPI and emphasized the role of procedural and anatomical factors, such as implantation depth and membranous septum length. Similarly, a meta-analysis of 2,707 patients found no strong association between baseline clinical variables and PPI risk. Instead, anatomical and procedural factors—such as short membranous septum length, deeper implantation depth, and annular/leaflet calcification—were significantly associated with increased PPI rates.<sup>10</sup>

The lack of procedural detail in our study, such as implantation depth or pre-existing conduction abnormalities (e.g., PR interval, QRS duration, RBBB), limits our ability to assess these potentially crucial risk factors. Moreover, the high PPI rate may partly reflect institutional learning curves and the use of early-generation TAVI systems, which have since undergone significant technical refinements. Newer-generation devices like the Evolut PRO and SAPIEN 3 have demonstrated reduced PPI rates due to improved valve profiles and more precise deployment mechanisms.<sup>11,12</sup>

Clinical implications of PPI after TAVI remain a subject of ongoing debate. Several studies suggest that PPI may be associated with adverse long-term outcomes such as increased heart failure hospitalization, impaired left ventricular function, and higher mortality, particularly in pacing-dependent individuals.<sup>13,14</sup> However, other investigations have not confirmed these associations, underscoring the heterogeneity of this population and the need for individualized pacing strategies.<sup>15,16</sup>

From a clinical standpoint, our findings support the notion that traditional preprocedural variables alone are insufficient for accurate risk stratification. As Oestreich et al.<sup>17</sup> suggested, integrating multimodal imaging—including CT-based assessment of the membranous septum and aortic root orientation—with ECG markers may enhance prediction models and guide intra-procedural decision-making. Furthermore, procedural strategies such as high implantation techniques and cusp-overlap views have shown promise in reducing conduction system trauma and should be considered in centers aiming to minimize PPI burden.<sup>18</sup>

### Limitations

This study has several important limitations. First, the retrospective and single-center nature of the analysis, coupled with a relatively small sample size (n=60), restricts the statistical power to identify subtle but clinically relevant associations. Second, the data represent an early era of TAVI, with procedures performed between 2008 and 2011 using first-generation CoreValve devices. Given the substantial evolution in valve technology and implantation techniques over the past decade, the applicability of our findings to contemporary practice—characterized by newer-generation devices and refined procedural strategies—may be limited.

Third, the study lacked access to key procedural parameters, including implantation depth, valve-to-annulus oversizing ratio, and fluoroscopic views such as cusp-overlap techniques, all of which are known to impact conduction system outcomes. Furthermore, pre-existing conduction disturbances (e.g., PR interval, QRS duration, RBBB) were not systematically documented, and electroanatomical mapping was not utilized. These omissions precluded a more granular analysis of ECG predictors of PPI.

Finally, the study did not assess long-term clinical outcomes such as pacing dependency, heart failure hospitalizations, cardiovascular mortality, or functional recovery. These factors are critical to understanding the true prognostic implications of post-TAVI permanent pacing. Taken together, these limitations highlight the need for future prospective, multicenter investigations incorporating standardized procedural protocols, advanced imaging modalities, and extended clinical follow-up.

### CONCLUSION

PPI remains a common complication after TAVI, particularly with early-generation self-expanding valves. No single clinical or echocardiographic predictor was identified in our cohort, reflecting the multifactorial nature of conduction disturbances. Future research should focus on integrating



detailed imaging and procedural data to improve risk stratification and reduce unnecessary pacemaker use as TAVI technology evolves.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was conducted with the permission of the Ethics Committee of Mogadishu Somalia Turkiye Recep Tayyip Erdoğan Training and Research Hospital (Date: 09.04.2025, Decision No: 1197).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## REFERENCES

- Kim MH, Deeb GM, Eagle KA, et al. Complete atrioventricular block after valvular heart surgery and the timing of pacemaker implantation. *Am J Cardiol.* 2001;87(5):649-A10. doi:10.1016/s0002-9149(00)01448-x
- Rodés-Cabau J, Webb JG, Cheung A, et al. Transcatheter aortic valve implantation for the treatment of severe symptomatic aortic stenosis: a position statement from the Canadian Cardiovascular Society. *Can J Cardiol.* 2010;26(11):191-199.
- Khawaja MZ, Rajani R, Cook A, et al. Permanent pacemaker insertion after CoreValve transcatheter aortic valve implantation: incidence and contributing factors. *Circulation.* 2011;123(9):951-960. doi:10.1161/CIRCULATIONAHA.109.927152
- Sinhal A, Altwegg L, Pasupati S, et al. Atrioventricular block after transcatheter balloon-expandable aortic valve implantation. *Catheter Cardiovasc Interv.* 2008;1(3):305-309. doi:10.1016/j.jcin.2007.12.009
- Richardt G, Möllmann H, Neumann T, et al. Anatomic and procedural predictors of paravalvular aortic regurgitation after implantation of the Medtronic CoreValve system. *Circ Cardiovasc Interv.* 2010;3(20):524-530. doi:10.1161/CIRCINTERVENTIONS.110.957316
- Lilly S, Deshmukh A, Epstein A, et al. 2020 ACC expert consensus decision pathway on management of conduction disturbances in patients undergoing transcatheter aortic valve replacement: a report of the American College of Cardiology Solution Set Oversight Committee. *JACC.* 2020;76(20):2391-2411. doi:10.1016/j.jacc.2020.08.050
- Généreux P, Piazza N, Alu MC, et al. Valve academic research consortium 3: updated endpoint definitions for aortic valve clinical research. *J Am Coll Cardiol.* 2021;77(21):2717-2746. doi:10.1016/j.jacc.2021.02.038
- Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med.* 2014;370(19):1790-1798. doi:10.1056/NEJMoa1400590
- Eltchaninoff H, Prat A, Gilard M, et al. Transcatheter aortic valve implantation: early results of the FRANCE (FRench Aortic National CoreValve and Edwards) registry. *Eur Heart J.* 2011;32:191-7. doi:10.1093/eurheartj/ehq261
- Maier O, Piayda K, Afzal S, et al. Computed tomography derived predictors of permanent pacemaker implantation after transcatheter aortic valve replacement: a meta-analysis. *Catheter Cardiovasc Interv.* 2021;98(6):E897-E907. doi:10.1002/ccd.29805
- Mauri V, Reimann A, Stern D, et al. Predictors of Permanent pacemaker implantation after transcatheter aortic valve replacement with the SAPIEN 3. *JACC Cardiovasc Interv.* 2016;9(21):2200-2209. doi:10.1016/j.jcin.2016.08.034
- Harvey JE, Puri R, Grubb KJ, et al. Decreasing pacemaker implantation rates with Evolut supra-annular transcatheter aortic valves in a large real-world registry. *Cardiovasc Revasc Med.* 2024;69:1-9. doi:10.1016/j.carrev.2024.05.024
- Aljabbar T, Qiu F, Masih S, et al. Association of clinical and economic outcomes with permanent pacemaker implantation after transcatheter aortic valve replacement. *JAMA Network Open.* 2018;1(1):e180088. doi:10.1001/jamanetworkopen.2018.0088
- Sá MP, Jacquemyn X, Sun T, et al. Late outcomes of permanent pacemaker implantation after TAVR: meta-analysis of reconstructed time-to-event data. *JSCAI.* 2022;1(5):100434. doi:10.1016/j.jscai.2022.100434
- Giustino G, Van der Boon RM, Molina-Martin de Nicolas J, et al. Impact of permanent pacemaker on mortality after transcatheter aortic valve implantation: the PRAGMATIC (Pooled Rotterdam-Milan-Toulouse in Collaboration) Pacemaker substudy. *EuroIntervention.* 2016;12(9):1185-1193. doi:10.4244/EIJV12I9A192
- Sammour YM, Lak H, Gajulapalli RD, et al. Pacing-related differences after SAPIEN-3 TAVI: clinical and echocardiographic correlates. *Am J Cardiol.* 2023;197:24-33. doi:10.1016/j.amjcard.2023.04.001
- Oestreich BA, Mbai M, Gurevich S, et al. Computed tomography (CT) assessment of the membranous septal anatomy prior to transcatheter aortic valve replacement (TAVR) with the balloon-expandable SAPIEN 3 valve. *Cardiovasc Revasc Med.* 2018;19(5 Pt B):626-631. doi:10.1016/j.carrev.2017.12.012
- Pascual I, Hernández-Vaquero D, Alperi A, et al. Permanent pacemaker reduction using cusp-overlapping projection in TAVR: a propensity score analysis. *JACC Cardiovasc Interv.* 2022;15(2):150-161. doi:10.1016/j.jcin.2021.10.002

# The motivation to quit: smoking cessation rates in ACS versus elective PCI patients

 Gamze Yeter Arslan<sup>1</sup>,  Serdar Söner<sup>2</sup>

<sup>1</sup>Department of Cardiology, Kepez State Hospital, Antalya, Türkiye

<sup>2</sup>Department of Cardiology, Gazi Yaşargil Training and Research Hospital, University of Health Sciences, Diyarbakır, Türkiye

**Cite this article:** Arslan GY, Söner S. The motivation to quit: smoking cessation rates in ACS versus elective PCI patients. *J Cardiol Cardiovasc Surg.* 2025;3(2):25-28.

**Corresponding Author:** Gamze Yeter Arslan, dr.gamzeyetararslan@gmail.com

**Received:** 15/04/2025

**Accepted:** 24/06/2025

**Published:** 27/06/2025

## ABSTRACT

**Aims:** This study aimed to compare six-month smoking cessation rates in active smokers undergoing stent implantation either following an acute coronary syndrome (ACS) event or as part of an elective coronary angiography for stable coronary artery disease (CAD). Additionally, the research sought to identify clinical and psychological determinants associated with successful cessation in both groups.

**Methods:** This retrospective observational study included 300 current smokers (150 in the ACS group and 150 in the elective PCI group), aged between 35 and 80 years. Demographic data, comorbidities (including diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), heart failure with preserved ejection fraction [HFpEF] and heart failure with reduced ejection fraction [HFrEF]), and smoking status at six-month follow-up were collected. A psychological assessment using the Brief Illness Perception Questionnaire (BIPQ) was conducted in a entire cohort (n=300) to evaluate perceived severity and emotional impact. Statistical analyses included chi-square, t-tests, and multivariable logistic regression to determine independent predictors of cessation.

**Results:** At six months, the smoking cessation rate was significantly higher among ACS patients (58%) compared to those undergoing elective PCI (32%) ( $p<0.001$ ). Across the entire cohort, higher cessation rates were observed in individuals aged  $>50$  years, female patients, those with diabetes, and especially among patients with HFpEF. BIPQ results across the full cohort showed significantly higher scores for perceived illness severity and emotional response among the ACS group. In multivariable analysis, ACS presentation (OR=2.3,  $p<0.001$ ), HFpEF (OR=1.8,  $p=0.02$ ), and female gender (OR=1.6,  $p=0.04$ ) emerged as independent predictors of cessation.

**Conclusion:** It is interesting to note that smoking has been identified as a universal and powerful risk factor across all spectra of coronary artery disease, both acute and stable. However, it has been suggested that patients experiencing ACS may be more responsive to cessation efforts, possibly due to heightened emotional distress and perceived threat to life. Patients who are electively undergoing PCI, while equally at risk, may require different motivational strategies. It is suggested that these findings highlight the importance of integrating clinical context with psychological readiness when designing and delivering smoking cessation interventions in cardiology practice.

**Keywords:** Smoking cessation, acute coronary syndrome, elective PCI, stenting, cardiovascular risk factors, behavior change

## INTRODUCTION

Cigarette smoking remains a leading modifiable risk factor for both acute and chronic manifestations of coronary artery disease (CAD). While the association between smoking and cardiovascular morbidity is well-established, the clinical context in which patients are confronted with their diagnosis whether through an acute coronary syndrome (ACS) or an elective coronary angiography may influence their readiness and motivation to quit smoking.<sup>1</sup> Exploring the interplay between clinical presentation and smoking cessation can provide valuable insights for targeted intervention strategies. Coronary artery disease (CAD) is the leading cause of morbidity and mortality worldwide. Among the numerous risk factors, cigarette smoking remains one of the most

preventable causes of cardiovascular disease. The World Health Organization reports that smoking contributes to over 8 million deaths annually, with a substantial proportion related to cardiovascular events.<sup>2</sup> Numerous studies have confirmed the association between smoking and increased CAD risk. The INTERHEART study reported that smoking accounts for 36% of the global population-attributable risk for myocardial infarction.<sup>3</sup> The Framingham Heart Study also demonstrated a clear dose-response relationship between smoking intensity and CAD incidence. Furthermore, secondhand smoke exposure is associated with increased CAD events, highlighting the broader public health implications.<sup>4</sup>

Smoking is a leading risk factor for cardiovascular disease and continues to contribute significantly to global mortality. Despite public health efforts, smoking cessation rates remain low among patients with coronary artery disease. An ACS often represents a turning point in a patient's perception of health, potentially triggering motivation to quit smoking. In contrast, patients undergoing elective procedures may not perceive an immediate threat to life, and thus may be less motivated to alter risky behaviors.<sup>5</sup> This study investigates whether clinical urgency, as represented by ACS, is associated with higher smoking cessation rates than elective PCI.

**Study endpoints;** The primary endpoint of the study is the comparison of the proportion of individuals who completely quit smoking six months after undergoing stent implantation due to ACS versus those who received stents following elective coronary angiography. This endpoint aims to reveal the relationship between smoking cessation behavior and the mode of clinical presentation (urgent vs. elective). The secondary endpoints are as follows:

1. To evaluate the impact of comorbid conditions (diabetes, hypertension, COPD, and heart failure) on smoking cessation rates.
2. To compare smoking cessation rates according to the type of heart failure [heart failure with preserved ejection fraction (HFpEF) vs. heart failure with reduced ejection fraction (HFrEF)].
3. To analyze the influence of demographic variables such as age (>50 years) and gender on smoking cessation outcomes.
4. To assess the association between scores from the Brief Illness Perception Questionnaire (BIPQ) and smoking cessation, focusing on the following dimensions:<sup>6</sup>
  - Perceived severity of illness
  - Emotional response
  - Level of concern
  - Perceived control

These endpoints aim to provide a comprehensive evaluation of both clinical and psychological factors influencing smoking cessation among patients with coronary artery disease.

## METHODS

The study was conducted with the permission University of Health Sciences Gazi Yaşargil Training and Research Hospital Clinical Researches Ethics Committee (Date: 23.05.2025, Decision No: 466). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. This retrospective observational study included 300 patients who underwent coronary angiography and stent implantation in cardiology clinic between September 2024 and March 2025. Patients were divided into two groups: those presenting with ACS (n=150) and those undergoing elective PCI (n=150). Inclusion criteria were age between 35–80 years, active smoking status at admission, and complete follow-up data at 6 months. Exclusion criteria included history of psychiatric illness, participation in structured smoking cessation programs, or loss to follow-up.

## Statistical Analysis

Data collected included demographic characteristics (age, sex), comorbidities (diabetes mellitus, hypertension, COPD, HFpEF, HFrEF), and self-reported smoking status at 6 months. Statistical analysis was performed using SPSS v28. Continuous variables were assessed for normality using the Shapiro-Wilk test and expressed as mean±SD or median (IQR) as appropriate. Categorical variables were expressed as counts (percentages). Comparisons between groups were made using independent Samples t-tests or Mann-Whitney U tests for continuous variables and Chi-square or Fisher's exact test for categorical variables. Univariable logistic regression was used to identify variables associated with smoking cessation. Variables with p<0.10 were entered into multivariable logistic regression models. Statistical significance was set at p<0.05.

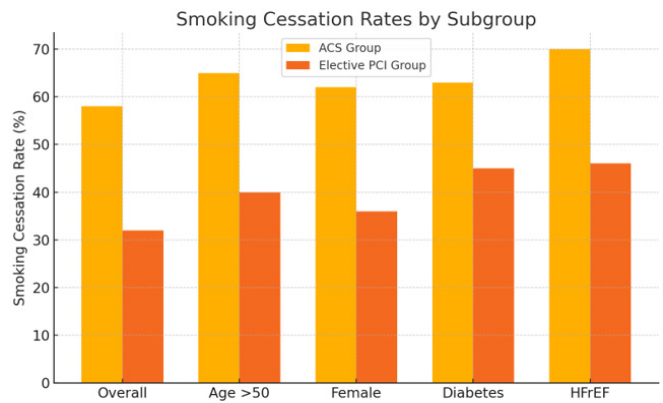
## RESULTS

A total of 300 patients were included in the study. Demographic and clinical characteristics are summarized in **Table 1**. The ACS group had a slightly higher prevalence of diabetes and reduced EF heart failure, while the elective PCI group had a higher incidence of COPD. At 6 months, smoking cessation was reported by 87 (58%) of ACS patients compared to 48 (32%) in the elective PCI group (p<0.001). Subgroup analysis showed significantly higher cessation rates among patients aged >50, females, diabetics, and those with HFrEF (**Figure**). **Table 2** summarizes smoking cessation rates by subgroup.

**Table 1.** Demographic and clinical characteristics of study participants

Variable	ACS group (n=150)	Elective PCI group (n=150)	p-value
Age >50 years (%)	109 (72.7%)	104 (69.3%)	0.53
Male gender (%)	92 (61.3%)	88 (58.7%)	0.68
Female gender (%)	58 (38.7%)	62 (41.3%)	0.68
Diabetes mellitus (%)	60 (40%)	48 (32%)	0.14
Hypertension (%)	64 (42.7%)	56 (37.3%)	0.36
COPD (%)	28 (18.7%)	35 (23.3%)	0.33
HFpEF (%)	16 (10.7%)	23 (15.3%)	0.24
HFrEF (%)	29 (19.3%)	21 (14.0%)	0.22
Subgroup	ACS group quit (%)	Elective PCI group quit (%)	p-value
Overall	58%	32%	<0.001
Age >50	65%	40%	0.01
Female	62%	36%	0.02
Diabetes	63%	45%	0.03
HFrEF	70%	46%	0.02
Perceived severity	8.1±1.0	6.6±1.3	<0.001
Emotional response	7.7±1.2	5.9±1.5	<0.001
Consequences	8.3±1.1	6.3±1.4	<0.001
Illness concern	7.5±1.4	6.0±1.6	<0.01

ACS: Acute coronary syndrome, PCI: Percutaneous coronary intervention, COPD: Chronic obstructive pulmonary disease, HFpEF: Heart failure with preserved ejection fraction, HFrEF: Heart failure with reduced ejection fraction. Values represent means±SD or percentages as indicated. Statistical significance defined as p<0.05



**Figure.** Comparison of smoking cessation rates between ACS and Elective PCI groups across key subgroups. The chart demonstrates consistently higher cessation rates among ACS patients, especially in those with HFrEF and diabetes

Table 2. Smoking cessation rates by subgroup at 6 months			
Subgroup	ACS group quit (%)	Elective PCI group quit (%)	p-value
Overall	58%	32%	<0.001
Age >50	65%	40%	0.01
Female	62%	36%	0.02
Diabetes	63%	45%	0.03
HFrEF	70%	46%	0.02
ACS: Acute coronary syndrome, PCI: Percutaneous coronary intervention, HFrEF: Heart failure with reduced ejection fraction. Values represent means±SD or percentages as indicated. Statistical significance defined as p<0.05			

Psychological evaluation using the BIPQ was conducted in a subset of 300 patients. ACS patients scored significantly higher on perceived severity and emotional response scales (Table 3). Multivariable logistic regression analysis identified ACS presentation and HFrEF as independent predictors of smoking cessation (Table 4).

Table 3. Psychological assessment scores (BIPQ Subset, 300)			
Domain	ACS group (n=150)	Elective PCI group (n=150)	p-value
Perceived severity	8.1±1.0	6.6±1.3	<0.001
Emotional response	7.7±1.2	5.9±1.5	<0.001
Consequences	8.3±1.1	6.3±1.4	<0.001
Illness concern	7.5±1.4	6.0±1.6	<0.01
ACS: Acute coronary syndrome, PCI: Percutaneous coronary intervention, Values represent means±SD. Statistical significance defined as p<0.05.			

Table 4. Multivariable logistic regression for smoking cessation			
Variable	Odds ratio	95% CI	p-value
ACS presentation	2.3	1.5 – 3.6	<0.001
HFrEF	1.8	1.1 – 2.9	0.02
Female gender	1.6	1.0 – 2.6	0.04
Age >50	1.4	0.9 – 2.3	0.08
ACS: Acute coronary syndrome, HFrEF: Heart failure with reduced ejection fraction, CI: Confidence interval, Values represent means±SD or percentages as indicated. Statistical significance defined as p<0.05			

DISCUSSION

This study demonstrates that patients presenting with ACS are more likely to quit smoking after PCI compared to those undergoing elective interventions. The findings suggest that the perceived threat of a life-threatening event such as ACS plays a significant motivational role. In addition, comorbidities such as diabetes and heart failure appear to increase cessation rates, possibly due to increased patient awareness of risk.

Psychological assessment reinforced this conclusion. Higher perceived severity and emotional response scores among ACS patients imply that emotional engagement and illness perception contribute to behavioral change. These results are consistent with the Health Belief Model and prior literature indicating that acute illness can serve as a teachable moment.

The benefits of smoking cessation are substantial and begin soon after quitting. Within 12 months, the risk of coronary events is reduced by nearly 50%, and long-term cessation normalizes cardiovascular risk.<sup>7</sup> Smoking cessation improves survival and reduces recurrent ischemic events in patients with established CAD.<sup>8</sup> Accordingly, international guidelines such as those by the ESC and AHA recommend routine assessment of smoking status and implementation of behavioral and pharmacologic interventions for cessation.<sup>9</sup>

This study’s strength lies in its comprehensive clinical and psychological evaluation. However, it is limited by its retrospective design and reliance on self-reported cessation without biochemical validation. Future studies should employ longitudinal designs and include structured smoking cessation interventions to validate these findings. In addition to perceived health threats, the fear of death experienced during an acute coronary event may play a substantial role in smoking cessation. Patients hospitalized with ACS often undergo emotionally intense situations such as emergency procedures, intensive monitoring, and discussions about mortality risks. This confrontation with potential fatality may trigger a psychological phenomenon known as ‘mortality salience, which can lead to significant behavior change in an effort to prolong life.<sup>10</sup> Such emotionally charged events often serve as powerful motivators, reinforcing the urgency and necessity to quit harmful habits like smoking.

Limitations

First of all our clinical study are retrospective, single centered, and has small number of patients. Future studies may be needed. Another limitation of this study is the lack of data regarding the duration and intensity of smoking (e.g., pack-years). Although cumulative tobacco exposure may influence nicotine dependence and the likelihood of cessation, such information was not consistently available in our retrospective cohort. Importantly, acute events such as ACS may serve as overriding motivational triggers regardless of baseline smoking duration. However, we acknowledge that not accounting for long-term smoking history may have



influenced cessation outcomes. Future prospective studies should include detailed assessments of smoking duration and dependence severity to better evaluate their impact on cessation success.

## CONCLUSION

The clinical presentation of smoking cessation has been demonstrated to exert a significant influence on the process. The present study found that ACS patients were more likely to quit smoking, as evidenced by both statistical and psychological data. It is hypothesised that targeting patients during periods of emotional and health vulnerability may increase the effectiveness of cessation programmes. Personalised interventions should consider both clinical and psychological profiles in order to maximise success. It is evident that cigarette smoking constitutes a significant and modifiable risk factor for CAD. In view of its extensive ramifications for vascular biology and clinical outcomes, smoking cessation should be a fundamental component of both primary and secondary cardiovascular prevention programmes. The implementation of more robust public health policies and clinical strategies is imperative in order to reduce tobacco use and prevent smoking-related cardiovascular events.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was conducted with the permission University of Health Sciences Gazi Yaşargil Training and Research Hospital Clinical Researches Ethics Committee (Date: 23.05.2025, Decision No: 466).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions







All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## REFERENCES

1. Critchley JA, Capewell S. Smoking cessation for the secondary prevention of coronary heart disease. *Cochrane Database Syst Rev*. 2004;4(1):CD003041. doi:10.1002/14651858.CD003041.pub3
2. Kotseva K, Wood D, De Backer G, et al. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients. *Eur J Cardiovasc Prev Rehabil*. 2009;16(2):121-137. doi:10.1097/HJR.0b013e3283294b1d
3. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. *J Consult Clin Psychol*. 1983;51(3):390-395. doi:10.1037/0022-006X.51.3.390
4. Leventhal H, Brissette I, Leventhal EA. The common-sense model of self-regulation of health and illness. In: Cameron LD, Leventhal H, eds. *The Self-Regulation of Health and Illness Behaviour*. London, UK: Routledge; 2003. doi:10.4324/9780203361063\_chapter\_2
5. Broadbent E, Petrie KJ, Main J, Weinman J. The Brief Illness Perception Questionnaire. *J Psychosom Res*. 2006;60(6):631-637. doi:10.1016/j.jpsychores.2005.10.020
6. Fiore MC, Jaén CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update*. Rockville, MD: US Department of Health and Human Services; 2008. doi:10.1037/e527352011-001
7. Tannenbaum MB, Hepler J, Zimmerman RS, et al. Appealing to fear: a meta-analysis of fear appeal effectiveness and theories. *Psychol Bull*. 2015;141(6):1178-1204. doi:10.1037/a0039729
8. Hay JL, Buckley TR, Ostroff JS. The role of cancer worry in cancer screening: a theoretical and empirical review of the literature. *Psychosomatics*. 2005;46(1):2-13. doi:10.1176/appi.psy.46.1.2
9. Clark AM, Spaling MA, Harkness K, et al. Determinants of effective heart failure self-care: a systematic review of patients' and caregivers' perceptions. *Heart*. 2014;100(9):716-721. doi:10.1136/heartjnl-2013-304852
10. Bandura A. *Social foundations of thought and action: a social cognitive theory*. Englewood Cliffs, NJ: Prentice Hall; 1986. doi:10.1037/13273-000



# Comparison of Pan-Immune Inflammatory Index in patients dialysed from catheters and fistulas

 Hakkı Öztürk<sup>1</sup>,  Duygu Felek<sup>2</sup>,  Artuner Varlıbaş<sup>3</sup>,  Aykut Hacıömeroğlu<sup>3</sup>,  
 Zekiye Nur Öztürk<sup>3</sup>,  Aydın Çifci<sup>3</sup>

<sup>1</sup>Infectious Diseases Epidemiologist, Private Ankara Balgat Dialysis Center, Ankara, Türkiye  
<sup>2</sup>Department of Internal Medicine, Faculty of Medicine, Yozgat Bozok University, Yozgat, Türkiye  
<sup>3</sup>Department of Internal Medicine, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

**Cite this article:** Öztürk H, Felek D, Varlıbaş A, Hacıömeroğlu A, Öztürk ZN, Çifci A. Comparison of Pan-Immune Inflammatory Index in patients dialysed from catheters and fistulas. *J Cardiol Cardiovasc Surg.* 2025;3(2):29-34.

**Corresponding Author:** Duygu Felek, d.kocamemik@gmail.com

**Received:** 28/05/2025

**Accepted:** 25/06/2025

**Published:** 27/06/2025

## ABSTRACT

**Aims:** Chronic kidney disease is a group of diseases associated with inflammatory processes, and the risk increases as the stage progresses. Increased inflammation in the disease is associated with mortality and morbidity, and diagnosis and treatment are very important. Arteriovenous fistula is recommended as the first choice for hemodialysis access. Some patients dialysed from catheters. We predict that catheters may cause a chronic inflammatory condition, and we planned this study to demonstrate this.

**Methods:** 242 patients from dialysis patients who applied to Kırıkkale University Internal Medicine Clinic, Ankara Private Balgat Dialysis Center and Yozgat Bozok University Internal Medicine Clinic were included in the study; demographic data (age, gender), history data (chronic diseases, continuously used medications), data regarding hemodialysis duration, laboratory data (HGB, WBC, PLT, MPV, neutrophil, monocyte, lymphocyte, C-reactive protein, urea, creatinine, glomerular filtration rate) of the patients were recorded. Pan-Immune Inflammatory Index (PII) ((neutrophil count x platelet count x monocyte count)/lymphocyte count) were calculated. Differences between hemodialysis vascular access and PII values were statistically analyzed in SPSS package program.

**Results:** According to hemodialysis vascular access routes, it was found that 182 (75.2%) of the patients had fistula dialysis, 60 (24.8%) had catheter dialysis and 85% of the individuals on catheter hemodialysis had permanent catheters, 15% had temporary catheters, 88% had jugular, and 12% had subclavian and femoral catheters. Inflammation levels were calculated with PII. While PII was calculated as  $21125.33 \pm 39621.37$  in patients undergoing hemodialysis through fistulas, it was calculated as  $29745.24 \pm 50905.25$  in patients undergoing hemodialysis through catheters ( $p=0.037^*$ ). In correlation analyses; A strong positive correlation was observed with lymphocyte, monocyte, neutrophil and platelet counts (respectively;  $0.242^{**}$ ,  $0.871^{**}$ ,  $0.888^{**}$ ;  $0.365^{**}$ ). A weak negative correlation was found with the duration of chronic kidney disease ( $-0.242^*$ ).

**Conclusion:** Since there is no directly related parameter developed for analyzing the level of inflammation, there is a need for formulation methods. PII is also a tool used for this purpose. In our study, we analyzed in which cases the increased oxidative stress in hemodialysis is higher with PII and the parameters that trigger it, and as a result, we found higher inflammation in patients hemodialyzed from catheters compared to patients hemodialyzed from fistulas. We concluded that the increased oxidative stress in chronic kidney disease can be further removed from the fistula by hemodialysis or that oxidative stress caused by foreign bodies such as catheters may be higher. For a more definitive decision, further examination is needed by evaluating before and after hemodialysis and examining individuals with chronic kidney disease who are on hemodialysis and those who are not.

**Keywords:** Chronic kidney disease, inflammation, Pan-Immune Inflammatory Index, catheter, fistula

## INTRODUCTION

Chronic kidney disease is a disease that causes systemic inflammatory processes; as the stage of the disease progresses, inflammation increases. Increasing inflammation in stage-5 dialysis patients has brought many problems with it.<sup>1,2</sup> Realizing and preventing this situation, which is quite difficult to detect, will contribute positively to mortality and morbidity.<sup>3</sup> The reference ranges of C-reactive protein, one

of the indicators of inflammation, have also become open to interpretation as the stage progresses in chronic kidney disease. However, since biomarkers such as C-reactive show a more significant increase in infection as well as inflammation, the need for new biomarkers to detect infection-related inflammation has increased.<sup>4</sup> Although there are many biomarker studies on this subject in the literature, many of

them have not been routinely used in clinical practice due to factors such as effective results and cost.<sup>5</sup> For this reason, it is still very valuable to detect inflammation with routinely studied tests in clinical practice.

Many studies have been conducted on inflammation in chronic kidney disease, such as hemopoietic cells, vitamin levels, nutritional status, and the presence of nutrition.<sup>6,7</sup> However, most of them have been treated by physicians, some of which are treatable and some of which are incurable. The modifiable factors of dialysis are; method, vascular access route, dialysate, dialyzer, and when these are examined, not every method is suitable for every patient, but the more widespread use of hemodialysis compared to peritoneal dialysis has made it more possible to investigate this group.<sup>8,9</sup> Various vascular interventional methods are used during dialysis treatment. The first of the two main methods is the use of a catheter in hemodialysis treatment, which allows blood to be taken out of the body, and the fistula method, which allows blood to return to the body by opening a direct vascular access.<sup>10,11</sup> These two methods can significantly affect patients' compliance with treatment, quality of life, and long-term survival. However, there are some complications associated with both methods and inflammatory processes that can affect the immune system.<sup>12</sup> During hemodialysis applications, some systemic inflammatory responses can be observed with both methods used. These responses can affect the response of patients to treatment, the development of infection, vascular occlusion and other cardiovascular complications. Therefore, evaluating the effects of both treatment methods on inflammatory processes is important for an optimal approach in the treatment process.<sup>13</sup>

Pan-Immune Inflammatory Index (PII) ((neutrophil count x platelet count x monocyte count)/lymphocyte count) is a tool used to measure systemic inflammation, and how this indicator changes in patients receiving dialysis treatment is an important research question. Whether catheter and fistula use have different effects on this inflammatory index can provide important information about the treatment processes of patients. Although fistula use is generally seen as longer lasting and less complicated, dialysis treatment with catheters is preferred for some patients because it provides faster access. The aim of the study is to better understand the advantages and disadvantages of both treatment methods by comparing their effects on inflammatory responses and to provide guidance for clinical applications.<sup>14,15</sup>

## METHODS

### Ethics

The study was initiated after obtaining ethics committee approval from Yozgat Bozok University Non-interventional Clinical Researches Ethics Committee (Date: 09.04.2025, Decision No: 457). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

### Patients and Methods

The retrospective study was planned to include dialysis patients who applied to Kırıkkale University Internal Medicine Clinic, Ankara Private Balgat Dialysis Center, and Yozgat Bozok University Internal Medicine Clinic between

January 2025 and February 2025. A total of 242 individuals were included in the study. The data to be obtained within the scope of the study were obtained from anamnesis and clinical course forms. In addition, they were recorded from the hospital information system and laboratory system. Demographic data (age, gender), data regarding the past history (chronic diseases, continuously used medications), data regarding the duration of hemodialysis, laboratory data (HGB, WBC, PLT, MPV, neutrophil, monocyte, lymphocyte, C-reactive protein, urea, creatinine, glomerular filtration rate) were recorded. PII ((neutrophil count x platelet count x monocyte count)/lymphocyte count), a biomarker used to measure systemic inflammation, was calculated. Differences between hemodialysis vascular access and PII values were analyzed statistically.

**Inclusion criteria:** Patients over 18 years of age with a diagnosis of chronic renal failure and on routine hemodialysis for at least one year.

**Exclusion criteria:** Patients under 18 years of age, patients on temporary hemodialysis (such as acute renal failure, intoxication, electrolyte imbalance), patients with signs of active infection, pregnancy, breastfeeding, patients with active malignancy, patients with a known history of rheumatologic disease, patients with a history of renal transplantation, patients receiving anti-inflammatory medical treatment, and patients who had surgery within the last 3 months.

### Statistical Analysis

Data were evaluated with SPSS 22.00 package program and descriptive statistics were expressed as number (n), frequency (%), mean (Mean), standard deviation ( $\pm$ SD) in statistical analyses. Kolmogorov-Smirnov test was used to analyze the normality distribution of the data. Chi-square test was used to compare categorical variables. Independent groups T-test was used to compare two groups for normally distributed data and nonparametric Mann-Whitney U Test was used for non-normally distributed data. Chi-square test was used to compare the data. Statistically,  $p < 0.05$  was considered significant.

## RESULTS

According to hemodialysis vascular access routes, 182 (75.2%) of the patients were dialyzed via fistula, 60 (24.8%) were dialyzed via catheter, 85% of the patients with hemodialysis via catheter had permanent catheters, 15% had temporary catheters, 88% had jugular catheters, and 12% had subclavian and femoral catheters. The mean duration of hemodialysis due to chronic renal failure was 6.37 years. The mean glomerular filtration rate was calculated as 7.28. Of the 242 individuals included in the study, 145 (59.9%) were male and 97 (40%) were female. There was no statistically significant difference between the two genders. The mean age of the individuals included in the study was calculated as 63.53 years and there was no statistically significant difference between the groups in terms of age.

Monocyte, lymphocyte, neutrophil and platelet levels were recorded. No statistically significant difference was found between the hemogram findings of the two groups; the results of the analysis were calculated as  $p = 0.731$ ,

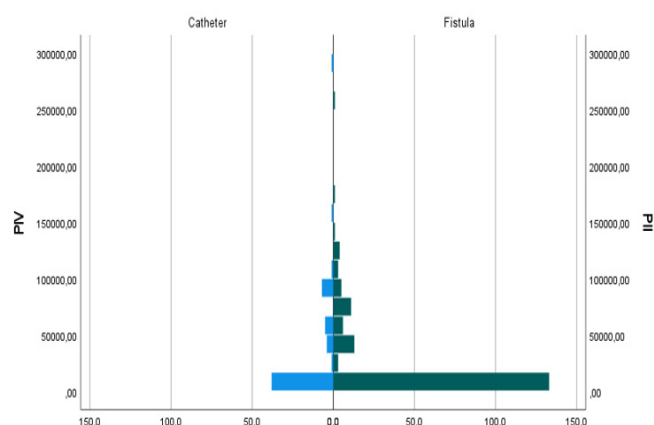
$p=0.244$ ,  $p=0.154$ ,  $p=0.654$ , respectively. PII was calculated as  $21125.33 \pm 39621.37$  in patients receiving hemodialysis through fistula and  $29745.24 \pm 50905.25$  in patients receiving hemodialysis through catheter ( $p=0.037^*$ ) (**Table 1**).

**Table 1.** Comparison of general data and Pan-Immune Inflammatory Index with hemodialysis access route

	Fistula (n=182)		Catheter (n=60)		P
	Mean	STD	Mean	STD	
Age (years)	63.53	11.41	63.57	16.73	0.304
Disease duration of time	6.81	7.11	5.05	5.57	0.050
Lymphocytes	4.44	8.21	4.69	8.54	0.731
Monocytes	4.16	5.63	5.32	10.79	0.244
Neutrophils	27.50	28.63	33.57	31.94	0.154
Platelets	200.17	68.40	202.60	76.91	0.654
CRP	16.14	22.70	17.61	26.61	0.492
PII	21125.33	39621.37	29745.24	50905.25	0.037*

CRP: C-reaktif protein, PII: Pan-Immune Inflammatory Index

Inflammation levels were calculated with the PII. Inflammation was found to be higher in individuals receiving hemodialysis through catheter compared to individuals receiving hemodialysis through fistula (**Figure**).



**Figure.** Hemodialysis vascular access route

PII (neutrophil count x platelet count x monocyte count)/lymphocyte count) calculation is a formulation that is directly proportional to neutrophil, platelet and monocyte counts and inversely proportional to lymphocyte count. When the correlation results were evaluated in accordance with this formula, strong positive correlations were observed with monocyte, platelet and neutrophil counts, while positive correlations were observed with lymphocyte counts, as expected. In correlation analyses, strong positive correlations were observed between PII and lymphocyte, monocyte, neutrophil and platelet counts (0.242\*\*, 0.871\*\*, 0.888\*\*, 0.888\*\*, 0.365\*\*, respectively). There was a weak negative correlation between duration of chronic kidney disease and PII (-0.242\*) (**Table 2**).

When the presence of chronic diseases other than chronic kidney disease was evaluated, it was observed that 137

patients had diabetes mellitus and 153 patients had hypertension. When the relationship between each of these diseases and PII was evaluated separately, PII was calculated as  $27533.12 \pm 49497.57$  in individuals with diabetes mellitus and PII was calculated as  $24809.33 \pm 43607.57$  in individuals with hypertension; although PII was higher in the presence of chronic diseases, the data were not statistically significant ( $p=0.053$ ;  $p=0.435$ ; respectively) (**Table 3**).

## DISCUSSION

Of the 242 individuals included in the study, 145 (59.9%) were male and 97 (40%) were female; the mean age of the individuals was calculated as  $63.53 \pm 12.89$  and there was no statistically significant difference between the groups in terms of age. The fact that there was no difference between the results of the statistical analysis in terms of age and gender increases the power of the study and the low effect rate of non-modifiable factors. In the most recent report of the Turkish Society of Nephrology, in which the practices and distributions related to hemodialysis across the country were given in 2023, the annual incidence of hemodialysis was calculated as 190.9 in men and 128.6 in women per million population, and it was observed that it was higher in men. It was also noted that the rate of hemodialysis increased with increasing age. In our study, the number of male patients was higher in the male gender in accordance with national data. In our study, 182 (75.2%) patients received dialysis from fistula and 60 (24.8%) from catheter, and 85% of the individuals who received hemodialysis from catheter had permanent catheters, 15% had temporary catheters; 88% had jugular, 12% had subclavian and femoral catheters. In our study, it was observed that the number of individuals receiving hemodialysis through fistula was higher than the number of individuals receiving hemodialysis through catheter and jugular vein was more preferred in the choice of vein for catheter. In the 2023 National Nephrology dialysis and transplantation registry report, it was found that arteriovenous fistula use was 26.58%, arteriovenous graft use was 0.18%, permanent catheter use was 51.44% and temporary catheter use was 21.80%.<sup>16</sup> Our patient profile showed a higher rate of fistula use, which is different from national data. In his evaluation of the vascular access route of hemodialysis patients in clinical practice, he drew attention to the selection of the appropriate method for the appropriate patient. He recommends fistula as the first choice because of the low risk of infection. Although there is evidence that the rate of hospitalization increases with the increased risk of infection caused by hemodialysis with central venous catheters, he concluded that there is insufficient evidence to explain the relationship with infection-induced hospitalization and consequently mortality. It emphasizes the importance of appropriate method and graft selection considering the risks of long-term vascular complications in fistulas.<sup>17</sup>

PII (neutrophil count x platelet count x monocyte count)/lymphocyte count) calculation was formulated as directly proportional to neutrophil, platelet and monocyte count and inversely proportional to lymphocyte count. When our correlation results were evaluated in accordance with this formulation, we observed a strong positive correlation with monocyte, neutrophil and platelet counts as expected (0.871\*\*, 0.888\*\*, 0.365\*\*, respectively), while the positive

**Table 2.** Correlation of Pan-Immune Inflammatory Index with general data and hemogram values

		CKD duration (years)	Lymphocyte	Monocyte	Neutrophil	Platelets	CRP	PII
CKD duration (years)	r							
	P							
Lymphocyte	r	-0.019						
	P	0.766						
Monocyte	r	-0.069	0.459					
	P	0.282	<0.001					
Neutrophil	r	-0.107	0.376	0.748				
	P	0.095	<0.001	<0.001				
Platelets	r	-0.065	0.298	0.215	0.255			
	P	0.316	<0.001	<0.001	<0.001			
CRP	r	0.108	0.029	-0.041	0.048	0.127		
	P	0.096	0.658	0.525	0.455	0.049		
PII	r	-0.127	0.242	0.871	0.888	0.365	<0.001	
	P	0.050	<0.001	<0.001	<0.001	<0.001	0.982	

CKD: Chronic kidney disease, CRP: C-reaktif protein, PII: Pan-Immune Inflammatory Index

**Table 3.** Association between Pan-Immune Inflammatory Index and chronic disease

	Yes	No	p
Diabetes mellitus	27533.12±49497.57	17420.29±30566.12	0.053
Hypertension	24809.33±43607.57	20384.64±41076.65	0.435

correlation with lymphocyte count (0.242\*\*) was thought to be due to the fact that other parameters in the hemogram were higher in individuals with higher lymphocytes. In inflammation, the increase in lymphocytes is not more than the increase in monocytes, neutrophils and platelets. In our study, the minimum duration of hemodialysis due to chronic renal failure was 1 year and the maximum duration was 55 years with a mean of 6.37 years. A weak negative correlation was observed between the duration of chronic kidney disease and PII (-0.242\*), suggesting that hemodialysis due to chronic renal failure reduces inflammation in the long term. Increased inflammation due to chronic renal failure is removed from the body by long-term hemodialysis and further investigation with data related to the frequency of hemodialysis is needed. Inflammation in chronic kidney disease is quite high and the factors that increase and decrease it have been investigated. Because it has been observed that inflammation increases mortality and morbidity.<sup>18</sup> In fact, inflammation has been one of the factors blamed for fibrosis in the clinical course of chronic kidney disease.<sup>19</sup> In our study, we examined the effect of catheter and fistula on systemic inflammation in the group in which end-stage inflammation was considered to be high rather than stage-related inflammation and we found that inflammation was higher in individuals receiving hemodialysis through catheter compared to individuals receiving hemodialysis through fistula. Many studies have addressed infection-related inflammation in hemodialysis patients with catheters.<sup>20</sup> However, it has been concluded that the catheter can be almost as safe as the fistula in patients with clean and regular care and can be used safely in pregnant women when hemodialysis is necessary. However, it was still emphasized that the safest method should be

preferred by informing about vascular access methods before pregnancy.<sup>21</sup> As a result, it was expected that the catheter with a foreign body increased the infection rate by forming a biofilm layer and the associated inflammation was found to be high.<sup>22</sup> However, in our study, we tried to minimize the effect of infection-related inflammation by studying in patients with no evidence of active infection. As a result, we observed that inflammation was high in the patient group with catheter even if there was no current infection. This result proved that there was a qualitative data proving that there was a condition related to inflammation caused by the foreign body. In the study conducted by Çantay et al.<sup>23</sup> in the gastrointestinal system, data on inflammation caused by foreign body were obtained and local inflammation was mentioned. However, the inflammation caused by a foreign body such as a catheter, which was present for a long time in our study, is expected to be more widespread and may reach detectable levels in systemic terms. On the other hand, the results of the analysis also raised the question of whether the catheter would be less effective than the fistula in clearing the existing inflammation. Because according to the analysis results found in the literature, many biomarker studies have been conducted to evaluate inflammation. Malyszko et al.<sup>24</sup> study on inflammation-associated neutrophil gelatinase; Doğan et al.<sup>25</sup> study on Apelin 13; Mohammed et al.<sup>26</sup> study on asymmetric dimethylarginine. It is obvious that these and similar biomarkers have no place in clinical practice. Because high cost and effective results limit the use of these and similar biomarkers. However, in addition to these biomarkers, prediction of inflammation with the results of routine analysis has also been the subject of the literature. The use of leukocyte-related inflammation index not only in hemodialysis patients but also in tremor and studies on inflammation prediction with hematologic laboratory data in patients with lupus are examples.<sup>27,28</sup> Studies have also been conducted in chronic kidney disease and there are studies on additional systemic inflammatory index.<sup>29,30</sup> Unlike the existing studies, our study also examines the relationship of the known increased inflammation with the vascular access route and the duration of chronic kidney disease. The finding



that inflammation was higher with increasing duration of chronic kidney disease did not show that the presence of a catheter increased inflammation more than a fistula, but supported that the catheter could not remove inflammation-related toxins as well as the fistula.

When the etiologic factors of hemodialysis patients were analyzed in our study, it was observed that diabetic and hypertensive nephropathy were the major etiologic factors. Although PII was found to be higher in the presence of chronic diseases other than chronic kidney disease, the data were not statistically significant. This result again increases the power of the study in the relationship between chronic kidney disease and PII. According to national nephrology registry data, diabetes mellitus rate was 34.87% and hypertension rate was 24.42% in individuals undergoing hemodialysis due to end-stage renal failure in our country; however, the frequency of hypertension was found to be higher in our patient profile.<sup>16</sup> In the literature, there are studies evaluating the presence of chronic disease and PII and in the study by Tuzimek et al.<sup>31</sup> no significant difference was observed in the systemic inflammation index used to predict acute coronary syndrome in diabetic patients. In the study by Huang et al.,<sup>32</sup> a positive correlation was observed between fragility fracture in postmenopausal anemic women with type 2 diabetes, indicating that the systemic inflammatory index is a useful tool in predicting this condition. Xiu et al.<sup>33</sup> evaluated the use of the systemic inflammation index as a predictive factor in hypertension follow-up and concluded that it can be used as an early warning parameter in the determination of mortality and poor prognosis. It has been observed that systemic inflammation index has a wide range of studies in chronic diseases.

## CONCLUSION

Inflammation is a problem that occurs in many diseases and conditions and it is very important to detect, prevent and attempt to reduce it. Unfortunately, it is not yet possible to predict the level of inflammation with a single biomarker. Since there is not yet a directly related parameter developed to analyze the level of inflammation, the need for formulation methods is obvious. In our study, PII was used for inflammation assessment. PII is a value calculated by neutrophil count x platelet count x monocyte count/lymphocyte count and has been proven to increase in inflammation. In our study, we analyzed in which conditions the oxidative stress increased in hemodialysis with PII is higher and what are the parameters that trigger it, and as a result, we found that inflammation was higher in patients undergoing hemodialysis through catheter compared to patients undergoing hemodialysis through fistula. It was thought that the increased oxidative stress in chronic kidney disease may be further removed by hemodialysis through fistula or inflammation caused by foreign body such as catheter may be higher. For a more definitive decision, further investigation is needed by examining pre- and post-hemodialysis evaluation in individuals with chronic kidney disease with and without hemodialysis.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was initiated after obtaining ethics committee approval from Yozgat Bozok University Non-interventional Clinical Researches Ethics Committee (Date: 09.04.2025, Decision No: 457).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## REFERENCES

1. Dai L, Golembiewska E, Lindholm B, Stenvinkel P. End-stage renal disease, inflammation and cardiovascular outcomes. *Contrib Nephrol*. 2017;191:32-33. doi:10.1159/000479254
2. Gupta J, Mitra N, Kanetsky PA, et al. Association between albuminuria, kidney function, and inflammatory biomarker profile in CKD in CRIC. *Clin J Am Soc Nephrol*. 2012;7(12):1938-46. doi:10.2215/CJN.02020212
3. Jankowska M, Cobo G, Lindholm B, Stenvinkel P. Inflammation and protein-energy wasting in the uremic milieu. *Contrib Nephrol*. 2017;191:58-71. doi:10.1159/000479256
4. Cobo G, Lindholm B, Stenvinkel P. Chronic inflammation in end-stage renal disease and dialysis. *Nephrol Dial Transplant*. 2018;33(3):35-40. doi:10.1093/ndt/gfy175
5. Akar HH, Köse M. Enflamatuvar biyobelirteçler. TÜSAD Kitapları: Çocuk Göğüs Hastalıkları Kitabı. 2016.
6. Balçık OY, Bora F, Köksoy S, Ersoy FF. Evre 3-5 kronik böbrek hastalarında hematopoetik hücrelerdeki vitamin D reseptör düzeyi ile inflamasyon belirteçlerinin değerlendirilmesi. *Akd Med J*. 2021;8(3):333-341. doi:10.53394/akd.1059539
7. Türkoğlu S, Yılmaz FC. Kronik böbrek hastalarında beslenme durumunun ve malnütrisyon inflamasyon skorunun belirlenmesi: kesitsel bir araştırma. *Türkiye Klinikleri Journal of Health Sciences*. 2022;7(3):678-684. doi:10.5336/healthsci.2022-88994
8. Korkmaz SA, Topbaş E. Böbrek sağlığının korunması ve böbrek hastalıklarının önlenmesinde ulusal ve uluslararası eylem planları. *NefroHemDergi*. 2023;18(1):45-61. doi:10.47565/ndthdt.2023.67
9. Seyahi N, Süleymanlar G. Türkiye'de renal replasman tedavilerinin güncel durumu: Türk Nefroloji Derneği kayıt sistemi 2014 yılı özet raporu. *Türk Neph Dial Transpl*. 2018;27(2):133-139. doi:10.5262/ndt.2016.1002.02
10. Bailie GR, Larkina M. Clinical outcomes and complications in hemodialysis patients with central venous catheters versus arteriovenous fistulas. *Kidney Int*. 2020;97(6):1193-1204. doi:10.1016/j.kint.2019.12.008
11. Foley RN, Collins AJ. End-stage renal disease in the United States: an update on the epidemiology and health outcomes. *Kidney Int*. 2011;79(4):290-296. doi:10.1038/ki.2010.446



12. Murray MD, Smith MR. Inflammatory markers in chronic kidney disease and dialysis. *Kidney Dis.* 2019;5(3):145-153. doi:10.1159/000504244
13. Pohl MA, Hsu RK. Immune system activation in dialysis patients: impact of arteriovenous access type. *Nephrol Dial Transplant.* 2022; 37(11):1982-1990. doi:10.1093/ndt/gfz139
14. Snaedal SJ, Gislason GH. Impact of central venous catheters on dialysis-related infection risk and outcomes. *Hemodial Int.* 2015;19(3):305-313. doi:10.1111/hdi.12285
15. Hernandez LA, Salazar JF. Comparative analysis of inflammatory responses in dialysis patients with different vascular access types. *Clin Nephrol.* 2017;88(2):86-92.
16. National Nephrology, Dialysis and Transplantation Registry Report of Turkey 2023.
17. Lok CE, Huber TS, Lee T, et al. KDOQI clinical practice guideline for vascular access: 2019 update. *Am J Kidney Dis.* 2020;75(4):1-164. doi:10.1053/j.ajkd.2019.12.001
18. Çiftçi D, Tüzün Özdemir S, Karadakovan A. Böbrek hastalıklarını önlemeye yönelik evrensel önlemler. Sunum. 2. Uluslararası Sağlık Araştırmaları Kongresi (ICOHER'22); 2022; İstanbul, Türkiye.
19. Panizo S, Martínez-Arias L, Alonso-Montes C, et al. Fibrosis in chronic kidney disease: pathogenesis and consequences. *Int J Mol Sci.* 2021; 22(1):408. doi:10.3390/ijms22010408
20. Ponce D, Nitsch D, Ikizler TA. Strategies to prevent infections in dialysis patients. *Semin Nephrol.* 2023;43(5):151467. doi:10.1016/j.semnephrol.2023.151467
21. Jesudason S, Hewawasam E, Moloney B, et al. Comparison of catheters or new arteriovenous fistulas for commencement of haemodialysis in pregnant women with chronic kidney disease: an international observational study. *J Nephrol.* 2022;35(6):1689-1698. doi:10.1007/s40620-022-01288-y
22. Can İN. Hastane kökenli pnömoni etkeni Klebsiella ve Acinetobacter kökenlerinde biyofilm yapımı ve antibakteriyel duyarlılığın araştırılması [tez]. İzmir: Dokuz Eylül Üniversitesi; 2021.
23. Çantay H, Anuk T, Sülü B, Binnetoğlu K, Allahverdi T, Gönüllü D. Üst gastrointestinal sistemde yabancı cisimlerin değerlendirilmesi: tanı ve tedavi. *The Med J Mustafa Kemal Univ.* 2021;12(44):186-190. doi:10.17944/mkutfd.935615
24. Malyszko J, Malyszko JS, Koc-Zorawska E, Kozminski P, Mysliwiec M. Neutrophil gelatinase-associated lipocalin in dialyzed patients is related to residual renal function, type of renal replacement therapy and inflammation. *Kidney Blood Press Res.* 2010;32(6):464-469. doi:10.1159/000321021
25. Doğan İ, Kahvecioğlu S, Eser B, et al. Periton diyaliz hastalarında serum apelin-13'ün inflamasyon ve kardiyak morfoloji için önemi. *Türk Nefroloji Diyaliz ve Transplantasyon Dergisi.* 2018;27(2):133-139.
26. Mohammed ZN. Diyaliz hastalarında galektin-3 ve asimetrik dimetilarginin (ADMA) ilişkisi. Selçuk Üniversitesi, Sağlık Bilimleri Enstitüsü. 2024.
27. Aygün D, Dundar B. The relationship between leukocyte-based inflammation indices and essential tremor. *Turk J Clin Lab.* 2024;15(3): 473-480. doi:10.18663/tjcl.1503503
28. Ermurat S, Tezcan D. Sistemik lupus eritematozus hastalarında inflamasyon belirtici ve yüksek hastalık aktivite göstergesi olarak yeni hematolojik indeksler. *Uludağ Üniversitesi Tıp Fakültesi Dergisi.* 2022; 48(2):189-196. doi:10.32708/uutfd.1110778
29. Gao C, Gao S, Zhao R, et al. Association between systemic immune-inflammation index and cardiovascular-kidney-metabolic syndrome. *Sci Rep.* 2024;14(1):19151. doi:10.1038/s41598-024-69819-0
30. Gu L, Xia Z, Qing B, et al. Systemic inflammatory response index (SIRI) is associated with all-cause mortality and cardiovascular mortality in population with chronic kidney disease: evidence from NHANES (2001-2018). *Front Immunol.* 2024;15:1338025. doi:10.3389/fimmu.2024.1338025
31. Tuzimek A, Dziedzic EA, Beck J, Kochman W. Correlations between acute coronary syndrome and novel inflammatory markers (systemic immune-inflammation index, systemic inflammation response index, and aggregate index of systemic inflammation) in patients with and without diabetes or prediabetes. *J Inflamm Res.* 2024;17:2623-2632. doi: 10.2147/JIR.S454117
32. Huang D, He Q, Pan J, et al. Systemic immune-inflammatory index predicts fragility fracture risk in postmenopausal anemic females with type 2 diabetes mellitus: evidence from a longitudinal cohort study. *BMC Endocr Disord.* 2024;24(1):256. doi:10.1186/s12902-024-01792-1
33. Xiu J, Lin X, Chen Q, et al. The aggregate index of systemic inflammation (AISI): a novel predictor for hypertension. *Front Cardiovasc Med.* 2023; 10:1163900. doi:10.3389/fcvm.2023.1163900

# Role of Systemic Immune-Inflammation Index in predicting multi-territorial atherosclerotic disease in peripheral arterial disease: a retrospective cohort study

 Faruk Serhatlıoğlu<sup>1</sup>,  Yücel Yılmaz<sup>2</sup>,  Cemre Tuğrul<sup>2</sup>,  Halis Yılmaz<sup>3</sup>,  
 Şaban Keleşoğlu<sup>4</sup>

<sup>1</sup>Department of Cardiovascular Surgery, Faculty of Medicine, Niğde Ömer Halisdemir University, Niğde, Türkiye

<sup>2</sup>Department of Cardiology, Kayseri City Training and Research Hospital, Kayseri, Türkiye

<sup>3</sup>Department of Cardiovascular Surgery, Faculty of Medicine, Erciyes University, Kayseri, Türkiye

<sup>4</sup>Department of Cardiology, Faculty of Medicine, Erciyes University, Kayseri, Türkiye

**Cite this article:** Serhatlıoğlu F, Yılmaz Y, Tuğrul C, Yılmaz H, Keleşoğlu Ş. Role of Systemic Immune-Inflammation Index in predicting multi-territorial atherosclerotic disease in peripheral arterial disease: a retrospective cohort study. *J Cardiol Cardiovasc Surg.* 2025;3(2):35-39.

**Corresponding Author:** Şaban Keleşoğlu, dr.s.k@hotmail.com

**Received:** 29/05/2025

**Accepted:** 26/06/2025

**Published:** 27/06/2025

## ABSTRACT

**Aims:** Death in patients with peripheral artery disease (PAD) is most often due to coronary artery disease (CAD) or cerebrovascular accidents (CVA). Systemic Immune-Inflammation Index (SII) can be used as a prognostic indicator in different cardiovascular diseases (CVD), including PAD. Our aim in this study was to investigate the predictive value of SII in detecting the coexistence of other CVD in patients with PAD.

**Methods:** The study included the results of 100 patients who were admitted to the cardiovascular surgery outpatient clinic of our hospital and diagnosed with PAD. PAD, CAD and carotid artery disease (CAAD) were diagnosed by history, physical examination, electrocardiography, duplex ultrasonography and ankle-brachial index (ABI) calculation. SII was determined as neutrophil count multiplied by platelet count and divided by lymphocyte count.

**Results:** 38 patients had CAAD, 28 had CAD, 19 had only PAD and 15 had all 3 diseases. Platelets levels ( $285 \pm 32.6$  vs  $234 \pm 9.6$ ,  $p < 0.001$ ), Neutrophils levels ( $4.9 \pm 1.1$  vs  $4.1 \pm 9.8$ ,  $p < 0.001$ ) and SII levels ( $4.9 \pm 1.1$  vs  $4.1 \pm 1.8$ ,  $p < 0.001$ ) were compared in both groups with and without other arterial diseases in terms of laboratory findings, while other laboratory findings were not statistically different between both groups ( $p < 0.05$ ).

**Conclusion:** In our study, we found that those with CAD or CAAD had higher SII levels than those with only PAD.

**Keywords:** Peripheral artery disease, Systemic Immune-Inflammation Index, multi-territorial atherosclerotic disease

## INTRODUCTION

Atherosclerosis is a systemic and inflammatory disease that can involve the entire arterial system. The most common types of atherosclerosis are coronary artery disease (CAD), carotid artery disease (CAAD) and peripheral artery disease (PAD). Studies have shown a link between the severity of atherosclerosis in one arterial territory and the occurrence of atherosclerotic disease in other territories.<sup>1-4</sup> In patients with CAAD and carotid artery stenosis  $\geq 70\%$ , 12.5% have PAD and 3.1% have CAD.<sup>5</sup> 24.5% of patients with PAD and 11.1% of patients with CAD have  $\geq 70\%$  carotid artery stenosis.<sup>6</sup> Therefore, in patients with PAD, the cause of death is mostly due to CAD or cerebrovascular events (CVAs).

The Systemic Immune-Inflammation Index (SII), a parameter of inflammation, is a prognostic indicator of adverse outcomes in various types of cancer.<sup>7-9</sup> Furthermore, recent studies have shown that SII, calculated by multiplying neutrophil and

platelet counts multiplied by lymphocyte count divided by lymphocyte count, can be used as a prognostic indicator in different cardiovascular diseases (CVD), including PAD.<sup>10-13</sup>

Our aim in this study was to investigate whether SII can be used to detect the coexistence of other CVDs in patients with PAD.

## METHODS

This study was prepared using data obtained from the Medical Master's Thesis titled "Risk of cardiovascular and cerebrovascular diseases in patients with PAD" which we completed in 2007 (Medical Specialization Thesis, Erciyes University, Faculty of Medicine, Department of Surgical Medical Sciences, Department of Cardiovascular Surgery, Kayseri, Türkiye, 2007 / Thesis No:193683). Our hospital's

Institute of Research Ethics reviewed this study involving human subjects. The study was conducted in accordance with the guidelines set out in the Declaration of Helsinki. The ethics committee was informed about the non-experimental design of the retrospective study and approved the study.

The study included the results of 100 patients who were admitted to the cardiovascular surgery outpatient clinic of our hospital and diagnosed with PAD between 02/2005-09/2006. History and physical examination were recorded. PAD, CAD and CAAD were diagnosed by history, physical examination, electrocardiography, duplex ultrasonography and ankle-brachial index (ABI) calculation. The diagnosis of ABI was made by measuring the systolic pressures of the posterior tibial artery and dorsalis pedis and dividing the higher value by the systolic pressure of the brachial artery. Similar measurements were made in both extremities and the lower ABI value was accepted as the patient's ABI value.<sup>14</sup> PAD classification was performed with Rutherford<sup>15</sup> grading. CAAD was investigated by duplex ultrasonography. The intima-media thickness of the right and left internal carotid artery and the bifurcation area was measured and the presence of a lesion was recorded.

Exclusion criteria for the study were as follows: Patients with a history of acute coronary syndrome, anemia, active infection or systemic inflammatory disease, autoimmune or chronic inflammatory disease, heart failure (ejection fraction <40%), chronic anti-inflammatory drug use, impaired liver and kidney function, ABI greater than 1.3.

Blood samples were collected between 08:00-10:00 in the morning. Antecubital venous blood samples were collected in tubes containing tripotassium EDTA as anticoagulant. All routine biochemical tests and hematologic parameters were evaluated using an autoanalyzer. SII was determined as neutrophil count multiplied by platelet count and divided by lymphocyte count.

### Statistical Analysis

The data analyses were performed using SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA). The distribution of quantitative variables was checked with the Shapiro-Wilk test. Descriptive data were presented as mean±standard deviation and median (interquartile range, IQR) depending on the normality of the distribution. Median and quartile ranges were given for non-normally distributed variables. An independent samples t-test was used for the comparison of quantitative variables with normal distribution, and the Mann-Whitney U test was used for quantitative variables without normal distribution. Categorical variables were compared using the Chi-square test. p values below 0.05 were accepted to show statistically significant.

## RESULTS

A total of 100 patients were included in the study. The mean age was 59.8±13.1 years. 93 of them were male. 58 patients were smokers. 38 patients had CAAD, 28 had CAD, 19 had only PAD and 15 had all 3 diseases. Diabetes mellitus (DM)

was present in 32 patients and hypertension (HT) was present in 46 patients. Patients were divided into 2 groups: those with PAD only and those with concomitant disease in other arterial systems. When demographic characteristics were compared, no difference was observed between the groups in terms of age, gender, history of DM/HT/dyslipidemia, smoking history, body-mass index, heart rate, blood pressure measurements and Rutherford classification ( $p<0.05$ ) (**Table 1**).

**Table 1.** Demographic characteristics of the study populations

	Another artery disease		p value
	Yes (n=81)	No (n=19)	
Variables			
Age (years)	57.8±8.6	61.2±10.1	0.502
Women gender (n, %)	5 (6.2%)	2 (10.5%)	0.455
Diabetes mellitus (n, %)	26 (32.1%)	6 (31.6%)	0.655
Hypertension (n, %)	36 (44.4%)	10 (52.6%)	0.672
Dyslipidemia	19 (23.5 %)	4 (21%)	0.391
Carotid artery disease (n, %)	38 (46.9%)	0 (46.3%)	-
Coronary artery disease (n, %)	28 (34.6%)	0 (6.9%)	-
Smoking (n, %)	47 (58%)	11 (57.9%)	0.145
Body-mass index (kg/m <sup>2</sup> )	28.3±4.1	29.5±4.8	0.931
Systolic blood pressure (mmHg)	133.6±13.7	132.8±15	0.654
Diastolic blood pressure (mmHg)	81.7±8.7	84±9.9	0.331
Heart rate	88.1±14.7	92.3± 8.5	0.07
Rutherford classifications (≥3)	22 (27.2%)	5 (26.3%)	0.717

Platelets levels (285±32.6 vs 234±9.6,  $p<0.001$ ), Neutrophils levels (4.9±1.1 vs 4.1±9.8,  $p<0.001$ ) and SII levels (4.9±1.1 vs 4.1±1.8,  $p<0.001$ ) were compared in both groups with and without other arterial diseases in terms of laboratory findings, while other laboratory findings were not statistically different between both groups ( $p<0.05$ ) (**Table 2**).

**Table 2.** Laboratory findings of the study populations

	Another artery disease		p value
	Yes (n=81)	No (n=19)	
Number of patients			
Glucose (mg/dl)	100.5±33.8	91.5±32.1	0.566
Serum creatinine (mg/dl)	0.91±0.41	0.95±0.39	0.620
AST (U/L)	25.2±7.3	22.7±7.9	0.667
ALT (U/L)	27.9±7.5	25.4±7.9	0.723
LDL cholesterol (mg/dl)	149.6±41.1	146.5±53.6	0.089
Hemoglobin (mg/dl)	13.5±2.4	13.8±2.5	0.606
Platelet (10 <sup>3</sup> /μL)	285±32.6	234±9.6	<0.001
White blood cell (10 <sup>3</sup> /μL)	9.4±6.3	8.3±4.1	0.132
Neutrophil (10 <sup>3</sup> /μL)	4.9±1.1	4.1±1.8	<0.001
Lymphocyte (10 <sup>3</sup> /μL)	2.09±0.7	2.25±0.8	0.056
SII	699 (443-1139)	431 (299-599)	<0.02

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase (U/L), LDL: Low-density lipoprotein, SII: Systemic Immune-Inflammation Index

## DISCUSSION

In this study, we reached results that may suggest that SII, which is considered a good inflammatory marker, can be used to predict the presence of CAAD and CAD in patients with PAD.

Peripheral arterial disease (PAD) is a group of diseases that are common and usually related to atherosclerosis, causing morbidity and mortality. It may occur due to living conditions, habits and occupation.<sup>16,17</sup> A significant proportion of patients with PAD have been reported to have CAD.<sup>18-20</sup> Some autopsy studies have shown that almost all patients with severe lower extremity PAD have extensive atherosclerotic disease in the coronary arteries.<sup>20</sup> In addition, a significant association between low ABI values and CAAD has been shown.<sup>21</sup>

As the severity of inflammation increases in the host, it is obvious that inflammation markers will increase accordingly. PAD patients had higher neutrophil counts than CAD patients, suggesting higher inflammation and thus more atherosclerosis in PAD than in CAD patients.<sup>22,23</sup> Bravetti et al.<sup>22</sup> showed that CAD patients with concurrent PAD had higher neutrophil counts than those with CAD alone. Similarly, Rossi et al.<sup>24</sup> in another study showed that blood leukocyte counts in patients with acute myocardial infarction increased in proportion to the plaque density in the carotid arteries. Vidacovic et al.<sup>25</sup> found that patients with atherosclerotic vascular disease had more elevated CRP levels when each peripheral arterial territory was included. In our study, we found that blood neutrophil counts were higher in patients with PAD, regardless of which arterial segment had atherosclerotic disease.

The ABI is an inexpensive and readily available test for the diagnosis of PAD. It has shown improved mortality prediction when PAD is determined to be present based on an ABI  $\leq$  0.9 and when combined with NLR.<sup>26</sup> A higher neutrophil count has been shown to be associated with major adverse cardiovascular events, death and a composite of myocardial infarction, stroke and death in patients with PAD.<sup>27</sup> Aykan et al.<sup>28</sup> claimed in a study that NLR is associated with the prevalence and complexity of PAD. A review by Bhat et al.<sup>29</sup> also evaluated that NLR was an independent predictor of early and mid-term amputation in patients with acute limb ischemia after embolectomy, a predictor of mortality and/or major amputation in critical limb ischemia, and an independent predictor of PAD severity. Songur et al.<sup>30</sup> found a correlation between PLR and higher amputation rate in patients with PAD. In addition, Yalim et al.<sup>31</sup> also claimed a correlation between PLR and NLR in multisite atherosclerosis.

There is a growing body of evidence suggesting that SII, calculated with three, is a stronger predictor of immune and inflammatory status in patients than single-component (neutrophils, lymphocytes, platelets) and two-component (PLR and NLR) inflammatory markers. There are studies showing that high SII levels are superior to NLR and PLR in predicting the risk of clinical outcomes in various diseases.<sup>7,9,11,12</sup> In addition, Zhang et al.<sup>32</sup> found that elevated SII on admission was independently associated with

the presence of plaque thickness and ulceration in acute ischemic stroke. Aktemur et al.<sup>33</sup> found that SII is an effective predictor of mortality risk in patients with iliac artery disease undergoing percutaneous intervention. Higher SII may indicate the possibility of more complex lower extremity arterial disease.<sup>13</sup> Oflar et al.<sup>13</sup> claimed that increased SII levels are an independent predictor of CAAD severity. In our study, we found that those with CAD or CAAD had higher SII levels than those with only PAD. When evaluated together with the literature, it can be speculated that individuals with more inflammation have higher SII levels. Although NLR and PLR levels were not evaluated, when considered together with other study results, it can be concluded that SII is a better inflammatory marker for the detection of those with more extensive atherosclerotic disease.

Considering our results in terms of physiopathologic mechanisms, neutrophils invade the plaque and initiate and/or exacerbate tissue damage and inflammation by directly and indirectly affecting both endothelial and smooth muscle cells through the mediators they secrete.<sup>35,36</sup> With endothelial damage, monocyte/lymphocyte migration to the subendothelial region and subsequent foam cells, fatty streaks, which are the first stage of atherosclerotic plaques, are formed, and then the atherosclerotic plaque progresses with the continuation of slow inflammation. In addition, proteolytic enzymes and growth factors released from monocytes (foam cells) and lymphocytes have important roles in damage and repair.<sup>37</sup> Lymphopenia occurs due to physiological stress and a mechanism such as decreased cell production, tissue-level redistribution or cell apoptosis.<sup>38</sup> With increased lymphocyte apoptosis within the atherosclerotic plaque, plaque development progresses and destabilization occurs within the plaque.<sup>38</sup> Platelets are a key component of the cellular process in hemostasis, as well as being important in maintaining vascular integrity in the absence of injury and protecting against spontaneous bleeding.<sup>39</sup> Platelets regulate lymphocyte activation and influence the function of lymphocyte subpopulations. They also contribute to the migration and proliferation of smooth muscle cells.<sup>37,40,41</sup>

## Limitations

This study has some limitations. The study included a small number of patients and was a single-center, retrospective study. The number of patients in our study may have been insufficient and our data set is quite old. This may have caused unintentional bias in our statistical results. In our study, we only evaluated the presence of CAAD. Therefore, we did not evaluate the carotid artery stenosis rate. Considering that the severity of carotid artery stenosis is related to LVH, this can be considered a limitation of our study. SII levels were calculated only during hospital admission. Furthermore, parameters potentially affecting atherosclerosis, such as VEGF, TGF $\alpha$ - $\beta$ , and NO, were not measured and the lack of a follow-up study does not provide insight into the long-term changes and effects of SII.

## CONCLUSION

Neutrophils and platelets positively influence inflammation and the development of atherosclerotic plaques, whereas a decrease in lymphocytes has a negative effect. These



findings suggest that SII may serve as a more accurate and comprehensive measure to predict immunologic and inflammatory/anti-inflammatory states in the individual. The results of the present study suggest that SII, a useful, simple, easily measurable and inexpensive indicator of inflammatory status, is a powerful inflammatory marker for predicting additional arterial system diseases (CAD and CAAD) in PAD patients. Larger and multicenter studies are needed to better analyze all possible predictors of disease development.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

This study was prepared using data obtained from the Medical Master's Thesis titled "Risk of cardiovascular and cerebrovascular diseases in patients with PAD" which we completed in 2007 (Medical Specialization Thesis, Erciyes University, Faculty of Medicine, Department of Surgical Medical Sciences, Department of Cardiovascular Surgery, Kayseri, Türkiye, 2007 / Thesis No:193683).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.





## REFERENCES

1. Tanimoto S, Ikari Y, Tanabe K, et al. Prevalence of carotid artery stenosis in patients with coronary artery disease in Japanese population. *Stroke*. 2005;36(10):2094-2098. doi:10.1161/01.STR.0000185337.82019.9e
2. Kallikazaros I, Tsioufis C, Sideris S, Stefanadis C, Toutouzas P. Carotid artery disease as a marker for the presence of severe coronary artery disease in patients evaluated for chest pain. *Stroke*. 1999;30(5):1002-1007. doi:10.1161/01.str.30.5.1002
3. Steinvil A, Sadeh B, Arbel Y, et al. Prevalence and predictors of concomitant carotid and coronary artery atherosclerotic disease. *J Am Coll Cardiol*. 2011;57(7):779-783. doi:10.1016/j.jacc.2010.09.047
4. Qureshi AI, Alexandrov AV, Tegeler CH, et al. Guidelines for screening of extracranial carotid artery disease: a statement for healthcare professionals from the multidisciplinary practice guidelines committee of the American Society of Neuroimaging; cosponsored by the Society of Vascular and Interventional Neurology. *J Neuroimaging*. 2007;17(1):19-47. doi:10.1111/j.1552-6569.2006.00085.x
5. Kurvers HA, van der Graaf Y, Blankensteijn JD, Visseren FLJ, Eikelboom BC, SMART Study Group. Screening for asymptomatic internal carotid artery stenosis and aneurysm of the abdominal aorta: comparing the yield between patients with manifest atherosclerosis and patients with risk factors for atherosclerosis only. *J Vasc Surg*. 2003;37(6):1226-1233. doi:10.1016/s0741-5214(02)75140-9
6. Cheng SW, Wu LL, Lau H, Ting AC, Wong J. Prevalence of significant carotid stenosis in Chinese patients with peripheral and coronary artery disease. *Aust N Z J Surg*. 1999;69(1):44-47. doi:10.1046/j.1440-1622.1999.01501.x
7. Ji Y, Wang H. Prognostic prediction of Systemic Immune-Inflammation Index for patients with gynecological and breast cancers: a meta-analysis. *World J Surg Oncol*. 2020;18(1):197. doi:10.1186/s12957-020-01974-w
8. Huang Y, Gao Y, Wu Y, Lin H. Prognostic value of Systemic Immune-Inflammation Index in patients with urologic cancers: a meta-analysis. *Cancer Cell Int*. 2020;20:499. doi:10.1186/s12935-020-01590-4
9. Zhang Y, Lin S, Yang X, Wang R, Luo L. Prognostic value of pretreatment Systemic Immune-Inflammation Index in patients with gastrointestinal cancers. *J Cell Physiol*. 2019;234(5):5555-5563. doi:10.1002/jcp.27373
10. Huang J, Zhang Q, Wang R, et al. Systemic Immune-Inflammation Index predicts clinical outcomes for elderly patients with acute myocardial infarction receiving percutaneous coronary intervention. *Med Sci Monit*. 2019;25:9690-9701. doi:10.12659/MSM.919802
11. Yang YL, Wu CH, Hsu PF, et al. Systemic Immune-Inflammation Index (SII) predicted clinical outcome in patients with coronary artery disease. *Eur J Clin Invest*. 2020;50(5):e13230. doi:10.1111/eci.13230
12. Huang T, Peng Q, Zhang Y, Zhu Z, Fan X. The Systemic Immune-Inflammation Index (SII) and coronary artery lesions in Kawasaki disease. *Clin Exp Med*. 2024;24(1):4. doi:10.1007/s10238-023-01265-0
13. Ofar E, Akdeniz E, Yıldız C, et al. Evaluation of systemic immune-inflammation index for predicting severity of lower extremity arterial disease. *Vascular*. 2024;32(4):797-803. doi:10.1177/17085381241251772
14. Decrinis M, Doder S, Stark G, Pilger E. A prospective evaluation of sensitivity and specificity of the ankle/brachial index in the follow-up of superficial femoral artery occlusions treated by angioplasty. *Clin Invest*. 1994;72(8):592-597. doi:10.1007/BF00227451
15. Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg*. 1997;26(3):517-538. doi:10.1016/s0741-5214(97)70045-4
16. Scalise E, Costa D, Gallelli G, et al. Biomarkers and social determinants in atherosclerotic arterial diseases: a scoping review. *Ann Vasc Surg*. 2025;113:41-63. doi:10.1016/j.avsg.2024.12.076
17. Khan H, Girdhar NR, Massin SZ, et al. Current prognostic biomarkers for peripheral arterial disease: a comprehensive systematic review of the literature. *Metabolites*. 2025;15(4):224. doi:10.3390/metabol15040224
18. Gersh BJ, Rihal CS, Rooke TW, Ballard DJ. Evaluation and management of patients with both peripheral vascular and coronary artery disease. *J Am Coll Cardiol*. 1991;18(1):203-214. doi:10.1016/s0735-1097(10)80241-4
19. Barzilay JI, Kronmal RA, Bittner V, Eaker E, Foster ED. Coronary artery disease in diabetic and nondiabetic patients with lower extremity arterial disease: a report from the Coronary Artery Surgery Study Registry. *Am Heart J*. 1998;135(6 Pt 1):1055-1062. doi:10.1016/s0002-8703(98)70072-9
20. Mautner SL, Mautner GC, Hunsberger SA, Roberts WC. Comparison of composition of atherosclerotic plaques in saphenous veins used as aortocoronary bypass conduits with plaques in native coronary arteries in the same men. *Am J Cardiol*. 1992;70(18):1380-1387. doi:10.1016/0002-9149(92)90285-7
21. Murabito JM, Evans JC, Larson MG, et al. The ankle-brachial index in the elderly and risk of stroke, coronary disease, and death: the Framingham Study. *Arch Intern Med*. 2003;163(16):1939-1942. doi:10.1001/archinte.163.16.1939
22. Brevetti G, Piscione F, Silvestro A, et al. Increased inflammatory status and higher prevalence of three-vessel coronary artery disease in patients with concomitant coronary and peripheral atherosclerosis. *Thromb Haemost*. 2003;89(6):1058-1063.
23. Erren M, Reinecke H, Junker R, et al. Systemic inflammatory parameters in patients with atherosclerosis of the coronary and peripheral arteries. *Arterioscler Thromb Vasc Biol*. 1999;19(10):2355-2363. doi:10.1161/01.atv.19.10.2355
24. Rossi A, Franceschini L, Fusaro M, et al. Carotid atherosclerotic plaque instability in patients with acute myocardial infarction. *Int J Cardiol*. 2006;111(2):263-266. doi:10.1016/j.ijcard.2005.08.030
25. Vidakovic R, Schouten O, Kuiper R, et al. The prevalence of polyvascular disease in patients referred for peripheral arterial disease. *Eur J Vasc Endovasc Surg*. 2009;38(4):435-440. doi:10.1016/j.ejvs.2009.05.006
26. Amrock SM, Weitzman M. Multiple biomarkers for mortality prediction in peripheral arterial disease. *Vasc Med*. 2016;21(2):105-112. doi:10.1177/1358683X15621797
27. Haumer M, Amighi J, Exner M, et al. Association of neutrophils and future cardiovascular events in patients with peripheral artery disease. *J Vasc Surg*. 2005;41(4):610-617. doi:10.1016/j.jvs.2005.01.013



28. Aykan AÇ, Hatem E, Kalaycıoğlu E, et al. Neutrophil-to-lymphocyte ratio may be a marker of peripheral artery disease complexity. *Anatol J Cardiol*. 2016;16(7):497-503. doi:10.5152/AnatolJCardiol.2015.6240
29. Bhat T, Teli S, Rijal J, et al. Neutrophil to lymphocyte ratio and cardiovascular diseases: a review. *Expert Rev Cardiovasc Ther*. 2013; 11(1):55-59. doi:10.1586/erc.12.159
30. Songur M, Simsek E, Faruk O, Kavasoglu K, Alagha S, Karahan M. The platelet-lymphocyte ratio predict the risk of amputation in critical limb ischemia. *J Vasc Med Surg*. 2014;02(04):158. doi:10.4172/2329-6925.1000158
31. Yalim Z, Aldemir M, Emren SV. Association of inflammatory markers with multisite artery disease in patients with peripheral arterial disease. *Clin Investig Arterioscler*. 2021;33(2):55-61. doi:10.1016/j.arteri.2020.08.002
32. Zhang L, Xu X, Zhang X, Jiang S, Hui P. Systemic Immune-Inflammation Index is associated with ulcerative plaque in patients with acute ischemic stroke: a single center exploratory study. *J Clin Ultrasound*. 2024;52(3):295-304. doi:10.1002/jcu.23632
33. Aktemur T, Demirci G, Tasbulak O, et al. A simple predictor for long-term mortality after percutaneous iliac artery intervention: Systemic Immune Inflammatory Index. *Ann Vasc Surg*. 2023;96:276-283. doi:10.1016/j.avsg.2023.03.012
34. Kelesoglu S, Yilmaz Y, Elcik D, et al. Increased serum Systemic Immune-Inflammation Index is independently associated with severity of carotid artery stenosis. *Angiology*. 2023;74(8):790-797. doi:10.1177/00033197221144934
35. Candemir M, Kiziltunç E, Nurkoç S, Şahinarslan A. Relationship between Systemic Immune-Inflammation Index (SII) and the severity of stable coronary artery disease. *Angiology*. 2021;72(6):575-581. doi:10.1177/0003319720987743
36. Balta S, Celik T, Mikhailidis DP, et al. The relation between atherosclerosis and the neutrophil-lymphocyte ratio. *Clin Appl Thromb Hemost*. 2016;22(5):405-411. doi:10.1177/1076029615569568
37. Ross R. Atherosclerosis--an inflammatory disease. *N Engl J Med*. 1999; 340(2):115-126. doi:10.1056/NEJM199901143400207
38. Núñez J, Sanchis J, Bodí V, et al. Relationship between low lymphocyte count and major cardiac events in patients with acute chest pain, a non-diagnostic electrocardiogram and normal troponin levels. *Atherosclerosis*. 2009;206(1):251-257. doi:10.1016/j.atherosclerosis.2009.01.029
39. Li N. Platelet-lymphocyte cross-talk. *J Leukoc Biol*. 2008;83(5):1069-1078. doi:10.1189/jlb.0907615
40. Demirtas S, Karahan O, Yazici S, et al. The relationship between complete blood count parameters and Fontaine's Stages in patients with peripheral arterial disease. *Vascular*. 2014;22(6):427-431. doi:10.1177/1708538114522227
41. Duran M, Gunebakmaz O, Uysal OK, et al. Relation between mean platelet volume and coronary collateral vessels in patients with acute coronary syndromes. *J Cardiol*. 2013;61(4):295-298. doi:10.1016/j.jjcc.2012.12.011

# Recurrent cardiac papillary fibroelastoma with multiple organ embolism. Is it really benign?: a case report

 Osman Fehmi Beyazal<sup>1</sup>,  Özer Kandemir<sup>2</sup>,  İsmail Sapmaz<sup>2</sup>,  Yaman Zorlutuna<sup>2</sup>

<sup>1</sup>Department of Cardiovascular Surgery, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

<sup>2</sup>Department of Cardiovascular Surgery, Bayındır Söğütözü Hospital, Ankara, Türkiye

**Cite this article:** Beyazal OF, Kandemir Ö, Sapmaz İ, Zorlutuna Y. Recurrent cardiac papillary fibroelastoma with multiple organ embolism. Is it really benign?: a case report. *J Cardiol Cardiovasc Surg.* 2025;3(2):40-42.

**Corresponding Author:** Osman Fehmi Beyazal, osmanfehmi beyazal@gmail.com

**Received:** 05/05/2025

**Accepted:** 25/06/2025

**Published:** 27/06/2025

## ABSTRACT

Cardiac papillary fibroelastomas are the second most common benign heart tumor after myxomas. They are usually asymptomatic but may cause embolic symptoms. In this case report, we present a patient who developed acute thrombosis in the lower extremity and was operated for cardiac papillary fibroelastoma in addition to embolectomy. In addition, tumor recurrence developed 2 years later, multiple embolisms occurred in the kidney and spleen, and aortic valve replacement was performed.

**Keywords:** Cardiac papillary fibroelastoma, heart tumor, embolism

## INTRODUCTION

Cardiac papillary fibroelastomas (CFE), accounting for <10% of all cardiac tumors, are the second most common benign heart tumor after myxomas.<sup>1</sup> They are usually asymptomatic and diagnosed incidentally. However, according to the localization and size of the tumor; stroke, myocardial infarction, pulmonary embolism, embolism in extremity arteries, renal artery and splenic artery may occur, sudden cardiac death may develop.<sup>2</sup> In this case report, we present a patient who first developed acute thrombosis in the iliac artery, therefore embolectomy was performed and then cardiac mass was removed, and two years later, kidney and spleen infarction developed and aortic valve replacement (AVR) was performed due to the recurrence of the tumor in the aortic valve.

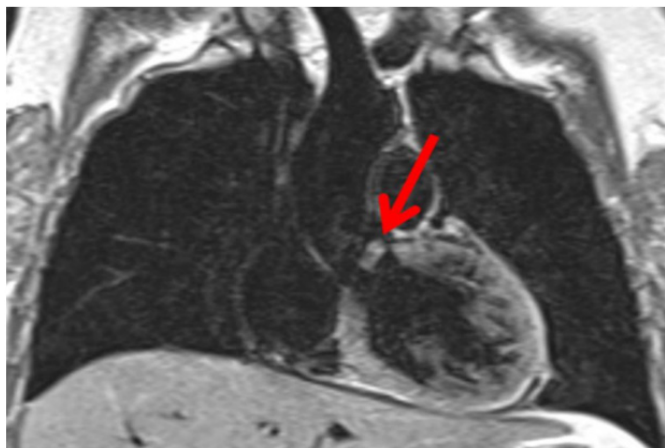
## CASE

Patient consent was obtained for this study. A 50-year-old female patient was admitted to an external center with the complaint of pain in her right leg and embolectomy was performed due to the detection of acute thrombus in the right iliac artery. She was referred to us after a 12x12 mm mass was detected at the level of the aortic valve in the transthoracic echocardiography (TTE). Her vital signs were stable, and there was no abnormality in her examination, history and laboratory parameters. However, due to sudden onset of pain, coldness and color change in the left leg, left femoral embolectomy was performed. She was then operated with a median sternotomy, and a fragile, lobulated mass extending over the aortic valve noncoronary leaflet was removed.

No dysfunction was observed in the aortic valve. Fibrous material was detected in the pathology report of the operation material. After the left femoral embolectomy, the material sent to pathology was also found to be fibrinous material. The patient did not develop any complications in the follow-up, and was discharged with 300 mg of acetylsalicylic acid (ASA).

Two years later, a solid mass of 10x9 mm was detected in the left leaflet of the aortic valve in the TTE of the patient who developed dyspnea. Ejection fraction: 40%, mild mitral regurgitation, moderate aortic regurgitation, and a maximum gradient of 27 mmHg in the aortic valve were detected. Thereupon, cardiac magnetic resonance (MR) was performed to evaluate the recurrence of the mass and other cardiac cavities, and a solid mass was observed in the same place (**Figure 1**). In addition, bilateral renal hypoechoic areas were detected in abdominal ultrasonography. On computed tomography of the abdomen, there was an ischemic lesion area of embolism and infarct areas in the right kidney in the middle and upper pole posterolaterally. There were ischemic areas in the upper pole posterior and lower pole of the left kidney, but no infarction had developed yet (**Figure 2**). In addition, an infarct area due to embolism was detected in the posterosuperior part of the spleen (**Figure 3**).

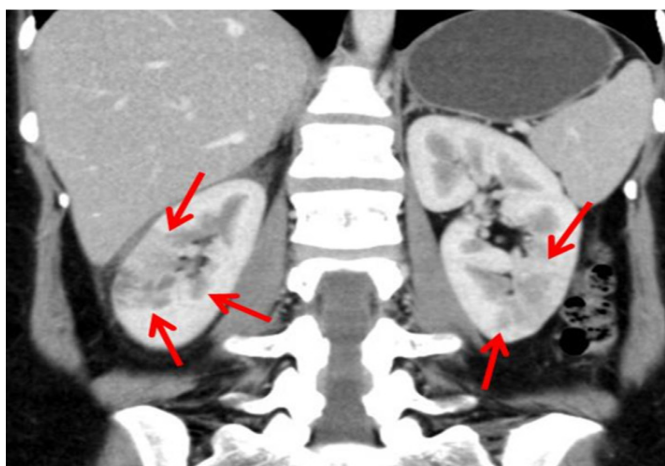
Thereupon, it was decided to re-operate the patient. Median sternotomy was performed at the same place, and there was a 1x1x0.5 cm rough, hard mass on the right aortic leaflet with a broad base, extending between the right and left leaflets, and restricting the movement of both leaflets. The mass



**Figure 1.** Red arrows indicate recurrent cardiac papillary fibroelastoma in the left leaflet of the aortic valve on cardiac magnetic resonance



**Figure 2.** Red arrows indicate ischemic and infarct areas in the kidney on computed tomography



**Figure 3.** Red arrows indicate the area of infarct due to embolism in the posterosuperior part of the spleen on computed tomography

was excised together with the dysfunctional aortic valve. The aortic root was enlarged with the Nick technique using a synthetic graft and a number 23 St. Jude mechanical valve (St. Jude Medical, Minneapolis, USA) was inserted. In the pathology report, it was observed that fibrous connective tissue was formed in the blood-fibrin association. In the

follow-up, the patient was extubated on time and discharged with ASA 300 mg and warfarin.

## DISCUSSION

Primary tumors of the heart are less common than secondary tumors. CFE comes after myxomas, which is the most common heart tumor, and is the second most common heart tumor and has a benign character.<sup>1</sup> CFE consists of a small papillary, pedunculated, avascular tumor covered by a single endothelial layer containing variable amounts of elastic fibrils in the form of collagenous connective tissue in the hyaline stroma.<sup>3</sup> The worldwide prevalence of CFE during autopsies and open heart surgery ranges from 0.02% to 0.45%, respectively.<sup>4</sup> CFE occurs in the aortic valve in 29%, the mitral valve in 25%, the tricuspid valve in 17%, and the pulmonary valve in 13%.<sup>5</sup>

Patients are mostly asymptomatic. Although it is histologically benign, it varies according to the location, size, growth rate and embolization tendency of the tumor; It can cause life-threatening complications such as stroke, valve dysfunction, embolism, myocardial infarction, pulmonary embolism and sudden death. Mechanisms of thromboembolism include tumor embolization and thrombus formation on the tumor. Tumor size may not be an indicator for thromboembolism risk.<sup>6</sup>

Warfarin or antiplatelet therapy can be used in the treatment of small and asymptomatic lesions and may be useful in preventing thromboembolic events.<sup>7</sup> However, surgical removal of tumors larger than 1 cm is recommended due to the risk of embolization and sudden death.<sup>4</sup> Although the need for surgery in small and asymptomatic cases is controversial, embolization has also been reported in a 3 mm tumor.<sup>8</sup> In our case, the size of the tumor was more than 1 cm and we excised it surgically because it was symptomatic. After the first operation, valve functions were observed to be normal and the patient was discharged without complications. However, two years later, recurrence developed in the same place. This time, aortic valve functions were also observed to be impaired. For this reason, this time we had to remove the aortic valve along with the mass, and therefore we performed AVR.

Recurrence is not common because CFE is benign. In our case, the first complaint of the patient was distal arterial embolism, which developed at close intervals and twice. At his second visit, in addition to the recurrence of the tumor, ischemic findings and infarct areas were also detected in the kidney and spleen. Since the coexistence of these conditions is very rare, we think that this case report contributes to the literature. Therefore, cardiac evaluation is extremely important in patients presenting with embolism in the extremity arteries and visceral organs. In the case of recurrent and multiple embolism in patients with a previous history of cardiac tumors, it should be kept in mind that benign tumors may also develop recurrence, and imaging methods such as MR or transesophageal echocardiography (TEE) should be investigated. In addition, the surgical material should

be examined pathologically in patients presenting with embolism.

## CONCLUSION

Although cardiac fibroelastomas are benign, recurrence can be seen. It can cause embolization and should be kept in mind in the differential diagnosis of patients presenting with embolism. Although there is no definite consensus on surgical removal in asymptomatic patients, they should be surgically removed in symptomatic patients.

## ETHICAL DECLARATIONS

### Informed Consent

The patient signed and free and informed consent form.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## REFERENCES

1. Baikoussis NG, Dedeilias P, Argiriou M, et al. Cardiac papillary fibroelastoma; when, how, why? *Ann Card Anaesth*. 2016;19(1):162-165. doi:10.4103/0971-9784.173040
2. Esteban-Lucia L, De la Fuente Batista S, Kallmeyer Mayor AM, Cortes Garcia M. Cardioembolic stroke secondary to an aortic valve fibroelastoma: an increasingly recognized rare cause of stroke. *Stroke*. 2021;52(4):e111-e114. doi:10.1161/STROKEAHA.120.029361
3. Mathis S, Lamy M, Ciron J, et al. Paroxysmal sneezing at the onset of syncope and transient ischemic attack revealing a papillary cardiac fibroelastoma. *Case Rep Neurol Med*. 2014;2014:734849. doi:10.1155/2014/734849
4. Iqbal I, Ullah W, Khan MAA, Haq S, Cheema MA. A case of fibroelastoma with widespread embolism to the brain, kidney, and spleen. *Cureus*. 2019;11(6):e4798. doi:10.7759/cureus.4798
5. Grinda JM, Couetil JP, Chauvaud S, et al. Cardiac valve papillary fibroelastoma: surgical excision for revealed or potential embolization. *J Thorac Cardiovasc Surg*. 1999;117(1):106-110. doi:10.1016/s0022-5223(99)70474-5
6. Boğa M, Durmaz S, Kurtoglu T, Gürcün U, Çulhacı N, Yılmaz M. A rare cause of embolism: cardiac papillary fibroelastoma. *Meandros Med Dent J*. 2018;19(2):171. doi:10.4274/meandros.2109
7. Öz K, Aktürk İF, Ulukan MÖ, Ersoy B, Ereğ E. An unusual presentation of a cardiac papillary fibroelastoma: a case report. *Turkish Journal of Thoracic and Cardiovascular Surgery*. 2014;22(4):826-829. doi:10.5606/tgkdc.dergisi.2014.9549
8. Shahian DM, Labib SB, Chang G. Cardiac papillary fibroelastoma. *Ann Thorac Surg*. 1995;59(2):538-541. doi:10.1016/0003-4975(94)00857-4