E-ISSN 2148-9211

CVSI

CARDIOVASCULAR SURGERY *and* INTERVENTIONS

Official Electronic Journal of the Turkish Society of Cardiovascular Surgery

Turkish Society of Cardiovascular Surgery 1988

Volume: 11 / Number: 3 / November 2024

E-ISSN 2148-9211

CARDIOVASCULAR SURGERY AND INTERVENTIONS

Volume 11 - Number 3 - November 2024

Cardiovascular Surgery and Interventions is the official and periodical journal of the Turkish Society of Cardiovascular Surgery.
It is published three times a year.

The Cardiovascular Surgery and Interventions is indexed in the following database:
TÜBİTAK, ULAKBİM (Turkish Medical Abstracts), Google Scholar, Advanced Sciences Index, Directory of Research Journals Indexing, International Institute of Organized Research (I2OR), International Innovative Journal Impact Factor (IIJIF), Citefactor, ResearchBib, Asos Index, Scientific Indexing Services, J-Gate, Root Indexing, Eurasian Scientific Journal Index, Infobase, Index Copernicus International, SOBIAD, Türkiye Citation Index and TurkMedline

Türk Kalp ve Damar Cerrahisi Derneği adına Sahibi ve Sorumlu Yazı İşleri Müdürü
Levent Yılık

Editorial Contact Person
Şahin Bozok, MD.
Email: drsahinbozok@gmail.com

Executive office / Yönetim Yeri ve Adresi:
Türk Kalp ve Damar Cerrahisi Derneği
Ataşehir Mah., Ataşehir Bulvarı, 48 Ada,
Mimoza 2/2, K: 2, D: 6,
34758 Ataşehir, İstanbul, Türkiye
Tel: +90 216 - 456 14 54
Fax: +90 216 - 456 14 54
Email: info@tkdcd.org
URL: http://www.tkdcd.org

Publisher / Yayıncı
Bayçınar Tıbbi Yayıncılık ve Reklam Hiz. Tic. Ltd. Şti.
Örnek Mah., Dr. Suphi Ezgi Sok., Saray Apt., No: 11, D: 6,
34704 Ataşehir, İstanbul, Türkiye
Tel: +90 216 - 317 41 14
Email: info@baycinartibbiyayincilik.com
Yayıncı Sertifika No: 52284

Type of publication: Periodical
Publication date: October 21, 2024

The control of conformity with the journal standards and the typesetting of the articles in this journal, the control of the English abstracts and references and the preparation of the journal for publishing were performed by Bayçınar Medical Publishing.

Contents

ORIGINAL ARTICLES

CASE REPORTS

LETTERS TO THE EDITOR

Cardiovasc Surg Int 2024;11(3):223
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.53697
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Letter to the Editor Open Access

Response to Letter to the Editor: "Analysis of incorrect referrals to the cardiovascular surgery outpatient clinic"

Ömer Faruk Rahman[1], Fevzi Ayyıldız[2]

[1]Department of Cardiovascular Surgery, Burdur State Hospital, Burdur, Türkiye
[2]Department of Cardiovascular Surgery, Aydın Adnan Menderes University Faculty of Medicine, Aydın, Türkiye

Received: October 10, 2024 ***Accepted:*** October 10, 2024 ***Published online:*** October 17, 2024

We would like to thank the author for their interest in our article titled *"Analysis of Incorrect Referrals to the Cardiovascular Surgery Outpatient Clinic."*[1] We find the OECD (Organisation for Economic Co-operation and Development) data shared by the author, highlighting the insufficiency of the number of physicians, to be noteworthy. As emphasized in our article, ensuring accurate patient referrals to the appropriate outpatient clinics is of critical importance, particularly considering the increasing number of admissions and the growing workload on healthcare professionals. We believe that the recent increase in residency positions in medical specialization in Türkiye may help address the shortage of physicians in the coming years. However, we believe that an increase in the number of physicians alone will not be sufficient to prevent incorrect outpatient clinic referrals.

As we stated in the limitations of our article, we believe that studies investigating the reasons for incorrect patient presentations to the cardiovascular surgery outpatient clinic could provide important contributions to addressing the issue. For this reason, we have recently completed a new study evaluating the causes of incorrect outpatient clinic referrals. We believe that the results of our new study will provide significant insights for identifying key areas to target to prevent incorrect referrals.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Erkan MH. Comment on "Analysis of incorrect referrals to the cardiovascular surgery outpatient clinic". Cardiovasc Surg Int 2024;11:223-2. doi: 10.5606/e-cvsi.2024.1746.

Corresponding author: Ömer Faruk Rahman, MD. İzmir Bakırçay Üniversitesi Tıp Fakültesi, Kalp ve Damar Cerrahisi Anabilim Dalı, 35665 Menemen, İzmir, Türkiye.
E-mail: omerfaruk.rahman@bakircay.edu.tr

Citation:
Rahman ÖF, Ayyıldız F. Response to Letter to the Editor: "Analysis of incorrect referrals to the cardiovascular surgery outpatient clinic". Cardiovasc Surg Int 2024;11(3):223. doi: 10.5606/e-cvsi.2024.53697.

Cardiovasc Surg Int 2024;11(3):143-150
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1693
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Reduction in lung injury in an experimental ischemia-reperfusion model with tranexamic acid: A biochemical and histopathological assessment

Muhammet Fethi Sağlam[1], Zerrin Pulathan[2], Süleyman Caner Karahan[3], Esin Yuluğ[4]

[1]Department of Cardiovascular Surgery, Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara, Türkiye
[2]Department of Cardiovascular Surgery, Karadeniz Technical University Faculty of Medicine, Trabzon, Türkiye
[3]Department of Medical Biochemistry, Karadeniz Technical University Faculty of Medicine, Trabzon, Türkiye
[4]Department of Histology and Embryology, Karadeniz Technical University Faculty of Medicine, Trabzon, Türkiye

Received: June 05, 2024 ***Accepted:*** June 05, 2024 ***Published online:*** September 03, 2024

ABSTRACT

Objectives: This study aimed to investigate the effectiveness of tranexamic acid in reducing lung injury associated with ischemia-reperfusion in rats.

Materials and methods: Twenty-three male Sprague-Dawley rats (aged 2-3 months and weighing 250±30 g) were divided into three groups: sham, ischemia-reperfusion (IR) injury, and tranexamic acid (TA) groups. The rats in the IR and TA groups underwent abdominal aortic clamping for 1 h, followed by 2 h of reperfusion. The TA group received 100 mg/kg tranexamic acid intravenously before clamping. Biochemical and histological evaluations were performed.

Results: Compared to those in the sham group, the plasma myeloperoxidase, malondialdehyde, and serum ischemia-modified albumin levels in the IR group were significantly higher, indicating oxidative stress. Compared to those in the IR group, the ischemia-modified albumin levels in the TA group were significantly lower. Histopathological analysis revealed lung damage in the IR group, which was reduced in the TA group, although the difference was not significant.

Conclusion: Tranexamic acid reduces oxidative stress and local inflammatory responses, mitigating lung reperfusion injury. However, further studies are needed to explore its efficacy in different models and at different doses.

Keywords: Inflammation, ischemia-reperfusion injury, lung injury, oxidative stress, tranexamic acid.

Ischemia is the temporary reduction or cessation of blood flow to a tissue, and reperfusion is the restoration of blood flow.[1] This reduction in blood flow causes tissue damage depending on the duration of ischemia and tissue properties.[2,3] Reperfusion can lead to necrosis, tissue edema, and systemic damage, potentially causing multiple organ failure.[4]

Despite surgical advancements, ischemia-reperfusion (IR) injury remains a key issue in cardiovascular surgery as it can occur after abdominal aortic surgery, emboli, thrombosis, and arterial injuries.[5-7]

The pathogenesis of IR involves tissue injury triggering systemic reactions, neutrophil activation, cytokine release, and the formation of radicals and proteases.[8] In ischemic tissues, blood stasis and hypoxia cause endothelial damage and thrombosis. During reperfusion, tissue plasminogen activator activates plasmin, increasing tissue destruction. Fibrin degradation products block capillaries, affecting distant organs such as the lungs.[9,10]

Studies on IR injury often use chemicals to suppress neutrophils, but research on antifibrinolytic agents is limited.[11,12] These studies show the effects of ischemia and reperfusion on organs, but the pathology is not fully understood.[13-15] Studies show that damage to

Corresponding author: Muhammet Fethi Sağlam, MD. Ankara Yıldırım Beyazıt Üniversitesi Tıp Fakültesi, Kalp ve Damar Cerrahisi Anabilim Dalı, 06800 Çankaya, Ankara.
E-mail: dr.m.fethisaglam@gmail.com

Citation:
Sağlam MF, Pulathan Z, Karahan SC, Yuluğ E. Reduction in lung injury in an experimental ischemia-reperfusion model with tranexamic acid: A biochemical and histopathological assessment. Cardiovasc Surg Int 2024;11(3):143-150. doi: 10.5606/e-cvsi.2024.1693

reperfused tissues and organs is caused by neutrophil products.[10,11] Suppressing neutrophils can prevent damage, indicating a need for further study. Hence, this study aimed to investigate the effect of tranexamic acid (TA) on damage to distant organs caused by aortic ischemia and reperfusion in rats.

MATERIALS AND METHODS

This study utilized 23 healthy male Sprague-Dawley rats (aged 2-3 months and weighing 250±30 g) bred in the laboratory of Karadeniz Technical University Faculty of Medicine. The temperature in the housing and experimental environment was maintained between 20°C and 26°C. The rats were fasted for 12 h before the experiment. The study protocol was approved by the Local Ethics Committee for Animal Experiments of Karadeniz Technical University Faculty of Medicine (date: 18.03.2009, no: 2009/243/1). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Analgesia and anesthesia were achieved by intraperitoneally administering xylazine hydrochloride (Rompun; Bayer AG, Leverkusen, Germany) and ketamine hydrochloride (Ketalar; Pfizer Inc., New York, NY, USA) to the rats in the laboratory. The rats were weighed using an electronic scale, and their weights were recorded. The midline of the abdomen and the anterior neck region were shaved. Under a microscope, a transverse incision was made in the anterior neck region. The left carotid artery and right internal jugular vein were explored and cannulated. The arterial line was connected to a monitor (4113-K Model; Nihon-Kohden, Tokyo, Japan) using a three-way stopcock and transducer set.

After catheterization and monitorization, a median laparotomy was performed by dissecting the skin, subcutaneous tissue, and muscle tissue in the midline of the abdomen. The retroperitoneal region was opened, and the abdominal aorta was explored. After exploration, all subjects received heparin (Nevparine; Mustafa Nevzat İlaç Sanayi A.Ş., İstanbul, Türkiye) to achieve anticoagulation. After heparin administration, saline was given to the subjects in IR group, and TA (Transamin-Fako İlaç A.Ş. İstanbul, Türkiye) was administered via a central venous catheter to the subjects in TA group. In IR and TA groups, the abdominal aorta was clamped with a bulldog clamp at the infrarenal level to induce aortic ischemia. Ischemia was confirmed by the absence of a pulse distal to the clamp, which was also verified by a handheld Doppler device. The ischemia period lasted for 60 min.

In IR and TA groups, the aortic clamp was removed after 1 h of ischemia, and reperfusion was initiated. The revascularization of the previously ischemic areas was confirmed by the return of palpable femoral artery pulses and verified using a handheld Doppler device. Reperfusion lasted for 2 h. At the end of the experiment, arterial blood was collected from the carotid arteries for biochemical analysis, and the rats were then euthanized.

To determine the effect of TA on lung injury in an experimental aortic IR model, rats were divided into three groups: the sham (control) group (n=9), the IR group (n=7), and the TA group (n=7). In the sham group, laparotomy was performed without inducing IR, and blood and tissue samples were taken at the end of the third hour. In the IR group, laparotomy was performed, and the abdominal aorta was explored. Saline was administered via a central venous catheter before clamping the aorta at the infrarenal level to induce 1 h of aortic ischemia. Following ischemia, the clamp was removed, and reperfusion was maintained for 2 h. Blood and tissue samples were collected at the end of the reperfusion period. In the TA group, laparotomy was performed, and the abdominal aorta was explored. To induce 1 h of ischemia, tranexamic acid was administered via a central venous catheter 5 min before aortic clamping. After the ischemic period, the clamp was released, and reperfusion was maintained for 2 h. Blood and tissue samples were collected at the end of the reperfusion period.

After the experimental process, arterial blood was collected from the carotid artery using a blood gas syringe and a 10 mL syringe. The collected blood was transferred into biochemistry tubes, EDTA (ethylenediaminetetraacetic acid) tubes, and citrate tubes. Median sternotomy was performed to expose the trachea, pericardium, and heart. Both of the pleurae were opened to access the lungs. The left lung was clamped at the main bronchus, and an cannula was inserted into the trachea through the neck region. The tip of the cannula was advanced into the right main bronchus for bronchoalveolar lavage (BAL). Phosphate-buffered saline was

administered to the right lung, and the lavage fluid was aspirated and transferred to biochemistry tubes. This process was repeated, resulting in 4 mL of BAL fluid. The left lung was resected and washed with saline to remove clots and particles, and tissue samples were collected for biochemical analysis. The tissue samples were placed in Eppendorf tubes and kept on ice.

Serum alanine transaminase, lactate dehydrogenase, and D-dimer levels were measured, and lactate dehydrogenase levels were also measured in the BAL fluid. The serum and plasma samples obtained by centrifugation were stored at −80°C. Lung tissues were also stored at −80°C for biochemical analysis. The lung tissues collected for histopathological examination were fixed in 10% formaldehyde and processed for further analysis.

At the end of the experiment, tissue samples were taken from specific parts of the lungs of all rats and fixed in 10% formaldehyde. The tissue fragments were dehydrated through a graded alcohol series and cleared with xylene solution. Paraffin blocks of the tissues were prepared, and 5-µm thick sections were cut with a microtome (Leica RM2255; Wetzlar, Germany). After deparaffinization, the sections were stained with hematoxylin-eosin. Histopathological evaluation was performed by a blinded histologist who was unaware of the study groups. Lung tissue damage was assessed semiquantitatively in five different fields at high magnification (×400) using the following microscopic scoring criteria:[16] Grade 0, normal lung morphology; Grade 1, mild intraalveolar edema and mild inflammatory cell infiltration; Grade 2, moderate alveolar edema and moderate inflammatory cell infiltration; Grade 3, severe alveolar edema, severe inflammatory cell infiltration, and focal hemorrhage; Grade 4, diffuse inflammatory cell infiltration and damage to the alveolar structure. Each specimen was scored on a scale of 0 to 4. The mean histological score was calculated for each group.

Statistical analysis

Data were analyzed using the NCSS (Number Cruncher Statistical System) 2007 (NCSS LLC., Kaysville, UT, USA) package. Descriptive statistical methods (mean and standard deviation) were used to summarize the data. The distribution of the variables was assessed with the Shapiro-Wilk normality test. For normally distributed variables, one-way analysis of variance was used for intergroup comparisons. For nonnormally distributed variables, the Kruskal-Wallis test was used for intergroup comparisons. When significant differences were found, post hoc analyses were conducted using the Bonferroni-corrected Mann-Whitney U test to identify specific group differences. A p-value <0.05 was considered statistically significant.

RESULTS

Significant differences were observed in plasma myeloperoxidase (MPO) and malondialdehyde (MDA) levels between the sham and IR groups (p=0.001 for both comparisons) and between the sham and TA groups (p=0.001 for both comparisons), indicating increased inflammation and oxidative stress markers in these groups (Table 1).

Significant differences in tissue MPO and MDA levels were observed between the sham and IR groups

Table 1
Plasma parameters

	Sham group (n=9)	IR group (n=7)	TA group (n=7)	Sham *vs.* IR	Sham *vs.* TA	IR *vs.* TA
	Mean±SD	Mean±SD	Mean±SD	*p*	*p*	*p*
Plasma TAFI	41.56±27.46	50.00±22.82	44.55±10.31	0.53	0.79	0.65
Plasma TAT	2.87±0.14	3.06±0.25	3.07±0.22	0.12	0.11	0.95
D-dimer	0.23±0.04	0.27±0.07	0.27±0.04	0.34	0.28	0.92
Plasma MPO	1690.52±332.34	2795.87±374.96**	2551.23±476.90**	0.001*	0.001*	0.18
Plasma MDA	0.31±0.04	0.43±0.04**	0.46±0.04**	0.001*	0.001*	0.27

SD: Standard deviation; IR: Ischemia-reperfusion; TA: Tranexamic acid; TAFI: Thrombin-Activatable Fibrinolysis Inhibitor; TAT: Thrombin-Antithrombin Complex; MPO: Myeloperoxidase; MDA:Malondialdehyde; * p<0.05 *vs.* the IR group; ** p<0.05 *vs.* Sham group.

Table 2
Tissue parameters

	Sham group (n=9)	IR group (n=7)	TA group (n=7)	Sham *vs.* IR	Sham *vs.* TA	IR *vs.* TA
	Mean±SD	Mean±SD	Mean±SD	*p*	*p*	*p*
Tissue MPO	3533.76±219.32	3981.59±164.44**	4068.98±233.62**	0.001*	0.001*	0.23
Tissue MDA	4.52±0.13	5.66±0.48**	4.85±0.58*	0.001*	0.15	0.006*

SD: Standard deviation; IR: Ischemia-reperfusion; TA: Tranexamic acid; MPO: Myeloperoxidase; MDA: Malondialdehyde; * p<0.05 *vs.* IR group; ** p<0.05 *vs.* Sham group.

(p=0.001 for both comparisons) and between the sham and TA groups (p=0.001 for both comparisons), indicating increased levels of neutrophil activity and lipid peroxidation in these groups. Compared to those in the IR group, the tissue MDA levels in the TA group were significantly lower (p=0.006), suggesting that TA may help mitigate lipid peroxidation (Table 2).

Significant differences in serum ischemia-modified albumin (IMA) levels were detected between the sham and IR groups (p=0.007) and between the IR and TA groups (p=0.001), indicating varying levels of IMA (Table 3).

Significant differences were observed in partial pressure of carbon dioxide between the IR and TA groups (p=0.03) and in histological scores between the sham and IR groups (p=0.008) and the sham and TA groups (p=0.012), indicating varying levels of respiratory function and histological damage (Table 4).

Table 3
Serum parameters

	Sham group (n=9)	IR group (n=7)	TA group (n=7)	Sham *vs.* IR	Sham *vs.* TA	IR *vs.* TA
Parameters	Mean±SD	Mean±SD	Mean±SD	*p*	*p*	*p*
Serum IMA	0.44±0.03	0.51±0.03*	0.42±0.04**	0.007*	0.62	0.001*
Serum ALT	70.66±21.23	99.14±49.71	61.57±11.85	0.14	0.57	0.09
Serum LDH	882.00±521.22	933.42±441.73	770.28±344.26	0.78	0.57	0.53
BAL-LDH	657.55±424.39	676.85±401.52	801.42±310.81	0.92	0.49	0.46

SD: Standard deviation; IR: Ischemia-reperfusion; TA: Tranexamic acid; IMA: Ischemia-modified albumin; ALT: Alanine transaminase; LDH: Lactate dehydrogenase; BAL: Bronchoalveolar lavage; * p<0.05 *vs.* the IR group; ** p<0.05 *vs.* the Sham group.

Table 4
Arterial blood gas and histological parameters

	Sham group (n=9)	IR group (n=7)	TA group (n=7)	Sham *vs.* IR	Sham *vs.* TA	IR *vs.* TA
Parameters	Mean±SD	Mean±SD	Mean±SD	*p*	*p*	*p*
pH	7.22±0.14	7.18±0.14	7.30±0.03	0.68	0.32	0.17
PO_2	105.68±24.25	79.38±24.84	105.38±30.39	0.05	0.97	0.07
PCO_2	51.43±14.55	70.62±27.57	45.30±11.81*	0.07	0.40	0.03*
HCO_{3-}	21.12±3.05	20.21±3.13	20.08±2.97	0.55	0.45	0.88
BE	–5.50±5.17	–5.31±3.02	–4.84±3.70	0.90	0.65	0.76
SaO_2	94.40±6.42	84.82±20.41	95.50±2.98	0.10	0.82	0.09
Histological score	1.22±1.09	2.85±0.69**	2.71±0.75**	0.008*	0.012*	0.60

SD: Standard deviation; IR: Ischemia-reperfusion; TA: Tranexamic acid; PO_2: Partial pressure of oxygen; PCO_2: Partial pressure of carbon dioxide; HCO_{3-}: Bicarbonate; BE: Base excess; SaO_2: Oxygen saturation; * p<0.05 *vs.* IR group; ** p<0.05 *vs.* Sham group.

Histopathological examination of the lung tissues revealed normal lung tissue in the sham group. In the IR group, widespread leukocyte infiltration, thrombus in the arterioles, significant degeneration in the alveolar structure, and interalveolar hemorrhage were observed. In the TA group, leukocyte infiltration was decreased compared to that in the IR group, and no thrombi were observed in the arterioles. Interalveolar hemorrhage was also reduced compared to that in the IR group, but diffuse interstitial edema was still present. Hematoxylin-eosin-stained lung tissue samples examined under a light microscope are shown in Figure 1.

DISCUSSION

Reperfusion injury is a significant issue observed in various clinical conditions where ischemic tissues and organs are revascularized. Such conditions include thoracic aortic surgery, abdominal aortic surgery, surgical interventions on lower extremity arteries, and organ transplantation.[17,18] While local damage occurs in target organs in these situations, significant damage also occurs in distant organs, particularly the lungs.[19] Lung damage is a significant concern that increases mortality and morbidity.[20,21]

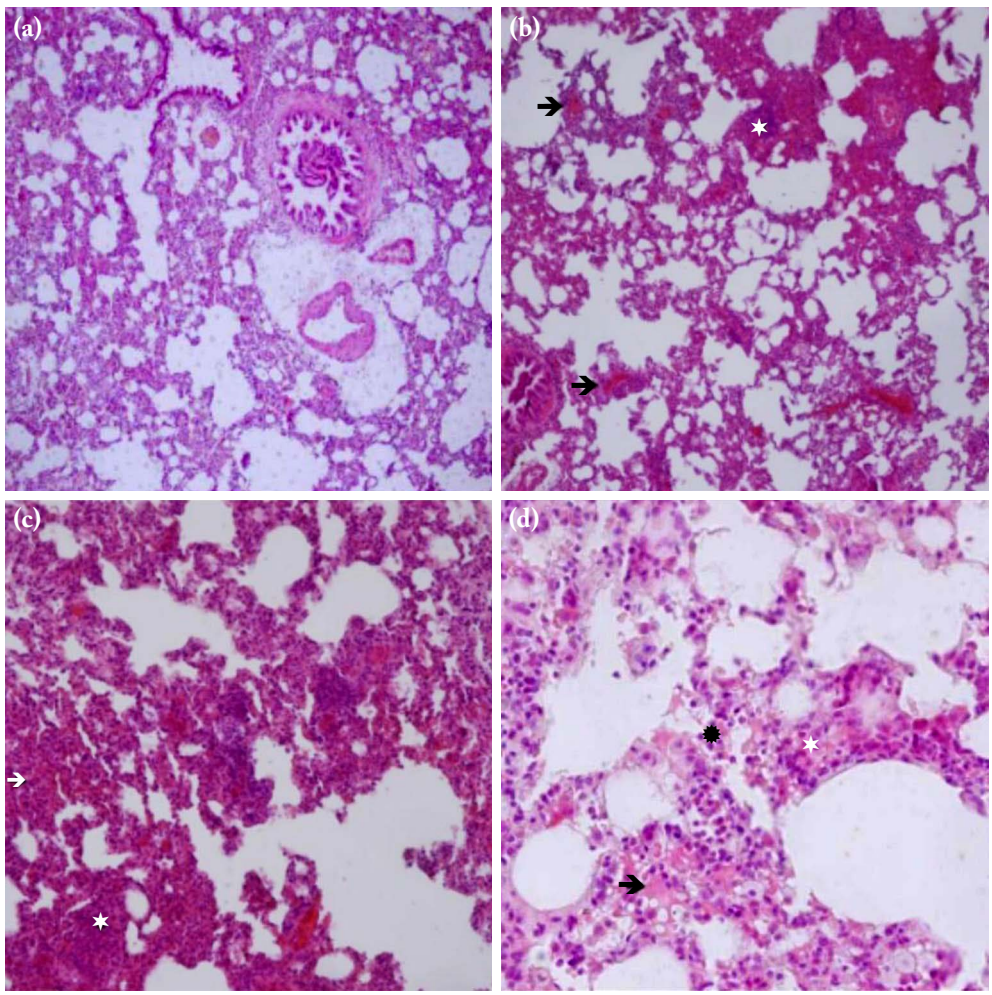


Figure 1. Histological examination of lung tissues. **(a)** Sham group, (H-E, ×100). **(b)** IR group, diffuse leukocyte infiltration (★) and thrombus in arterioles (➔) (H-E, ×100). **(c)** IR group, marked degeneration in alveolar structure (★), interalveolar hemorrhage (➔) (H-E, ×200). **(d)** TA group: Less interalveolar hemorrhage (★), damage to the alveolar structure (✹) and widespread interstitial edema (➔) compared to IR group (H-E, ×200).
IR: Ischemia-reperfusion; TA: Tranexamic acid.

The primary pathogenic factor in reperfusion injury is the generation of free radicals in tissues revascularized after ischemia. These free radicals cause necrosis by damaging cellular structures, particularly through lipid peroxidation of cell membranes. The main source of these free radicals is the neutrophils activated during this process.[22] Neutrophils activated during reperfusion at the site of local damage play a role in both local and distant organ damage. These neutrophils secrete various mediators, such as interleukin (IL)-2, IL-6, IL-8, and tumor necrosis factor-alpha, activating other circulating neutrophils and inflammatory cells, leading to a systemic inflammatory response. This systemic response causes tissue edema and destruction in distant organs due to neutrophilic inflammation.[5,12]

Our study aimed to evaluate the antifibrinolytic and anti-inflammatory effects of TA on stabilizing microthrombi in ischemic tissue and preventing the proinflammatory effects of fibrin degradation products. Our findings indicate that TA has a significant effect in this regard. The inhibitory effects of TA on leukocyte proteinases and its anti-inflammatory effects, as mentioned in the introduction, were evident in the study results. The ability of TA to reduce oxidative stress and modulate the inflammatory response aligns with these mechanisms.

Histopathological evaluation revealed that tissue damage was significantly greater in the IR group than in the sham group, and this damage was reduced with TA administration in the TA group, although the reduction was not statistically significant. Specifically, the IR group exhibited widespread leukocyte infiltration, significant degeneration of alveolar structures, interalveolar hemorrhage, and thrombosis in the arterioles. These findings are indicative of severe reperfusion injury in the lung tissue. In contrast, the TA group showed a reduction in leukocyte infiltration, alveolar damage, and thrombus formation compared to the IR group, suggesting that TA helps mitigate some aspects of reperfusion injury. However, widespread interstitial edema was still present in the TA group, indicating that TA did not completely prevent all histopathological changes associated with reperfusion injury.

In a study by Sirmali et al.,[23] using ascorbic acid in an experimental lower extremity IR model, polymorphonuclear leukocytes, edema, and congestion were observed in the lung tissue of the IR group, similar to the changes observed in our IR group. Our findings also align with those of Tekinbas et al.,[16] who reported that free radical production during one-lung ventilation caused significant lung injury, as evidenced by intra-alveolar edema, inflammatory cell infiltration, focal hemorrhage, and alveolar destruction.

The tissue MPO and MDA levels indicate local inflammation and oxidative stress, respectively. In our study, while MDA levels were significantly higher in the IR group than in the sham group and significantly lower in the TA group than in the IR group, MPO levels were not significantly lower in the TA group than in the IR group. This finding suggests that TA effectively reduces oxidative stress but may not significantly impact leukocyte activity, as measured by MPO. Pesei et al.[24] also reported increased tissue MPO levels as an indirect indicator of leukocyte activity in lung injury associated with pancreatitis.

In our study, the plasma levels of MPO and MDA were significantly greater in the IR group than in the sham group, indicating an increased systemic inflammatory response and oxidative stress. However, the lack of statistically significant increases in the TA group suggested that while TA did not sufficiently suppress this response, it did reduce oxidative stress. This finding is consistent with studies in the literature, indicating that TA reduces oxidative stress and modulates the inflammatory response. For instance, in a study by Şirin et al.,[25] no pathological findings were observed in the lung histology of rabbits given aprotinin in a lower extremity IR model, and it was concluded that the drug reduced reperfusion injury. Similarly, Köksal et al.[26] demonstrated that aprotinin reduced reperfusion injury more effectively than alpha-tocopherol in a rat IR model.

The serum IMA level is an indicator of oxidative stress following ischemia. In our study, serum IMA levels were significantly higher in the IR group than in the sham group, while they were significantly lower in the TA group than in the IR group. This finding indicates that TA significantly reduces oxidative stress. Turedi et al.[27] also reported increased serum IMA and MDA levels in patients who underwent cardiopulmonary resuscitation due to cardiac arrest in the emergency department, with an increase in serum IMA levels associated with early prognosis after cardiopulmonary resuscitation.

This study has some limitations. Firstly, the use of a single dose of tranexamic acid may not fully capture the dose-dependent effects of the drug. Additionally, the use of heparin may have influenced the antifibrinolytic effects of tranexamic acid, potentially confounding the results. The study focused on short-term outcomes without evaluating long-term effects. Finally, the small sample size for histopathological and biochemical analyses may have limited the statistical power to detect differences between groups.

In conclusion, TA may be useful for reducing inflammatory reactions and oxidative stress in IR injury. The significant results included a reduction in the serum IMA and MDA levels, indicating decreased oxidative stress. Although not all inflammatory markers showed significant decreases, the overall trend suggests potential benefits of TA in reducing inflammatory reactions. Further research is necessary to explore the effects of different doses and long-term effects of TA in various IR models. This study continues the limited number of reperfusion studies involving the TA in the literature, and our findings share common aspects with the results in the literature. More studies are needed to investigate the effects of different doses and long-term effects of TA. This study suggested that TA may be a potential therapeutic option for reducing reperfusion injury, particularly through its local anti-inflammatory effects and its role in reducing oxidative stress.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conseptualsation and writing: M.F.S., Z.P.; Conceptualisation: Z.P., E.Y.; Data Curation: S.C.K., Z.P., E.Y., M.F.S.; Methodology: M.F.S., Z.P.; Methodology and writing: M.F.S., Z.P.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. J Vasc Surg 2019;69:3S-125S.e40. doi: 10.1016/j.jvs.2019.02.016.
2. Almasri J, Adusumalli J, Asi N, Lakis S, Alsawas M, Prokop LJ, et al. A systematic review and meta-analysis of revascularization outcomes of infrainguinal chronic limb-threatening ischemia. J Vasc Surg 2018;68:624-33. doi: 10.1016/j.jvs.2018.01.066.
3. Hıdıroğlu M, Uğuz E, Özerdem G, Yıldız E, Berkan Ö. The proinflammatory cytokine-mediated protective effects of pentoxifylline, iloprost, and cilostazol on a mitigating lung injury induced by lower limb ischemia and reperfusion in rats. Turk Gogus Kalp Dama 2014;22:138-44.
4. Rampon GL, Simpson SQ, Agrawal R. Prone positioning for acute hypoxemic respiratory failure and ARDS: A review. Chest 2023;163:332-40. doi: 10.1016/j.chest.2022.09.020.
5. Cannistrà M, Ruggiero M, Zullo A, Gallelli G, Serafini S, Maria M, et al. Hepatic ischemia reperfusion injury: A systematic review of literature and the role of current drugs and biomarkers. Int J Surg 2016;33 Suppl 1:S57-70. doi: 10.1016/j.ijsu.2016.05.050.
6. Ge X, Meng Q, Wei L, Liu J, Li M, Liang X, et al. Myocardial ischemia-reperfusion induced cardiac extracellular vesicles harbour proinflammatory features and aggravate heart injury. J Extracell Vesicles 2021;10:e12072. doi: 10.1002/jev2.12072.
7. Isbir S, Akgun S, Ak K, Civelek A, Tekeli A, Cobanoglu A. Effect of acute lower limb ischemia/reperfusion injury on the free oxygen radical systems in lungs. Turk Gogus Kalp Dama 2000;8:632-634.
8. Akbari G. Role of zinc supplementation on ischemia/reperfusion injury in various organs. Biol Trace Elem Res 2020;196:1-9. doi: 10.1007/s12011-019-01892-3.
9. Liu Q, Liu Y, Li Y, Hong Z, Li S, Liu C. PUM2 aggravates the neuroinflammation and brain damage induced by ischemia-reperfusion through the SLC7A11-dependent inhibition of ferroptosis via suppressing the SIRT1. Mol Cell Biochem 2023;478:609-20. doi: 10.1007/s11010-022-04534-w.
10. Jiang W, Yin Y, Gu X, Zhang Z, Ma H. Opportunities and challenges of pain-related myocardial ischemia-reperfusion injury. Front Physiol 2022;13:900664. doi: 10.3389/fphys.2022.900664.
11. Qiu S, Li X, Zhang J, Shi P, Cao Y, Zhuang Y, et al. Neutrophil membrane-coated taurine nanoparticles protect against hepatic ischemia-reperfusion injury. Eur J Pharmacol 2023;949:175712. doi: 10.1016/j.ejphar.2023.175712.
12. Zhan Y, Ling Y, Deng Q, Qiu Y, Shen J, Lai H, et al. HMGB1-mediated neutrophil extracellular trap formation exacerbates intestinal ischemia/reperfusion-induced acute lung injury. J Immunol 2022;208:968-78. doi: 10.4049/jimmunol.2100593.
13. Fan XD, Zheng HB, Fan XS, Lu S. Increase of SOX9 promotes hepatic Ischemia/Reperfusion (IR) injury by activating TGF-β1. Biochem Biophys Res Commun 2018;503:215-21. doi: 10.1016/j.bbrc.2018.06.005.
14. Dong NN, Chen XL, Deng BL, Xie SC, Hu J. Effective constituents of essential oil from gleditsiae fructus abnormalis and anti-cerebral ischemia/reperfusion injury

mechanism: Based on GC-MS, network pharmacology, and experimental verification. Zhongguo Zhong Yao Za Zhi 2023;48:1076-86. Chinese. doi: 10.19540/j.cnki.cjcmm.20221102.703.
15. Özen A, Yiğit G, Yıldırım A, Gül EB, Yılmaz M, İşcan HZ. Our clinical experience in the management of COVID-19-related arterial thrombosis with acute limb ischemia. Cardiovascular Surgery and Interventions 2024;11:33-41. doi :10.5606/e-cvsi.2024.1609.
16. Tekinbas C, Ulusoy H, Yulug E, Erol MM, Alver A, Yenilmez E, et al. One-lung ventilation: For how long? J Thorac Cardiovasc Surg 2007;134:405-10. doi: 10.1016/j.jtcvs.2007.05.003.
17. Güney T, Kocman AE, Ozatik O, Akyüz F. The effect of fucoidin on kidney and lung injury in a rat infrarenal aortic ischemia-reperfusion model. Perfusion 2022;37:198-207. doi: 10.1177/0267659120982839.
18. Gokalp O, Eygi B, Gokalp G, Kiray M, Besir Y, Iscan S, et al. Which distant organ is most affected by lower extremity ischemia-reperfusion? Ann Vasc Surg 2020;65:271-81. doi: 10.1016/j.avsg.2020.01.008.
19. Ma Y, Zabell T, Creasy A, Yang X, Chatterjee V, Villalba N, et al. Gut ischemia reperfusion injury induces lung inflammation via mesenteric lymph-mediated neutrophil activation. Front Immunol 2020;11:586685. doi: 10.3389/fimmu.2020.586685.
20. Ho YJ, Hsu HC, Wu BH, Lin YC, Liao LD, Yeh CK. Preventing ischemia-reperfusion injury by acousto-mechanical local oxygen delivery. J Control Release 2023;356:481-92. doi: 10.1016/j.jconrel.2023.03.018.
21. Kızıloğlu İ, Daylan A, Şener A, Aygün H, Bozok Ş. Acute mesenteric ischemia in the surgical intensive care unit: Analysis of clinical characteristics and risk factors for mortality. Cardiovascular Surgery and Interventions 2023;10:154-60. doi: 10.5606/e-cvsi.2023.1562.
22. Szijártó A. Free radicals and hepatic ischemia-reperfusion. Orv Hetil 2015;156:1904-7. doi: 10.1556/650.2015.30305.
23. Sirmali M, Uz E, Sirmali R, Kilbaş A, Yilmaz HR, Altuntaş I, et al. Protective effects of erdosteine and vitamins C and E combination on ischemia-reperfusion-induced lung oxidative stress and plasma copper and zinc levels in a rat hind limb model. Biol Trace Elem Res 2007;118:43-52. doi: 10.1007/s12011-007-0010-3.
24. Pesei ZG, Jancsó Z, Demcsák A, Németh BC, Vajda S, Sahin-Tóth M. Preclinical testing of dabigatran in trypsin-dependent pancreatitis. JCI Insight 2022;7:e161145. doi: 10.1172/jci.insight.161145.
25. Şirin H, Sarıbülbül O, Cerrahoğlu M, Baltalarlı A, Ortaç R, Saçar M, et al. Alt ekstremite iskemi reperfüzyonunun yol açtığı pulmoner hasarda aprotinin'in koruyucu etkinliği. Turk Gogus Kalp Dama 2001;9:233-37.
26. Koksal C, Bozkurt AK, Sirin G, Konukoglu D, Ustundag N. Aprotinin ameliorates ischemia/reperfusion injury in a rat hind limb model. Vascul Pharmacol 2004;41:125-9. doi: 10.1016/j.vph.2004.05.004.
27. Turedi S, Gunduz A, Mentese A, Dasdibi B, Karahan SC, Sahin A, et al. Investigation of the possibility of using ischemia-modified albumin as a novel and early prognostic marker in cardiac arrest patients after cardiopulmonary resuscitation. Resuscitation 2009;80:994-9. doi: 10.1016/j.resuscitation.2009.06.007.

Cardiovasc Surg Int 2024;11(3):151-156
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1682
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Aortic remodeling following elective endovascular aortic repair

Ferit Çetinkaya[1], Mehmet Ali Türkçü[2], Bahadır Aytekin[3], Ertekin Utku Ünal[4], Hakkı Zafer İşcan[3]

[1]Department of Cardiovascular Surgery, Ağrı Training and Research Hospital, Ağrı, Türkiye
[2]Department of Cardiovascular Surgery, Elbistan State Hospital, Kahramanmaraş, Türkiye
[3]Department of Cardiovascular Surgery, Ankara City Hospital, Ankara, Türkiye
[4]Department of Cardiovascular Surgery, Ufuk University Faculty of Medicine, Ankara, Türkiye

Received: May 18, 2024 ***Accepted:*** July 27, 2024 ***Published online:*** September 03, 2024

ABSTRACT

Objectives: This study aimed to investigate the changes in the aneurysm morphology during mid-term follow-up after endovascular aortic repair (EVAR).

Patients and methods: A total of 192 patients (180 males, 12 females; mean age: 69±5.1 years; range, 46 to 88 years) with infrarenal abdominal aortic aneurysms, who underwent elective EVAR between June 2016 and July 2021, who had at least one year of follow-up, and who possessed preoperative and postoperative computed tomography angiography scans, were included in the retrospective study.

Results: The median aneurysm diameter decreased from 61.0 to 57.5 mm (p<0.001). The median upper neck diameter increased from 24.0 to 26.0 mm (p<0.001). The median lower neck diameter also increased from 24.0 to 26.0 mm (p<0.001). The median infrarenal neck angle decreased from 35.0^0 to 30.0^0 (p<0.001). The mean aneurysm length decreased from 131.6±18.5 to 130.5±18.6 mm (p<0.001).

Conclusion: This study suggests that the aneurysm sac contracts over the years following successful EVAR, while the infrarenal neck angle decreases, and the neck diameter expands due to the radial force of the endograft.

Keywords: Abdominal aort aneurysm; EVAR; neck, remodeling.

Abdominal aortic aneurysm is a frequently encountered condition, particularly in older individuals, and is associated with risk factors such as hypertension and atherosclerosis.[1] Endovascular aortic repair (EVAR) has gained increasing prominence in the treatment of infrarenal abdominal aortic aneurysms.[2] The 2019 European Society for Vascular Surgery guidelines recommend EVAR as the primary treatment option in suitable and elderly cases.[3]

Structural changes in the aneurysm morphology are crucial to monitor in post-EVAR surveillance.[4,5] Over the years, various alterations in the aneurysm sac and neck structure have been observed, attributed to the pressure exerted by the endograft and the thrombotic reduction of the sac in most patients.

The cessation of sac expansion is one of the primary objectives in EVAR treatment. Studies on post-EVAR sac morphology have demonstrated that EVAR effectively halts sac expansion in the majority of patients.[6,7] Additionally, the effects of aneurysm neck structure on success, its associations with type 1A endoleak risks, and post-EVAR alterations have also been among the researched topics in recent years.[8,9] This study aimed to elucidate the changes in aneurysm sac and neck structure during mid-term follow-up following EVAR.

PATIENTS AND METHODS

Patients who underwent elective EVAR at the Türkiye Yüksek İhtisas Hospital and Ankara Bilkent City Hospital between January 2016 and July 2021 were included in the retrospective study. Patients who presented with ruptured aortic aneurysms or required additional interventions during the

Corresponding author: Ferit Çetinkaya, MD. Ağrı Eğitim ve Araştırma Hastanesi, Kalp ve Damar Cerrahisi Kliniği, 04200 Ağrı, Türkiye.
E-mail: cetinkaya1234@gmail.com

Citation:
Çetinkaya F, Türkçü MA, Aytekin B, Ünal EU, İşcan HZ. Aortic remodeling following elective endovascular aortic repair. Cardiovasc Surg Int 2024;11(3):151-156. doi: 10.5606/e-cvsi.2024.1682.

same hospitalization, such as thoracic EVAR or percutaneous transluminal angioplasty, were excluded from the study. The patients were selected from our endovascular intervention database where comorbidities and pre-, peri-, and postoperative data were registered. Complementary clinical data were retrieved from patient records. Computed tomography angiography (CTA) measurements were conducted prospectively. Out of 262 patients, 192 patients (180 males, 12 females; mean age: 69±5.1 years; range, 46 to 88 years) with preoperative and postoperative CTAs, as well as recorded oversize rates, were included (Figure 1). All patients underwent EVAR under the same cardiovascular team. The endograft size was chosen to be 10% to 20% oversize for all patients. Computed tomography angiography measurements were performed by a single operator using the 3Mensio Vascular (3mensio Medical Imaging BV, Maastricht, Netherlands) program (Figure 2). The upper neck diameter was measured at the level just below the renal arteries, and the lower neck diameter was measured at the top of the aneurysm sac. All procedures were performed by the same endovascular team. The indication for EVAR intervention in abdominal aortic aneurysms was set for those with a sac diameter >55 mm. Additionally, patients with aneurysms with a diameter >40 mm that expanded >10 mm per year or those presenting with abdominal pain symptoms were also indicated for intervention. A written informed consent was obtained from each patient. The study protocol was approved by the Ankara City Hospital Ethics Committee (date: 1217, no: E1-20-1217). The study was conducted in accordance with the principles of the Declaration of Helsinki.

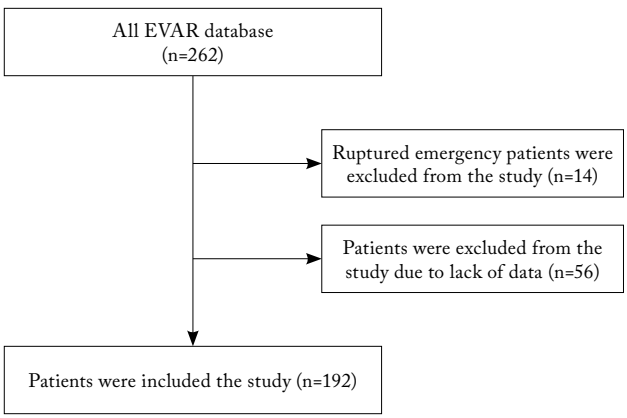


Figure 1. Flowchart of the study.
EVAR: Endovascular aortic repair.

Statistical analyses

Data were analyzed using IBM SPSS version 19.0 software (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to assess the fit of numeric variables to the normal distribution. Descriptive statistics were reported as frequency and percentage. Normally distributed data were reported as mean ± standard deviation (SD), and data not conforming to normal distribution were presented as median (min-max). To assess statistical significance, the chi-square test was used to determine the difference and relationship between categorical data. The Mann-Whitney U test and Student's t-test were used to assess the relationship between nominal data and numerical values. A p-value <0.05 was considered statistically significant.

RESULTS

The patients' characteristics are presented in Table 1. Thirty-nine percent of the patients had coronary artery disease. The perioperative characteristics of the patients are provided in Table 2. General anesthesia was administered to 89.2% of the patients. Modular endografts

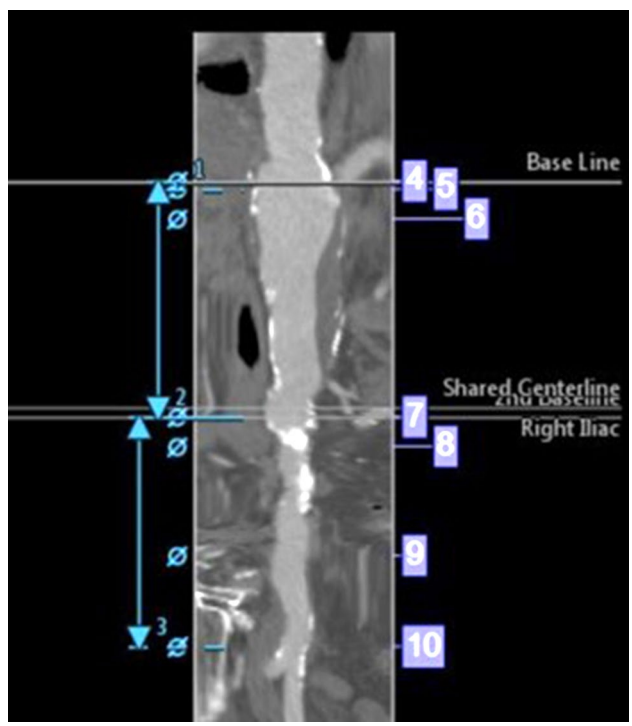


Figure 2. An example of diameter measurements from the 3MensioVascular program.

Table 1
Baseline characteristics of the patients (n=192)

	n	%	Mean±SD	Median	Min-Max
Age (year)			69.4±5.1	69.0	46.0-88.0
Ejection fraction			48.5±7.4	50.0	20.0-67.0
Sex					
Male	180	93.7			
Diyabetes mellitus	24	12.5			
Hypertension	135	70.0			
Hyperlipidemia	55	28.6			
Chronic obstructive pulmonary disease	44	22.9			
Chronic kidney disease	18	9.3			
Peripheral artery disease	12	6.2			
Coronary artery disease	75	39.0			
Coronary artery bypass graft	29	15.1			
Congestive heart disease	5	2.8			
Transient ischemic attact/cerebrovascular disease	11	5.7			
Cancer	6	3.1			
Symptomatic patient	84	43.7			
History of abdominal surgery	6	3.1			
Smoking	102	53.1			

SD: Standard deviation.

were used in 95.4% of the cases, while unibody (AFX, Endologix; Irvine, CA, USA) endografts were used in 4.6%. The median duration of intensive care unit stay was 6.4 (1-120) h, and the median hospital stay was 2.9 (1-19) days.

The median follow-up duration was 28 months (interquartile range, 37 to 21 months). Endoleaks were observed in 18.3% (n=33) of the patients during follow-up. Type 1A endoleaks were detected in 3.8% (n=7) of cases, all of which underwent secondary interventions. Type 1B, type 2, and type 3 endoleaks were observed in 3.3% (n=6), 6.6% (n=12), and 4.1% (n=8) of cases, respectively. All patients with type 2 endoleaks had a benign course and were managed medically. For other patients with endoleaks, treatments included nine aortic extensions, nine iliac extensions, three balloon dilations, two crossover procedures, one iliac extension with embolectomy, one iliac extension with crossover, and two open surgeries. The frequency of endoleak-independent complications was 3.9%, with iliac graft thrombosis

Table 2
Perioperative features

Parameters	Median	Min-Max
Procedure time (min)	120.0	30.0-360.0
Scopy time (min)	12.0	4.0-52.0
Opaque amount (mL)	50.0	0-140.0
Length of stay in intensive care (h)	4.0	1.0-120.0
Length of stay in the hospital (day)	2.0	1.0-19.0

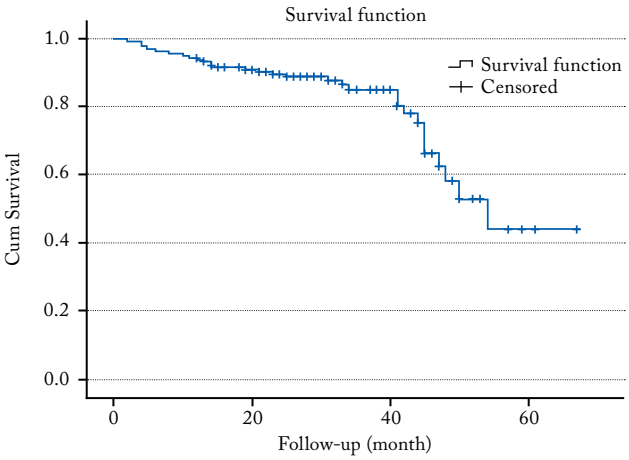


Figure 3. Kaplan-Meier survival analysis.

being the most common (n=5). These five patients underwent embolectomy and additional iliac extension graft placement. The mortality rate was determined to be 18.3% (n=33) during follow-up (Figure 3). Among these, 17 were of cardiac origin, seven were aortic-related mortalities, eight were due to noncardiac causes, and one was of unknown etiology.

Morphological changes in patients' aneurysms, both preoperatively and postoperatively, are detailed in Table 3. In 6.3% (n=12) of patients, the aneurysm sac was enlarged by >5 mm during mid-term follow-up. In 81.7% (n=157) of cases, the aneurysm sac diameter remained stable or decreased. When considering all patients, the median aneurysm diameter reduced significantly from 61.0 to 57.5 mm (p<0.001). The median upper neck diameter (diameter at the lowest renal artery level) increased from 24.0 to 26.0 mm (p<0.001). The median lower neck diameter (before the aneurysm sac level) also increased from 24.0 to 26.0 mm (p<0.001). The median infrarenal neck angle decreased from 35.0° to 30.0° (p<0.001). The mean aneurysm length decreased from 131.6±18.5 to 130.5±18.6 mm (p<0.001).

DISCUSSION

Coronary tomography angiography measurements play a critical role in the monitoring

Table 3
Morphological changes in aneurysm after EVAR

	Mean±SD	Median	Min-Max	Test value	*p*
Aneurysm sac diameter (mm)					
Preoperative		61.0	54.0-118.0	-7.867	**<0.001**
Postoperative		57.5	31.0-113.0		
Upper neck diameter (mm)					
Preoperative		24.0	16.0-34.0	-11.193	**<0.001**
Postoperative		26.0	20.0-60.0		
Lower neck diameter (mm)					
Preoperative		24.0	15.0-38.0	-9.734	**<0.001**
Postoperative		26.0	18.0-38.0		
Neck length (mm)					
Preoperative		28.0	8.0-72.0	-0.581	0.56
Postoperative		28.0	8.0-74.0		
Infrarenal neck angulation (degree)					
Preoperative		35.0	0.0-90.0	-6.229	**<0.001**
Postoperative		30.0	0.0-110.0		
Aneurysm length (mm)					
Preoperative	131.6±18.5			4.25	**<0.001**
Postoperative	130.5±18.6				

SD: Standard deviation; EVAR: Endovascular aortic repair.

of patients following EVAR treatment to detect morphological changes in aneurysm sacs and necks.[10] This study focused on the mid-term follow-up of EVAR patients who received oversizing in the range of 10 to 20%. As expected, in this study, among patients with a stable or decreasing sac diameter (n=157, 81.7%), the average aneurysm sac diameter statistically significantly decreased by 3.5 mm after EVAR treatment. Soler et al.[4] reported that, during an mean follow-up of 24.6±4.1 months, over 51.8% of patients experienced a reduction of 10 mm or more in aneurysm sac diameter following EVAR.

The upper and lower neck diameters exhibited statistically significant expansion (2 mm), while no significant changes were observed in neck length. In patients with observed aortic neck dilatation, no complications related to the neck dilatation were observed. Kret et al.[11] noted that the average neck diameter expanded by 1 to 3 mm following EVAR and found it to be associated with oversizing regardless of the endograft brand. Oliveira et al.[12] reported an average aortic neck dilatation of 3 to 4 mm after EVAR. In our study, all oversizing ratios fell within the 10 to 20% range. These similar findings validate and elaborate on the specific measurements supported by our study.

The present study also revealed a statistically significant decrease of approximately 5° in infrarenal neck angulation. Ishibashi et al.[13] found that infrarenal neck angles >60° decreased by 20% in a two-year follow-up study.

The significant 1-mm reduction in aneurysm length is presumed to be due to the upward movement of the aneurysm related to its shrinkage. Wever et al.[14] found that in 14 patients with shrinking aneurysm sacs following EVAR, the average aneurysm length between the renal arteries and aortic bifurcation reduced by 4 mm after one year of follow-up. The impact of endograft aneurysm shrinkage on aneurysm morphology is a noteworthy outcome of this study.

Endovascular aortic repair often involves selecting grafts oversized approximately 10 to 20%, as recommended by endograft companies. The median 2-mm expansion observed in the upper and lower limits of the aneurysm neck, as documented in the study's results, is primarily attributed to the radial strength of the oversized grafts. This neck expansion was observed in all patients during immediate post-EVAR follow-up angiographies. Additionally, no neck expansion due to endoleak was found in control CTAs among patients with endoleak.

Unibody (AFX, Endologix) endografts were used in the early years of this study, and these patients were included in the study. This may have increased our total endoleak rates due to type 3 endoleak.

Although the routine follow-up of EVAR patients is currently performed using two-dimensional CTA measurements, recent studies have demonstrated the increased value of three-dimensional volumetric monitoring.[15,16] We believe that with advancing technology and artificial intelligence in the coming years, volumetric monitoring will become more convenient and is likely to replace diameter measurements in routine follow-ups. On the other hand, open surgery will stay as a good alternative to EVAR, both in cases of EVAR complications and in patients who are anatomically unsuitable for endovascular treatment.[16]

There are some limitations to this study. This study is a retrospective and single-center investigation. Given the precise CTA measurements in this study, there may be a margin of error in the measurements. Measurements were conducted by a single expert. The study included multiple endograft brands to mitigate bias risk. However, this may have introduced graft variety since different endograft brands may have varying radial strength. The study was conducted with a relatively small sample size and short follow-up due to limitations. Larger sample sizes and longer follow-up durations may provide more conclusive results.

In conclusion, in the mid-term follow-up after EVAR (median of 28 months), a median expansion of 2 mm in the aneurysm neck diameter was observed due to the radial force of the endograft. The infrarenal aneurysm neck angle decreased by a median of 5°, the aneurysm sac diameter reduced by a median of 3.5 mm, and the aneurysm length shortened by approximately 1 mm. While changes in neck morphology were associated with endograft dimensions and radial strength, alterations in sac morphology were directly linked to the success of EVAR treatment.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Writing: F.Ç.; Analysis and idea: H.Z.İ.; Critical review: E.U.Ü.; Data collection: M.A.T., B.A.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Sakalihasan N, Limet R, Defawe OD. Abdominal aortic aneurysm. Lancet 2005;365:1577-89. doi: 10.1016/S0140-6736(05)66459-8.
2. Mani K, Lees T, Beiles B, Jensen LP, Venermo M, Simo G, et al. Treatment of abdominal aortic aneurysm in nine countries 2005-2009: A vascunet report. Eur J Vasc Endovasc Surg 2011;42:598-607. doi: 10.1016/j.ejvs.2011.06.043.
3. Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. Eur J Vasc Endovasc Surg 2019;57:8-93. doi: 10.1016/j.ejvs.2018.09.020.
4. Soler RJ, Bartoli MA, Mancini J, Lerussi G, Thevenin B, Sarlon-Bartoli G, et al. Aneurysm sac shrinkage after endovascular repair: Predictive factors and long-term follow-up. Ann Vasc Surg 2015;29:770-9. doi: 10.1016/j.avsg.2014.12.016.
5. Antoniou GA, Alfahad A, Antoniou SA, Torella F. Prognostic significance of aneurysm sac shrinkage after endovascular aneurysm repair. J Endovasc Ther 2020;27:857-68. doi: 10.1177/1526602820937432.
6. Arko FR, Filis KA, Hill BB, Fogarty TJ, Zarins CK. Morphologic changes and outcome following endovascular abdominal aortic aneurysm repair as a function of aneurysm size. Arch Surg 2003;138:651-5. doi: 10.1001/archsurg.138.6.651.
7. İşcan HZ, Karahan M, Akkaya BB, Başar V, Aşkın G, Kubat E, et al. Long-term results of endovascular intervention with unibody bifurcation endograft for elective abdominal aortic aneurysm management. Rev Cardiovasc Med 2021;22:453-59. doi: 10.31083/j.rcm2202051.
8. Aytekin B, Deniz G, Çetinkaya F, Mola S, Tümer NB, Ünal EU, et al. The impact of large proximal aortic neck on endovascular aneurysm repair outcomes. Turk Gogus Kalp Dama 2023;31:489-97. doi: 10.5606/tgkdc.dergisi.2023.25255.
9. Çetinkaya F, İşcan HZ, Türkçü MA, Mavioğlu HL, Ünal EU. Predictive parameters of type 1A endoleak for elective endovascular aortic repair: A single-center experience. Ann Vasc Surg 2024;98:108-14. doi: 10.1016/j.avsg.2023.07.095.
10. Baderkhan H, Haller O, Wanhainen A, Björck M, Mani K. Follow-up after endovascular aortic aneurysm repair can be stratified based on first postoperative imaging. Br J Surg 2018;105:709-18. doi: 10.1002/bjs.10766.
11. Kret MR, Tran K, Lee JT. Change in aortic neck diameter after endovascular aortic aneurysm repair. Ann Vasc Surg 2017;43:115-20. doi: 10.1016/j.avsg.2016.11.013.
12. Oliveira NF, Bastos Gonçalves FM, de Vries JP, Ultee KH, Werson DA, Hoeks SE, et al. Mid-term results of EVAR in severe proximal aneurysm neck angulation. Eur J Vasc Endovasc Surg 2015;49:19-27. doi: 10.1016/j.ejvs.2014.10.001.
13. Ishibashi H, Ishiguchi T, Ohta T, Sugimoto I, Yamada T, Tadakoshi M, et al. Remodeling of proximal neck angulation after endovascular aneurysm repair. J Vasc Surg 2012;56:1201-5. doi: 10.1016/j.jvs.2012.04.014.
14. Wever JJ, Blankensteijn JD, Broeders IA, Eikelboom BC. Length measurements of the aorta after endovascular abdominal aortic aneurysm repair. Eur J Vasc Endovasc Surg 1999;18:481-6. doi: 10.1053/ejvs.1999.0882.
15. Franchin M, Serafini M, Tadiello M, Fontana F, Rivolta N, Venturini M, et al. A morphovolumetric analysis of aneurysm sac evolution after elective endovascular abdominal aortic repair. J Vasc Surg 2021;74:1222-31.e2. doi: 10.1016/j.jvs.2021.03.034.
16. Akansel S, Erdoğan BS, Sargın M, Sokullu O, Kurç E, Aka SA. Late surgical conversion after failed endovascular aortic repair: Our single-institutional experience. Cardiovasc Surg Int 2023;10:79-88. doi: 10.5606/e-cvsi.2023.1493.

Cardiovasc Surg Int 2024;11(3):157-163
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1670
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Relationship between sacroiliitis and tricuspid annular plane systolic excursion in patients with ankylosing spondylitis

Osman Cure[1], Elif Ergül[2], Mustafa Cetin[2], Kadir Ikkilic[3], Bayram Kizilkaya[4]

[1]Department of Internal Medicine, Division of Rheumatology, Recep Tayyip Erdoğan University Faculty of Medicine, Rize, Türkiye
[2]Department of Cardiology, Recep Tayyip Erdoğan University Faculty of Medicine, Rize, Türkiye
[3]Department of Hematology, Recep Tayyip Erdoğan University Faculty of Medicine, Rize, Türkiye
[4]Department of Internal Medicine, Recep Tayyip Erdoğan University Faculty of Medicine, Rize, Türkiye

Received: April 05, 2024 ***Accepted:*** July 08, 2024 ***Published online:*** September 03, 2024

ABSTRACT

Objectives: The study aimed to assess the association between sacroiliitis and tricuspid annular plane systolic excursion (TAPSE), a measure utilized to predict right ventricular systolic function in individuals with ankylosing spondylitis (AS).

Patients and methods: Demographic, clinical, laboratory, medical, and echocardiographic information of 90 AS patients (54 males, 36 females; mean age: 42.7±12.4 years; range, 23 to 72 years) between March 2018 and July 2023 was prospectively recorded. The patients were divided into two groups: those with normal (≥15 mm) TAPSE values (Group 1; n=69) and those with low (<15 mm) TAPSE values (Group 2; n=21). The groups were compared in terms of TAPSE values.

Results: In Group 2, the disease duration was longer (p=0.049), the use of tumor necrosis factor inhibitors was higher (p=0.046), and the rate of sacroiliitis was lower (p=0.012). Bath Ankylosing Spondylitis Disease Activity Index was higher in Group 2. In logistic regression analysis, there was an independent relationship between sacroiliitis in AS patients and Group 2 (odds ratio=0.088, 95% confidence interval: 0.008-0.960, p=0.046). Sacroiliitis had a close association with decreased right ventricular function in patients with AS.

Conclusion: There was an independent relationship between sacroiliitis and TAPSE in patients with AS.

Keywords: Ankylosing spondylitis, right ventricular function, tricuspid annular plane systolic excursion.

Ankylosing spondylitis (AS) is a chronic inflammatory disease that affects and causes damage to axial and peripheral joints. It creates a significant health and socioeconomic burden on society.[1] Ankylosing spondylitis affects approximately 0.2 to 1.2% of the population and is 2.5 times more prevalent in males compared to females. Apart from joints, it most commonly causes anterior uveitis in the eyes and can also lead to significant organ damage in the cardiovascular system, lungs, kidneys, and nervous system.[2,3]

It is known that AS is not only due to aortic pathology but is also associated with cardiac complications such as left ventricular diastolic dysfunction, pericarditis, conduction disorders (atrioventricular or branch block), rarely mitral insufficiency, heart failure, and cardiomegaly.[4,5] Almost all patients with cardiac involvement are HLA (human leukocyte antigen)-B27 positive.[6,7] Mortality and morbidity are increased in AS patients with right ventricular (RV) cardiopulmonary disease. Tricuspid annular plane systolic excursion (TAPSE) is one of the noninvasive parameters used to evaluate the systolic functions of the RV and is known as the annular movement of the tricuspid valve in the normal heart. The normal TAPSE value is 15 to 20 mm. A TAPSE value <15 mm indicates RV dysfunction.[8,9] In AS patients, RV functions may be

Corresponding author: Osman Cure, MD. Recep Tayyip Erdoğan Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Romatoloji Bilim Dalı, 53020 Rize, Türkiye
E-mail: creosman61@gmail.com

Citation:
Cure O, Ergül E, Cetin M, Ikkilic K, Kizilkaya B. Relationship between sacroiliitis and tricuspid annular plane systolic excursion in patients with ankylosing spondylitis. Cardiovasc Surg Int 2024;11(3):157-163. doi: 10.5606/e-cvsi.2024.1670.

affected due to cardiac pathologies such as pulmonary arterial hypertension (PAH) and valve disease.[6,7] Hence, this study aimed to evaluate the relationship of TAPSE with sacroiliitis in AS patients.

PATIENTS AND METHODS

Ninety patients (54 males, 36 females; mean age: 42.7±12.4 years; range, 23 to 72 years) who visited the rheumatology clinic of the Recep Tayyip Erdoğan University Faculty of Medicine between March 2018 and July 2023 were enrolled in the cross-sectional prospective study. The patients were divided into two groups: those with normal TAPSE values (Group 1; n=69) and those with low TAPSE values (Group 2; n=21). The diagnosis of AS was determined according to the criteria outlined by the Assessment of Spondyloarthritis International Society.[10] Individuals under 18 years of age, individuals diagnosed with other rheumatological disorders, congestive heart failure, or severe valve disease, patients with a prosthetic heart valve, individuals with a history of lung disease, pulmonary hypertension, congenital heart disease, renal failure (estimated glomerular filtration rate <30 mL/min/1.7 m^2), or active infection, and patients with a history of malignancy were excluded. A written informed consent was obtained from each patient. The study protocol was approved by the Recep Tayyip Erdoğan University Faculty of Medicine Ethics Committee (date: 21.09.2023, no: 2023/220). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The patients' age, sex, body mass index, smoking status, comorbidities, and medication history were recorded. Disease duration was defined from the initial symptom onset. Laboratory tests were conducted on venous blood samples obtained from the patients following an 8-h fasting period. Complete blood count, serum creatinine, glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, C-reactive protein, and erythrocyte sedimentation rate were analyzed. Cigarette use was calculated in pack-years. Direct sacroiliac radiography and magnetic resonance imaging were conducted for sacroiliitis in patients presenting with inflammatory low back pain. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index were calculated for the participants.[11] Echocardiography was performed by the same experienced cardiologist.

Detailed two-dimensional transthoracic echocardiography was performed in all patients using Philips Epiq 7 with a 1 to 5 MHz X5-1 transducer (Philips Medical Systems Inc., Andover, MA, USA). Left atrial, left ventricular end-diastolic, and left ventricular end-systolic diameters and pulse and continuous Doppler measurements, E and A wave velocities, and deceleration time were quantified with standard two-dimensional M-mode echocardiographic images in accordance with current guideline recommendations.[13] Left ventricular ejection fraction was determined using the modified Simpson method. Left ventricular septal and posterior wall thicknesses were measured in the parasternal long axis view at the end of diastole. These measurements were used to calculate the left ventricular mass using the formula validated by Devereux et al.[12] left ventricular mass index=left ventricular mass/body surface area (body weight × 0.425 × height × 0.725 × 0.007184).[13,14]

Tricuspid annular plane systolic excursion was assessed as the complete excursion of the tricuspid annulus from its peak position after atrial contraction to its lowest point during ventricular systole, and TAPSE measurements were conducted in compliance with the most recent guidelines.[15] Patients with a TAPSE value ≥15 mm were considered to have a normal TAPSE and included in Group 1, while those with a TAPSE value <15 mm were considered to have decreased TAPSE and were included in Group 2.

Statistical analysis

The statistical analysis was performed using IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Numerical variables were presented as mean ± standard deviation (SD), while categorical variables were represented as percentages. Variables were evaluated for normal distribution through visual methods (histograms and probability plots) and analytical techniques (Kolmogorov-Smirnov/Shapiro-Wilk tests). To compare means between groups for normally distributed variables, the one-way analysis of variance was employed. Categorical variables were compared using either the chi-square test or Fisher exact test. Cross tabulations were used for comparison of the

TABLE 1
Demographic, medical, laboratory, and echocardiographic data of AS patients comparing Groups 1 and 2

	Group 1 (n=69)			Group 2 (n=21)			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
	Demographic data						
Age (year)			43.1±12.4			41.7±11.1	0.671
Sex							
Male	45	65.2		9	42.9		**0.058**
BMI (kg/m^2)			27.9±5.1			26.7±4.5	0.379
Disease duration (year)			8.2±5.7			11.3±8.1	**0.049**
Diabetes mellitus	6	8.7		1	4.8		0.481
Hypertension	16	23.2		4	19		0.473
Hyperlipidemia	35	50.7		11	52.4		0.547
Smoking	29	42.6		8	38.1		0.457
BASDAI score			4.03±2.2			5±2.3	0.089
BASFI score			2.9±2.4			3.4±2.4	0.431
Uveitis	8	11.6		2	9.5		0.574
Peripheral arthritis	11	15.9		4	19		0.483
Lower back pain	67	97.1		20	95.2		0.554
Enthesitis	10	14.5		3	14.3		0.644
Dactylitis	2	2.9		1	4.8		0.554
Sacroiliitis	68	98.6		18	85.7		0.012
	Medical treatment						
Beta blocker	5	7.2		3	14.3		0.275
CCB	11	15.9		1	4.8		0.172
ACEI	7	10.1		2	9.5		0.650
ARB	7	10.1		1	4.8		0.400
Diuretics	11	15.9		3	14.3		0.580
Statins	5	7.2		1	4.8		0.572
OAD	3	4.3		1	4.8		0.662
NSAID	27	39.1		4	19.1		0.073
Anti TNF-α	40	58		17	81		0.046
IL-17A inhibitors	2	2.9		0	0		0.586
	Laboratory data						
WBC (×10^3/L)			7.8±2.5			7.7±1.8	0.811
HGB (g/L)			14±1.6			13.6±1.7	0.343
Glucose (mg/dL)			97.5±15.4			101.7±27	0.386
SCREA (mg/dL)			0.79±0.16			0.74±0.18	0.260
eGFR (mL/min/1.73 m^2)			105.1±16.5			107.3±14.1	0.560
HbA1c (%)			5.6±0.71			5.6±0.28	0.980
HLA B27 positive	36	52.9		13	61.9		0.321

TABLE 1
Continued

Variables	Group 1 (n=69) n	%	Mean±SD	Group 2 (n=21) n	%	Mean±SD	*p*
	Echocardiography data						
LVEF (%)			61.4±3.8			62.45.2	0.374
Mitral E wave			84.2±19.6			82.8±21.7	0.767
Mitral A wave			76.1±21.8			76.4±22.3	0.909
EA ratio			1.18±0.39			1.1±0.38	0.793
EE ratio			8.6±3.5			9.2±4.7	0.537
Deceleration time			206.1±57.3			195±52	0.389
LVMI (g/m^2)			81.3±24.4			82.5±30.5	0.857

SD: Standard deviation; BMI: Body mass index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CCB: Calcium channel blocker; ACEI: Angiotensin converting enzyme inhibitors; ARB: Angiotensin receptor blockers; OAD: Oral Antidiabetic Drugs; NSAID: Nonsteroidal Anti-inflammatory Drugs; TNF-α: Tumor necrosis factor-alpha; WBC: White blood count; HGB: Hemoglobin; SCREA: Serum creatinine; eGFR: Glomerular filtration rate; HbA1c: Hemoglobin A1C; HLA B27: Human leukocyte antigen B27; LVEF: Left ventricular ejection fraction; IL: Interleukin.

proportions of patients with categorical variables. After comparing the groups, the parameters were first evaluated with univariate logistic regression analysis to determine the predictors of Group 2, and the parameters found to be statistically significant as a result of this evaluation were evaluated with multivariate logistic regression analysis (enter method). A p-value <0.05 was considered statistically significant.

RESULTS

In Group 1, 11 patients had peripheral arthritis and 68 patients had sacroiliitis, while in Group 2, four patients had peripheral arthritis and 18 patients had sacroiliitis. A comparison of the data obtained between the two groups is presented in Table 1. In Group 2, disease duration was longer (p=0.049), anti-tumor necrosis factor use was higher (p=0.046), and sacroiliitis was lower (p=0.012). Although it did

TABLE 2
Investigating the relationship between sacroiliitis and decreased TAPSE values in AS patients using logistic regression analysis

Variables	Univaraite OR	95% CI Lower-upper	*p*	Multivariate OR	95% CI Lower-upper	*p*
Sex Male	0.400	0.148-1.083	0.071			
Disease duration	1.071	0.997-1.150	0.061			
Sacroiliitis	0.088	0.009-0.900	0.040	0.088	0.008-0.960	**0.046**
BASDAI score	1.212	0.969-1.516	0.092			
NSAID	0.366	0.111-1.205	0.098			
Anti TNF-α	3.081	1.103-10.123	0.032	3.086	0.901-10.570	0.073

TAPSE: Tricuspid annular plane systolic excursion; AS: Ankylosing spondylitis; OR: Odds ratio; CI: Confidence interval; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; NSAID: Nonsteroidal anti-inflammatory drugs; TNF-α: Tumor necrosis factor-alpha.

not reach statistical significance, the BASDAI score was higher in Group 2.

To determine the factors that predicted decreased TAPSE values in Group 2, univariate logistic regression analysis was performed using parameters that showed statistically significant differences between the groups (Table 2). Afterward, multivariate logistic regression analysis was performed using the parameters that remained significant in univariate analysis. As a result, we concluded that the presence of sacroiliitis in patients with AS had an independent association with Group 2 (odds ratio=0.088, 95% confidence interval 0.008-0.960, p=0.046). Sacroiliitis had a close association with decreased RV function in patients with AS.

DISCUSSION

Ankylosing spondylitis is a chronic inflammatory disease that leads to characteristic spinal deformities, such as flattening of lumbar lordosis and kyphosis, mainly as a result of axial involvement.[16] The inflammatory condition in the thoracic vertebrae and costovertebral joints gradually leads to fusion and ossification of the spine, resulting in increased dorsal kyphosis and thoracic stiffness.[17] Severe spinal kyphosis causes fatigue in the diaphragm and other muscles, intra-abdominal discomfort, and decreased lung function.[18] Decreased chest expansion and lung parenchymal abnormalities are significant factors linked to pulmonary dysfunction.[19]

Pulmonary arterial hypertension is more common in connective tissue autoimmune disorders such as systemic sclerosis, mixed connective tissue disease, and Sjögren's syndrome; however, there are limited studies on the association between ankylosing spondylitis and PAH. Inflammation and interstitial lung disease in connective tissue diseases are important mechanisms that play a role in the formation and progression of PAH. The risk of right heart failure and death is increased in these patients due to elevated pulmonary artery pressure. Pulmonary arterial hypertension symptoms in autoimmune diseases are nonspecific. Clinical evaluation, physical examination, respiratory function tests, echocardiographic measurements, and right heart catheterization are used in the diagnosis of PAH. In the study conducted by Colalillo et al.,[20] they reported that decreased TAPSE and TAPSE/systolic pulmonary artery pressure ratio in echocardiographic measurements in systemic sclerosis patients had predictive importance for the diagnosis of PAH and mortality.[21]

Studies have found a higher prevalence of death from cardiovascular disease in AS patients than the general population, particularly from congestive heart failure and ischemic heart disease.[22,23] In echocardiographic studies in AS, the prevalence of aortic valve insufficiency and diastolic left ventricular dysfunction was increased.[23,24] It has been suggested that the cause of left ventricular dysfunction may be impaired filling and relaxation of the left ventricle due to inflammation or fibrosis in the myocardium due to disease activity in AS patients.[22,23] While previous studies have examined left ventricular functions in AS patients, there is limited research on RV function in this population. In a study conducted by Karoli et al.,[25] echocardiography of 56 AS patients revealed PAH in 60.7%, RV dilatation in 30.4%, RV hypertrophy, and thickening of the interventricular symptoms in 37.5%. In this study, they found PAH to be common in AS patients. These changes were found to be correlated with thoracic spinal lesions and long disease duration. In another study on 55 AS patients with predominant spinal lesions, grade 3 sacroiliitis on plain radiographs, and long disease duration, PAH, RV hypertrophy, and RV dilatation were detected in 70.96%, 47.3%, and 34.5%, respectively.[26] There are cases in the literature describing the relationship between AS and PAH.[7,27] In our study, similar to previous literature, Group 2, which exhibited lower TAPSE values, had longer disease duration and higher disease activity scores. The longer duration of disease in Group 2, in which TAPSE was lower, may have caused changes in the myocardium over time. Excessive contraction of the myocardium may have caused a decrease in myocardial fibers over time and eventually led to the development of fibrosis. Myocardial fibrosis may also have caused a decrease in TAPSE. It has been demonstrated that RV fibrosis strongly correlates with RV function.[28] The value of RV fibrosis is still debated. Fibrotic remodeling may be a protective adaptation to some extent to preserve ventricular shape and function against increased pressures.[29] In AS, which is a chronic inflammatory disease, inflammation can increase myofibroblast activation, which may result in fibrosis.[30] Since patients who did not develop

pulmonary hypertension were included in this study, the increased TAPSE in patients with sacroiliitis might reflect an adaptive change that occurred in these patients in the early period.

In the lung, AS causes ankylosis in the thoracic vertebrae, fusion in the costovertebral joints, sternoclavicular joint, enthesitis in the manubrium, chest wall restriction, pleural thickening, apical fibrosis, and chest pain, causing difficulty in breathing and a decrease in respiratory functions. Additionally, obstructive sleep apnea syndrome is increased in these patients compared to the normal population. Pain in the waist and hips due to sacroiliitis and lumbar involvement are factors that affect lumbar flattening and breathing. Due to these changes, pressure increases in the pulmonary artery and RV functions are affected.[31] In our study, we found that TAPSE was increased in the group with sacroiliitis. It may suggest that there may be an increase in RV functions in patients with sacroiliitis to compensate for the decrease in lung capacity caused by pain or that it may be a finding due to pericardial involvement.

There are some limitations to this study. This single-center study involved a relatively small number of patients, which may limit the applicability of the results to a broader population. The limitations of the study include not using additional parameters and advanced imaging methods to assess the RV structure and functions in AS patients.

In conclusion, this is the first study to explore the correlation between sacroiliitis and TAPSE values in AS patients. This study found an independent relationship between sacroiliitis and TAPSE in patients with AS. Changes in cardiac function may occur in patients with AS without clinically significant myocardial damage. Transthoracic echocardiography, which is a noninvasive procedure to detect these functions at an early stage, can be used more frequently in daily practice.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Development of study concept and design: O.C.; Acquisition, analysis and interpretation of the data: E.E., O.C.; Statistical analysis: M.C.; Writing: O.C., K.I.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Hwang MC, Ridley L, Reveille JD. Ankylosing spondylitis risk factors: A systematic literature review. Clin Rheumatol 2021;40:3079-93. doi: 10.1007/s10067-021-05679-7.
2. Ouardi NE, Djossou JH, Taoubane L, Ghassem MA, Toufik H, Majjad A, et al. Extra-articular manifestations in patients with ankylosing spondylitis: Baseline characteristics from the RBSMR study. Mediterr J Rheumatol 2022;33:316-21. doi: 10.31138/mjr.33.3.316.
3. Rueda-Gotor J, Ferraz-Amaro I, Genre F, González Mazón I, Corrales A, Portilla V, et al. Cardiovascular and disease-related features associated with extra-articular manifestations in axial spondyloarthritis. A multicenter study of 888 patients. Semin Arthritis Rheum 2022;57:152096. doi: 10.1016/j.semarthrit.2022.152096.
4. Moyssakis I, Gialafos E, Vassiliou VA, Boki K, Votteas V, Sfikakis PP, et al. Myocardial performance and aortic elasticity are impaired in patients with ankylosing spondylitis. Scand J Rheumatol 2009;38:216-21. doi: 10.1080/03009740802474672.
5. Lautermann D, Braun J. Ankylosing spondylitis--cardiac manifestations. Clin Exp Rheumatol 2002;20(6 Suppl 28):S11-5.
6. Kaya EB, Okutucu S, Aksoy H, Karakulak UN, Tulumen E, Ozdemir O, et al. Evaluation of cardiac autonomic functions in patients with ankylosing spondylitis via heart rate recovery and heart rate variability. Clin Res Cardiol 2010;99:803-8. doi: 10.1007/s00392-010-0187-x.
7. Hung YM, Cheng CC, Wann SR, Lin SL. Ankylosing spondylitis associated with pulmonary arterial hypertension. Intern Med 2015;54:431-4. doi: 10.2169/internalmedicine.54.3160.
8. Aloia E, Cameli M, D'Ascenzi F, Sciaccaluga C, Mondillo S. TAPSE: An old but useful tool in different diseases. Int J Cardiol 2016;225:177-83. doi: 10.1016/j.ijcard.2016.10.009.
9. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: A report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685-713;. doi: 10.1016/j.echo.2010.05.010.
10. Rudwaleit M, van der Heijde D, Landewé R, Akkoc N, Brandt J, Chou CT, et al. The Assessment of Spondylo Arthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis 2011;70:25-31. doi: 10.1136/ard.2010.133645.
11. Zochling J. Measures of symptoms and disease status in ankylosing spondylitis: Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of

Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), and Health Assessment Questionnaire for the Spondylarthropathies (HAQ-S). Arthritis Care Res (Hoboken) 2011;63 Suppl 11:S47-58. doi: 10.1002/acr.20575.

12. Devereux RB, Casale PN, Wallerson DC, Kligfield P, Hammond IW, Liebson PR, et al. Cost-effectiveness of echocardiography and electrocardiography for detection of left ventricular hypertrophy in patients with systemic hypertension. Hypertension 1987;9:II69-76. doi: 10.1161/01.hyp.9.2_pt_2.ii69.
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2015;16:233-70. doi: 10.1093/ehjci/jev014.
14. Hosey-Cojocari C, Chan SS, Friesen CS, Robinson A, Williams V, Swanson E, et al. Are body surface area based estimates of liver volume applicable to children with overweight or obesity? An in vivo validation study. Clin Transl Sci 2021;14:2008-16. doi: 10.1111/cts.13059.
15. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1-39.e14. doi: 10.1016/j.echo.2014.10.003.
16. Agrawal P, Tote S, Sapkale B. Diagnosis and treatment of ankylosing spondylitis. Cureus 2024;16:e52559. doi: 10.7759/cureus.52559.
17. Berdal G, Halvorsen S, van der Heijde D, Mowe M, Dagfinrud H. Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitis than in matched population controls and is associated with impaired spinal mobility: A comparative study. Arthritis Res Ther 2012;14:R19. doi: 10.1186/ar3699.
18. Liu J, Kang N, Zhang Y, Hai Y. Systemic changes associated with quality of life after surgical treatment of kyphotic deformity in patients with ankylosing spondylitis: A systematic review. Eur Spine J 2020;29:794-802. doi: 10.1007/s00586-020-06322-w.
19. Cho H, Kim T, Kim TH, Lee S, Lee KH. Spinal mobility, vertebral squaring, pulmonary function, pain, fatigue, and quality of life in patients with ankylosing spondylitis. Ann Rehabil Med 2013;37:675-82. doi: 10.5535/arm.2013.37.5.675.
20. Colalillo A, Hoffmann-Vold AM, Pellicano C, Romaniello A, Gabrielli A, Hachulla E, et al. The role of TAPSE/sPAP ratio in predicting pulmonary hypertension and mortality in the systemic sclerosis EUSTAR cohort. Autoimmun Rev 2023;22:103290. doi: 10.1016/j.autrev.2023.103290.
21. Vonk MC, Vandecasteele E, van Dijk AP. Pulmonary hypertension in connective tissue diseases, new evidence and challenges. Eur J Clin Invest 2021;51:e13453. doi: 10.1111/eci.13453.
22. Nurmohamed MT, van der Horst-Bruinsma I, Maksymowych WP. Cardiovascular and cerebrovascular diseases in ankylosing spondylitis: Current insights. Curr Rheumatol Rep 2012;14:415-21. doi: 10.1007/s11926-012-0270-6.
23. Biesbroek PS, Heslinga SC, Konings TC, van der Horst-Bruinsma IE, Hofman MBM, van de Ven PM, et al. Insights into cardiac involvement in ankylosing spondylitis from cardiovascular magnetic resonance. Heart 2017;103:745-52. doi: 10.1136/heartjnl-2016-310667.
24. Chetrit M, Khan MA, Kapadia S. State of the art management of aortic valve disease in ankylosing spondylitis. Curr Rheumatol Rep 2020;22:23. doi: 10.1007/s11926-020-00898-4.
25. Karoli NA, Rebrov AP, Novikova LS, Luk'ianova LV. Heart affection in patients with ankylosing spondiloarthritis. Ter Arkh 2005;77:80-4.
26. Karoli NA, Rebrov AP. Pulmonary hypertension, involvement of the right and left cardiac parts in patients with ankylosing spondylarthritis. Klin Med (Mosk) 2004;82:31-4.
27. Yang TY, Chen YH, Siao WZ, Jong GP. Case report: A Rare manifestation of pulmonary arterial hypertension in ankylosing spondylitis. J Pers Med 2022;13:62. doi: 10.3390/jpm13010062.
28. Roller FC, Wiedenroth C, Breithecker A, Liebetrau C, Mayer E, Schneider C, et al. Native T1 mapping and extracellular volume fraction measurement for assessment of right ventricular insertion point and septal fibrosis in chronic thromboembolic pulmonary hypertension. Eur Radiol 2017;27:1980-91. doi: 10.1007/s00330-016-4585-y.
29. Andersen S, Nielsen-Kudsk JE, Vonk Noordegraaf A, de Man FS. Right ventricular fibrosis. Circulation 2019;139:269-85. doi: 10.1161/CIRCULATIONAHA.118.035326.
30. Weber KT, Sun Y, Bhattacharya SK, Ahokas RA, Gerling IC. Myofibroblast-mediated mechanisms of pathological remodelling of the heart. Nat Rev Cardiol 2013;10:15-26. doi: 10.1038/nrcardio.2012.158.
31. Danve A. Thoracic manifestations of ankylosing spondylitis, inflammatory bowel disease, and relapsing polychondritis. Clin Chest Med 2019;40:599-608. doi: 10.1016/j.ccm.2019.05.006.

Cardiovasc Surg Int 2024;11(3):164-169
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1716
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Investigation of atrioventricular block and inflammation interaction versatility and cardiac pacemakers' effects on this versatility

Onur Akhan[1], Ersin Yildirim[1], Suleyman Kursad Ozel[1], Ege Alp Dagdeviren[1], Tuncay Guzel[2], Mehmet Kis[3]

[1]Department of Cardiology, Şehit Prof. Dr. İlhan Varank Training and Research Hospital, İstanbul, Türkiye
[2]Department of Cardiology, Gazi Yaşargil Training and Research Hospital, Diyarbakır, Türkiye
[3]Department of Cardiology, Dokuz Eylül University Faculty of Medicine, İzmir, Türkiye

Received: August 05, 2024 ***Accepted:*** August 17, 2024 ***Published online:*** September 16, 2024

ABSTRACT

Objectives: This study aimed to examine inflammation markers before and three months after permanent pacemaker implantation in individuals with complete atrioventricular block to establish if cardiac conduction system disorders and pacemaker treatment affect inflammation.

Patients and methods: This retrospective cohort study included 44 complete atrioventricular block patients (24 females, 20 males; mean age: 73.4±9.2 years; range, 64 to 82 years) who underwent dual chamber (DDD) pacemakers implantation between January 1, 2023 and December 31, 2023. The hospital information system provided demographic, clinical, and laboratory data. Preprocedure and postprocedure three-month follow-up C-reactive protein, hemogram-related parameters, and inflammation scores were compared.

Results: The most common comorbidities, listed in order of frequency, were hypertension (95.4%), atherosclerotic heart disease (81.8%), diabetes mellitus (43.1%), heart failure (31.8%), and stroke (11.3%). Regarding laboratory measurements and inflammatory scores of the patients, only the mean platelet volume had a statistically significant difference just before (88.11±6.23 fL) and three months after (87.46±5.43 fL) the procedure was (p=0.002).

Conclusion: As an established indicator of inflammation, the notable decrease in mean platelet volume at the three-month follow-up suggests that inflammation may not only contribute to but also result from atrioventricular block. Long-term follow-up is needed to observe the impact of cardiac pacemakers, and further studies with innovative physiological pacing methods are required to evaluate these effects.

Keywords: Atrioventricular block, cardiac pacemaker, inflammation, inflammation score.

Cardiac diseases, cardiac surgery, and systemic disorders, categorized as infiltrative, rheumatologic, endocrine, and genetic neuromuscular degenerative diseases, can lead to heart block by affecting the myocardium and the conduction system.[1,2] Abnormalities in cardiac conduction are a reliable predictor of mortality and heart failure. Nevertheless, a preventative approach has not yet been formulated. Autopsy examinations indicate the presence of fibrosis in the conduction system, although the underlying reason remains undisclosed. Inflammation is well-acknowledged as an indicator of fibrosis.[3] Studies with follow-up periods of 7 and 11 years have emphasized that high-sensitivity C-reactive protein elevation at baseline can predict incident conduction system disease in the general population.[3,4]

Irrespective of acute heart damage, systemic inflammation can have a detrimental impact on atrioventricular conduction. Gap junctions that include connexin43 and connect cardiomyocytes with inflammation-related cells, including macrophages, are acknowledged as crucial elements regulating conduction in the atrioventricular node. Lazzerini et al.[5] presented evidence that

Corresponding author: Onur Akhan, MD. Dr. İlhan Varank Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, 34785 Sancaktepe, İstanbul, Türkiye.
E-mail: akhanonur@gmail.com

Citation:
Akhan O, Yildirim E, Ozel SK, Dagdeviren EA, Guzel T, Kis M. Investigation of atrioventricular block and inflammation interaction versatility and cardiac pacemakers' effects on this versatility. Cardiovasc Surg Int 2024;11(3):164-169. doi: 10.5606/e-cvsi.2024.1716.

an increase in interleukin (IL)-6, which leads to systemic inflammation, might acutely exacerbate atrioventricular conduction by suppressing connexin43.

Recently, novel scoring techniques have been implemented to assess the extent of inflammation. The monocyte-to-lymphocyte ratio, one of these scores, exhibited a substantial association with the occurrence of new-onset cardiac conduction block throughout a follow-up period of roughly 10 years.[6] Patients without preexisting conduction system disorders who underwent transcatheter aortic valve replacement and had elevated neutrophil-to-lymphocyte ratio on the day of the treatment were more likely to require a permanent pacemaker.[7] In recent studies, the systemic immune-inflammation index (SII), which is defined as neutrophils multiplied by platelets/lymphocytes, has been linked to the development of complete atrioventricular block in patients with ST-segment elevation myocardial infarction and the necessity of a permanent pacemaker in patients with drug-related atrioventricular block.[8,9] Çelik et al.[10] discovered a substantial correlation between the occurrence of atrial fibrillation following coronary artery bypass surgery and the neutrophil-to-lymphocyte ratio.

While inflammation is known to cause atrioventricular block, it is worth considering the inverse relationship. If such a scenario is present, it is necessary to scrutinize the impact of cardiac pacemaker therapy on this condition.

This study aimed to assess the inflammation markers before and three months after the permanent pacemaker implantation in patients with complete atrioventricular block and investigate whether cardiac conduction system disorders also affect the inflammation process and, if so, whether permanent pacemaker treatment alters this inflammation process.

PATIENTS AND METHODS

In this retrospective cohort study, the inflammation-related parameters and scores of 44 patients (24 females, 20 males; mean age: 73.4±9.2 years; range, 64 to 82 years) who underwent dual chamber (DDD) pacemakers implantation due to total atrioventricular block at the Şehit Prof. Dr. İlhan Varank Training and Research Hospital, Department of Cardiology between January 1, 2023 and December 31, 2023 were evaluated and compared before and three months after the procedure.

Patient data from the hospital's information system included basic demographic data, baseline and three-month C-reactive protein values, and hemogram parameters. The calculated inflammation scores included neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelet-to-lymphocyte ratio, SII (neutrophils×platelets/lymphocytes), and pan-immune-inflammation value (neutrophils × monocytes × platelets/lymphocytes).

This study included only patients diagnosed with complete atrioventricular block and DDD pacemaker implantation. Patients with a previous diagnosis of cardiac conduction system disease, patients with cardiac conduction system disorders other than complete atrioventricular block, patients with pacemaker-related infectious diseases, patients who received cardiac pacemaker treatment other than DDD pacemaker, patients who experienced an acute cardiac syndrome or stroke in the last year, those with uncontrolled hypertension or diabetes mellitus, patients diagnosed with heart failure within the last year not receiving optimal medical treatment for heart failure, acute infection cases, and conditions with a diagnosis of a systemic disease causing an active inflammatory process during an attack episode were excluded. A written informed consent was obtained from each patient. The study protocol was approved by the Şehit Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (date: 26.6.2024, no: E-46059653-050.99-24750597). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

The statistical analysis was conducted using the IBM SPSS version 24.0 software (IBM Corp., Armonk, NY, USA). Initially, the normality of continuous data distribution was assessed using the Kolmogorov-Smirnov test. The mean ± standard deviation (SD) was provided for continuous data, while the number and frequency were used for categorical variables. Student's t-test was employed to compare continuous variables that were continuous. Subsequently, a comparative examination of

Table 1
Baseline clinical and demographic features

Parameters	n	%	Mean±SD
Age (year)	44		73.4±9.2
GFR (mL/min/1.73 m²)	44		64.7±17.4
Sex			
Male	24	54.5	
Hypertension	42	95.4	
Diabetes mellitus	19	43.1	
Heart failure	14	31.8	
Stroke	5	11.3	
Atherosclerotic heart disease	36	81.8	

SD: Standard deviation; GFR: Glomerular filtration rate.

categorical variables was conducted utilizing Pearson's chi-square and Fisher exact tests. A p-value <0.05 was considered statistically significant.

RESULTS

Hypertension, atherosclerotic heart disease, diabetes mellitus, heart failure, and stroke were the most prevalent comorbidities in the study cohort in order of frequency (Table 1). Atrial and ventricular sensing and pacing thresholds and impedance values are shown in Table 2.

The mean platelet volume value was the only statistically significant difference observed when comparing laboratory parameters of the patients just before (88.11±6.23 fL) and three months after (87.46±5.43 fL) the procedure (p=0.002). No differences regarding inflammatory scores were identified in the comparisons (Table 3).

Table 2
Cardiac pacemaker characteristics

Parameters	Mean±SD
Atrial pacing threshold (V)	0.87±0.25
Atrial sensing threshold (mV)	3.27±1.23
Atrial impedance (Ohms)	525.0±112.8
Ventricular pacing threshold (V)	0.81±0.19
Ventricular sensing threshold (mV)	12.53±3.92
Ventricular impedance (Ohms)	689.4±148.6

SD: Standard deviation.

DISCUSSION

The cardiac pacemaker system comprises three main components: cellular ion channels, isolated tissue, and an energy reservoir. This system is influenced by inflammatory processes even during the prenatal period.[11] Research has shown that inflammation adversely affects the cardiac conduction system by triggering fibrotic processes.[1,3,4] It has been shown that IL-6 affects connexin43 gap junctions in cardiomyocytes through a newly revealed mechanism.[5] Inflammation observed during cardiac intervention and surgery has provided indications for the necessity of a permanent pacemaker.[7-9] Moreover, the connection between inflammatory processes and cardiomyopathy and ventricular arrhythmias has recently been uncovered.[12,13]

Cardiac pacemaker therapy has been utilized as a treatment modality since 1960 for patients suffering from cardiac conduction system disorders.[14] Nevertheless, adverse consequences that can impact inflammation due to pacemaker therapy have been noted. These complications include the early lead fixation effect, suture inflammation, postcardiac injury syndrome, and pacemaker- and lead-related infections.[15-18]

These considerations aside, it may come to mind that the atrioventricular block itself is a cause of inflammation after the development of atrioventricular block. To achieve this objective, we investigated the inflammatory markers and scores of patients who developed complete atrioventricular block and

Table 3
Clinical laboratory findings

	Procedure Day*			After 3 month			
	Mean±SD	Median	Q1, Q3	Mean±SD	Median	Q1, Q3	*p*
CRP (mg/dL)	10.84±8.77			10.44±8.61			0.835
WBC (10^3/μL*)	7.93±2.29			7.98±2.78			0.889
Neutrophil (10^3/μL*)	6.76±2.81			5.40±2.25			0.349
Lymphocyte (10^3/μL*)	1.84±0.74			1.74±0.73			0.203
Monocyte (10^3/μL*)	0.55±0.21			0.54±0.21			0.948
Hemoglobin (gr/dL)	12.14±1.91			12.48±1.98			0.093
Hematocrit (%)	37.03±5.50			37.86±5.65			0.191
MCV (fL)	88.11±6.23			87.46±5.43			0.156
RDW (%)	14.40±1.70			14.55±1.46			0.480
MPV (fL)	9.90±1.24			9.58±1.39			**0.002**
Platelet (10^3/μL*)	225.00±78.77			232.46±76.23			0.265
M/L	0.38±0.34			0.38±0.26			0.986
N/L		2.65	1.84-4.41		2.90	1.89-4.67	0.326
P/L		120.66	80.71-151.60		132.08	89.96-190.17	0.090
SII		532.14	343.93-1187.90		871.15	378.56-1249.71	0.578
PIV		265.38	153.67-673.30		541.03	177.92-718.95	0.669

SD: Standard deviation; CRP: C-reactive protein; WBC: White blood cell; MCV: Mean corpuscular volume; RDW: Red cell distribution width; MPV: Mean platelet volume; M/L: Monocyte/lymphocyte; N/L: Neutrophil/lymphocyte; P/L: Platelet/lymphocyte; SII: Systemic immune-inflammation index; PIV: Panimmune-inflammation value; * Just before the procedure.

underwent DDD pacemaker implantation before and three months after the procedure.

The prevalence of inflammation-related atrial high-rate episodes in patients with cardiac pacemakers, as reported in the literature, prompted us to consider this subject.[19-21] The results of our study did not reveal any statistically significant differences, except for a decrease in mean platelet volume in the third month of the follow-up compared to baseline (87.46±5.43 fL *vs.* 88.11±6.23 fL; p=0.002).

A literature review showed that MPV could be an indicator of platelet activation and microvascular complications, as well as a marker of inflammation. Furthermore, it has been demonstrated that minor postcardiac surgery may be associated with the development of atrial fibrillation.[22-24] Therefore, our study's findings provide limited but relevant insights that align with its objectives.

The potential effects of the atrioventricular block on inflammation may not be adequately observed by restricting the follow-up period of the study to three months, as it is known in the literature that the effects of inflammation on the development of new atrioventricular block begin approximately two years later.[4] The investigation is also scheduled to undergo long-term follow-ups.

Another point that needs to be focused on is the recently implemented His-Purkinje conduction system pacing method. This novel cardiac pacing method has demonstrated the ability to maintain stable pacing thresholds over mid-term follow-ups and achieve low rates of lead revision in patients diagnosed with atrioventricular block.[25] The more physiological nature of this system for the cardiac conduction system may result in more suggestive results for the objectives of our study. This subject may be clarified in future research, specifically through innovative pacing methods like left bundle pacing.

The study's limitations include the fact that it is retrospective, it can be conducted in a single

center with a limited number of patients, and the limited follow-up period. Despite the exclusion of patients with newly diagnosed acute coronary syndrome, stroke, uncontrolled hypertension, and diabetes mellitus within the past year to mitigate the impact of comorbidities on inflammation, the results of the study may have been influenced by the presence of these conditions. Although we excluded all pacemaker-related infectious diseases, the study may have been exposed to unforeseeable effects.

In conclusion, inflammation is a cause of cardiac conduction system disorders, but it is unclear whether these disorders also lead to inflammation. In the present study, the difference in the mean platelet volume observed in the follow-up after DDD pacemaker application in patients with complete atrioventricular block may be a clue in clarifying this situation. Although we believe that our study will give ideas for future studies, it is evident that long-term follow-ups are necessary to clarify this issue.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conceptualization: O.A., E.Y.; Data collection: O.A., E.A.D.; Data analysis and investigation: O.A., E.Y., S.K.O., E.A.D.; Methodology: O.A., E.Y., T.G.; Reviewing-editing: O.A., E.Y., S.K.O., E.A.D., T.G., M.K.; Writing: O.A., E.Y., T.G., M.K.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Sabzwari SRA, Tzou WS. Systemic diseases and heart block. Cardiol Clin 2023;41:429-48. doi: 10.1016/j.ccl.2023.03.008.
2. Aksoy E, Sunar H. Conduction system abnormalities after isolated surgical aortic valve replacement. Cardiovasc Surg Int 2023;10:161-9. doi: 10.5606/e-cvsi.2023.1542
3. Frimodt-Møller EK, Gottdiener JS, Soliman EZ, Kizer JR, Vittinghoff E, Psaty BM, et al. Inflammation and incident conduction disease. J Am Heart Assoc 2023;12:e027247. doi: 10.1161/JAHA.122.027247.
4. Wu L, Wu M, Zhao D, Chen S, Wang G, Xu L, et al. Elevated high-sensitivity C-reactive protein levels increase the risk of new-onset cardiac conduction disorders. Cardiovasc Diabetol 2023;22:268. doi: 10.1186/s12933-023-01987-1.
5. Lazzerini PE, Acampa M, Cupelli M, Gamberucci A, Srivastava U, Nanni C, et al. Unravelling atrioventricular block risk in inflammatory diseases: Systemic inflammation acutely delays atrioventricular conduction via a cytokine-mediated inhibition of connexin43 expression. J Am Heart Assoc 2021;10:e022095. doi: 10.1161/JAHA.121.022095.
6. Li M, Li X, Gao H, Li P, Zhang L, Zhang X, et al. U-Shaped association between monocyte-lymphocyte ratio and risk of cardiac conduction block. J Inflamm Res 2023;16:5393-402. doi: 10.2147/JIR.S438722.
7. Totaro A, Testa G, Calafiore AM, Ienco V, Sacra V, Busti A, et al. Neutrophil to lymphocyte ratio predicts permanent pacemaker implantation in TAVR patients. J Card Surg 2022;37:5095-102. doi: 10.1111/jocs.17212.
8. Esin F, Esen S, Aktürk S, Pekersen Ö, Kiris T, Karaca M. Relationship between systemic immune inflammation index and development of complete atrioventricular block in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. BMC Cardiovasc Disord 2024;24:73. doi: 10.1186/s12872-024-03726-0.
9. Şenöz O, Erseçgin A. Systemic immune-inflammation index as a tool for predicting the need for a permanent pacemaker in patients with drug-induced atrioventricular block. Pacing Clin Electrophysiol 2021;44:1972-8. doi: 10.1111/pace.14377.
10. Çelik E, Çora A, Karadem KB. Are preoperative neutrophil/lymphocyte, platelet/lymphocyte, and platelet/neutrophil ratios markers in new-onset atrial fibrillation after coronary artery bypass grafting? Cardiovasc Surg Int 2020;7:113-20. doi: 10.5606/e-cvsi.2020.876
11. Frasch MG, Giussani DA. Impact of chronic fetal hypoxia and inflammation on cardiac pacemaker cell development. Cells 2020;9:733. doi: 10.3390/cells9030733.
12. Tung R, Bauer B, Schelbert H, Lynch JP 3rd, Auerbach M, Gupta P, et al. Incidence of abnormal positron emission tomography in patients with unexplained cardiomyopathy and ventricular arrhythmias: The potential role of occult inflammation in arrhythmogenesis. Heart Rhythm 2015;12:2488-98. doi: 10.1016/j.hrthm.2015.08.014.
13. Turpeinen AK, Vanninen E, Magga J, Tuomainen P, Kuusisto J, Sipola P, et al. Cardiac sympathetic activity is associated with inflammation and neurohumoral activation in patients with idiopathic dilated cardiomyopathy. Clin Physiol Funct Imaging 2009;29:414-9. doi: 10.1111/j.1475-097X.2009.00887.x.
14. Beck H, Boden WE, Patibandla S, Kireyev D, Gutpa V, Campagna F, et al. 50th Anniversary of the first successful permanent pacemaker implantation in the United States: Historical review and future directions. Am J Cardiol 2010;106:810-8. doi: 10.1016/j.amjcard.2010.04.043.
15. Varvarousis D, Goulas N, Polytarchou K, Psychari SN, Paravolidakis K, Konstantinidou A, et al. Biomarkers of myocardial injury and inflammation after permanent pacemaker implantation: The lead fixation type effect. J Atr Fibrillation 2018;10:1798. doi: 10.4022/jafib.1798.

16. Garg N, Moorthy N. A mysterious pacemaker suture: an uncommon foreign body reaction. Indian Pacing Electrophysiol J 2011;11:27-30.
17. Patel ZK, Shah MS, Bharucha R, Benz M. Post-cardiac injury syndrome following permanent dual-chamber pacemaker implantation. Cureus 2022;14:e21737. doi: 10.7759/cureus.21737.
18. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR, et al. Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections. J Am Coll Cardiol 2007;49:1851-9. doi: 10.1016/j.jacc.2007.01.072.
19. Simu GR, Tomoaia R, Rosu RO, Gusetu G, Puiu M, Cismaru G, et al. Galectin-3, inflammation, and the risk of atrial high-rate episodes in patients with dual chamber pacemakers. Int J Mol Sci 2023;24:7710. doi: 10.3390/ijms24097710.
20. Liao MT, Chen CK, Lin TT, Cheng LY, Ting HW, Liu YB. High-Sensitivity C-reactive protein is a predictor of subsequent atrial high-rate episodes in patients with pacemakers and preserved ejection fraction. J Clin Med 2020;9:3677. doi: 10.3390/jcm9113677.
21. Pastori D, Miyazawa K, Li Y, Shahid F, Hado H, Lip GYH. Inflammation and the risk of Atrial High-Rate Episodes (AHREs) in patients with cardiac implantable electronic devices. Clin Res Cardiol 2018;107:772-7. doi: 10.1007/s00392-018-1244-0.
22. Ramakrishnan A, Fontes ML, Lombard FW, Abdelmalak M, Hong Y, Shi Y, et al. Mean platelet volume and cardiac surgery-associated atrial fibrillation. J Cardiothorac Vasc Anesth 2021;35:2533-6. doi: 10.1053/j.jvca.2020.11.010.
23. Wang Y, Miao Y, Wan Q. Association of white blood cell count to mean platelet volume ratio with type 2 diabetic peripheral neuropathy in a Chinese population: A cross-sectional study. BMC Endocr Disord 2024;24:129. doi: 10.1186/s12902-024-01644-y.
24. Mi AE, Abdallah N, Eldars W. Mean platelet volume and platelet distribution width correlate with microvascular complications in Egyptian people with type 2 diabetes mellitus. Curr Diabetes Rev 2021;17:e080621193947. doi: 10.2174/1573399817666210608121024.
25. Vijayaraman P, Patel N, Colburn S, Beer D, Naperkowski A, Subzposh FA. His-Purkinje conduction system pacing in atrioventricular block: New insights into site of conduction block. JACC Clin Electrophysiol 2022;8:73-85. doi: 10.1016/j.jacep.2021.07.007.

Cardiovasc Surg Int 2024;11(3):170-176
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1714
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

A practical predictor for postoperative atrial fibrillation in patients with coronary artery bypass graft surgery: P-wave peak time in lead-V1

İlhan Koyuncu[1], Emin Koyun[2]

[1]Department of Cardiology, İzmir Bakırçay University, İzmir, Türkiye
[2]Department of Cardiology, Sivas Numune Hospital, Sivas, Türkiye

Received: July 30, 2024 ***Accepted:*** August 17, 2024 ***Published online:*** September 17, 2024

ABSTRACT

Objectives: The study aimed to examine the relationship between P-wave peak time (PWPT) and postoperative atrial fibrillation (POAF) in electrocardiograms recordings before the coronary artery bypass graft (CABG) surgery.

Patients and methods: The retrospective study was conducted with 203 patients who underwent CABG surgery between January 2015 and January 2023. Patients were divided into two groups: those who developed POAF (n=40; 30 males, 10 females; mean age: 68.1±8.7 years; range, 18 to 85 years) and those who did not (n=163; 122 males, 41 females; mean age: 62.9±9.7 years; range, 18 to 85 years). The PWPT was calculated on the patients' preoperative electrocardiograms.

Results: The PWPT in lead V1 (PWPT-V1) and age were identified as strong predictors of POAF in CABG patients. In the receiver operating characteristic curve analysis, it was found that a PWPT-V1 value >41.5 had 79% sensitivity and 73% specificity for the prediction of the POAF (area under the curve=0.806, p<0.001).

Conclusion: The PWPT-V1 can predict the development of POAF in patients undergoing CABG surgery. Thanks to this parameter, necessary prophylactic treatments can be performed in these patients before surgery. As a result, mortality and morbidity can be reduced in these patients.

Keywords: Atrial fibrillation, coronary artery bypass graft, P-wave indices, P-wave peak time

One of the common complications after cardiac surgery is atrial fibrillation (AF), and it is the most common type of arrhythmia after surgery.[1] In a study, it was found that postoperative AF (POAF) developed in 25 to 50% of patients depending on the surgical procedures.[2]

Although years have passed, developing surgical methods or preoperative treatments have not caused a decrease in the number of POAF in operated patients.[3] Postoperative AF still causes increased morbidity and mortality today. It is also among the important causes of health care costs.[4] Atrial fibrillation is more common in patients with POAF compared to patients in postoperative sinus rhythm.[5]

A study has shown that POAF is associated with an increased incidence of short-term complications after coronary artery bypass graft (CABG).[6] Additionally, it has been shown in a study that POAF is associated with the risk of death and thromboembolic complications in the long term.[7]

It is known that P-wave-related parameters reflect atrial reorganization, and it is associated with an increased risk of AF in CABG patients.[8] P-wave peak time (PWPT), a new electrocardiogram (ECG) parameter, shows that the conduction time in the interatrial and interatrial area increases, and a study has shown a relationship with AF.[9]

The study aimed to examine the relationship between PWPT and POAF in ECG recordings before

Corresponding author: İlhan Koyuncu, MD. İzmir Bakırçay Üniversitesi Kardiyoloji Anabilim Dalı, 35665 Menemen, İzmir, Türkiye
E-mail: dr_ilhann@hotmail.com

Citation:
Koyuncu İ, Koyun E. A practical predictor for postoperative atrial fibrillation in patients with coronary artery bypass graft surgery: P-wave peak time in lead-V1. Cardiovasc Surg Int 2024;11(3):170-176. doi: 10.5606/e-cvsi.2024.1714.

CABG surgery. If a relationship is found, PWPT could be used to identify patients at high risk for POAF and allow close monitoring of these patients after surgery, reducing mortality and morbidity in these patients.

PATIENTS AND METHODS

The retrospective study was conducted with 203 patients who underwent CABG surgery at the Bakırçay University Çiğli Training and Research Hospital, Department of Cardiology, between January 2015 and January 2023. The patients were in sinus rhythm on the ECG taken before CABG. The patients were divided into two groups: those who developed POAF (n=40; 30 males, 10 females; mean age: 68.1±8.7 years; range, 18 to 85 years) and those who did not (n=163; 122 males, 41 females; mean age: 62.9±9.7 years; range, 18 to 85 years). Electrocardiogram parameters, demographic characteristics, and blood parameters of the groups were compared. A written informed consent was obtained from each patient. The study protocol was approved by the İzmir Bakırçay University Ethics Committee (date: 18.10.2023, no: 1246). The study was conducted in accordance with the principles of the Declaration of Helsinki. The inclusion criteria were having no previous diagnosis of AF and having a documented sinus ECG before surgery. The exclusion criteria were as follows: patients with electrolyte disorders, patients without a preoperative ECG taken on the same day as the CABG surgery, patients with severe heart valve diseases and chronic renal failure, patients with pacemakers, patients using antiarrhythmic drugs, and patients with metabolic disorders.

Electrocardiograms taken on the day of the surgery were examined. The definition of POAF was made as follows: arrhythmia lasting more than 10 min and resolving spontaneously or after being treated with electrical/medical cardioversion.[8] Patients were closely monitored for arrhythmia throughout their hospital stay. An ECG was also taken when cardiac symptoms, such as palpitations, occurred. Patients who developed AF before discharge were included in the study.

Electrocardiograms were recorded in 12 leads, at 10 mm/mV and 25 mm/sec settings. Electrocardiograms were transferred digitally and

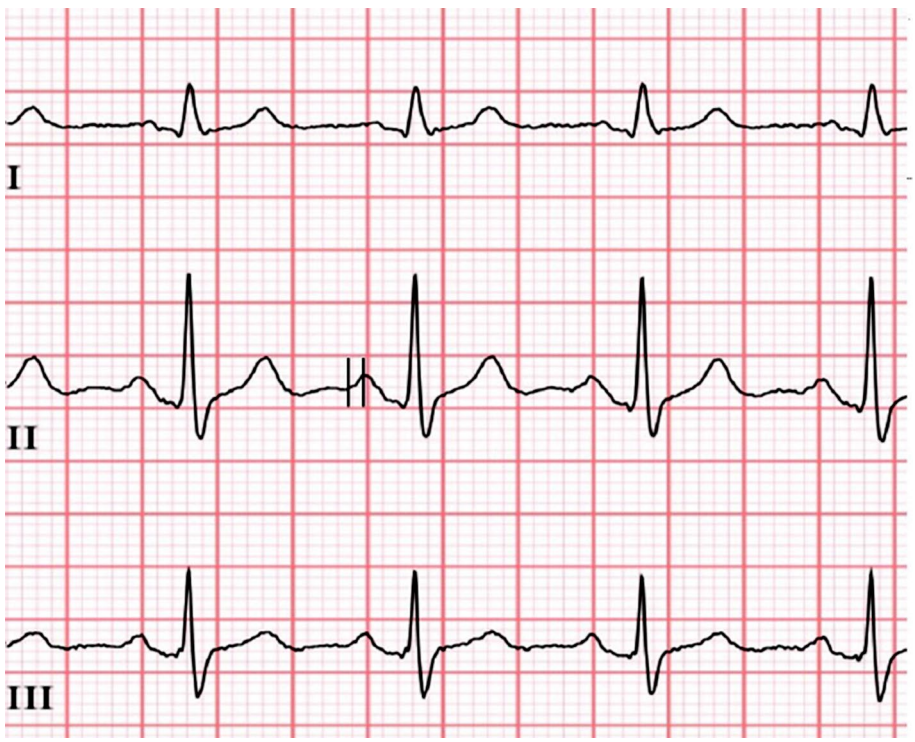


Figure 1. Calculation of P wave peak time on electrocardiographic.

loaded into software. Once the images were enlarged sufficiently, after the ECGs were evaluated by a cardiologist, they were evaluated again by another cardiologist to reduce bias. The PWPT was measured in leads D2 (PWPT-D2) and V1 (PWPT-V1; Figure 1). The beginning of the P-wave deflection determined the starting position of the measurement area. The peak of the P wave formed the last region of the measurement region. The PWPT was defined as the time between the onset of positive deflection and the peak of negative deflection during which P waves were biphasic in lead V1.

Statistical analysis

Data were analyzed using IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Histograms, Q-Q plots, and the Shapiro-Wilk test were used to evaluate whether the data met normality assumptions. A two-sample t-test and the Mann-Whitney U test were performed to compare quantitative variables between groups. The chi-square test was used to evaluate the relationship between categorical variables. The continuous data were presented as mean ± standard deviation (SD) based on the data distribution. The categorical variables were expressed as the frequency (n) and percentage (%). Logistic regression analysis was used to determine the risk factors affecting POAF status. Variables that were found to be statistically significant as a result of logistic regression analysis were evaluated with multiple logistic regression analysis. Receiver

Table 1
The baseline clinical and laboratory characteristics

	POAF (–) group (n=163)			POAF (+) group (n=40)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			62.9±9.7			68.1±8.7	**<0.001**
Sex							
Female	41	25.1		10	25		0.247
Body mass index (kg/m^2)			26.94±3.47			27.59±3.72	0.153
Hypertension	128	78.5		31	77.5		0.076
Diabetes mellitus	79	48.4		18	45		0.519
Hyperlipidemia	126	77.3		32	80		0.428
Cerebrovascular event	6	3.6		3	7.5		**0.023**
Smoking	62	38		12	30		0.152
Systolic blood pressure (mmHg)			143.73±20.8			147.4±19.52	0.154
Diastolic blood pressure (mmHg)			79.9±8.6			81.38±7.58	0.141
Gensini score			71.33±31.12			68.2±31.38	0.437
Creatinine (mg/dL)			0.93±0.44			0.85±0.29	0.36
Na (mmol/L)			140.2±3.4			138.6±2.5	0.853
K (mmol/L)			4.12±0.43			4.43±0.35	0.25
AST (U/L)			19.2±11.5			21.2±7.5	0.45
ALT (U/L)			16±14.1			20.1±16	0.17
Total cholesterol			193.54±48.03			180.93±46.17	0.06
LDL (mg/dL)			125.36±42.25			115.81±43.81	0.090
HDL (mg/dL)			34.1±5.7			32.9±4.8	0.07
White blood cell (10^3/uL)			8.2±2.4			8.1±2.2	0.30
Hemoglobin (g/dL)			10.9±1.8			11.4±2.1	0.81
Platelet (10^3/uL)			251.3±69.2			245.8±70.9	0.37

POAF: Postoperative atrial fibrillation; SD: Standard deviation; ALT: Alanine transaminase; AST: Aspartate transaminase; LDL-C: Low density lipoprotein cholesterol; HDL: High-density lipoprotein.

operating characteristic (ROC) analysis was performed to evaluate the predictive value of PWPT-V1 and age for POAF. The area under the curve (AUC) and the cutoff value were calculated for each parameter. Sensitivity and specificity were calculated to determine the diagnostic power of the scores. A p-value <0.05 was considered statistically significant.

RESULTS

When the baseline clinical and demographic characteristics of both groups were compared, the age of the patients in the POAF group was higher compared to the other group (p<0.001). The number of cerebrovascular events was also higher in the POAF group than in the other group (3 (7.5) *vs.* 6 (3.6), p=0.023). Total cholesterol count was observed at lower levels in the POAF group compared to the other group (180.93±46.17 *vs.* 193.54±48.03, p=0.037). There was no significant difference between the groups, except for age and cerebrovascular events (Table 1).

When the results of echocardiographic and electrocardiographic parameters of both groups were examined, partial interatrial block (IAB; 10 (25) *vs.* 7 (4.3), p<0.001), advanced IAB (8 (20) *vs.* 1 (0.6), p<0.001), PWPT-V1 (45.04±3.95 *vs.* 40.12±4.01, p<0.001), and PWPT-D2 (49.72±5.29 *vs.* 43.69±4.93, p<0.001) were higher in the POAF group compared to the other group (Table 2).

According to multiple logistic regression analysis, age (odds ratio [OR]=1.044, 95% confidence interval [CI]: 1.009-1.081, p=0.014), PWPT-V1 (OR=1.177,

Table 2
The echocardiographic and electrocardiographic results

	POAF (–) group (n=163)			POAF (+) group (n=40)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
LVEF (%)			53.63±9.72			52.86±9.81	0.475
Left atrium diameter (mm)			44.7±5.4			49.6±5.2	0.082
LVEDD (mm)			49.5±4.2			52.9±3.8	0.128
P-IAB	7	4.3		10	25		**<0.001**
A-IAB	1	0.6		8	20		**<0.001**
PWD (msec)			92.57±9.1			99.49±12.8	0.065
PWPT-V1 (msec)			40.12±4.01			45.04±3.95	**<0.001**
PWPT-D2 (msec)			43.69±4.93			49.72±5.29	**<0.001**

POAF: Postoperative atrial fibrillation; SD: Standard deviation; LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end-diastolic diameter; IAB: Interatrial block; PWD: P wave duration; PWPT: P wave peak time.

Table 3
The univariate and multivariate analysis for predicting POAF

	Univariate			Multivariate		
	OR	%95 CI	*p*	OR	%95 CI	*p*
Age	1.064	1.032-1.096	**<0.001**	1.044	1.009-1.081	**0.014**
PWPT-V1	1.318	1.229-1.414	**<0.001**	1.177	1.053-1.316	**0.004**
PWPT-D2	1.236	1.167-1.308	**<0.001**			
Cerebrovascular event	2.990	1.242-7.199	**0.015**			
A-IAB	26.500	7.443-94.355	**<0.001**	8.470	2.074-34.589	**0.003**
P-IAB	6.925	3.260-14.711	**<0.001**			

POAF: Postoperative atrial fibrillation; OR: Odss ratio; CI: Confidence interval; PWPT-V1: P-wave peak time in lead V1; PWPT-D2: P-wave peak time in lead D2; A-IAB: Advanced interatrial block; P-IAB: Partial interatrial block.

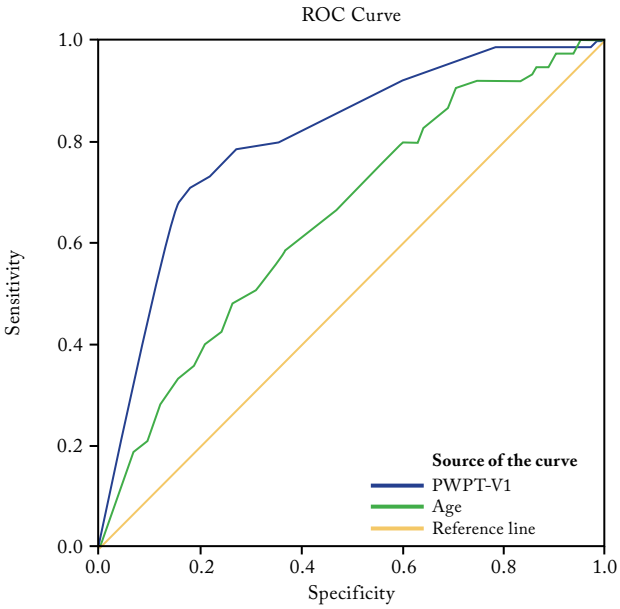


Figure 2. The ROC curve of POAF predictors in patients who underwent CABG surgery.

ROC: Receiver operating characteristics; POAF: Postoperative atrial fibrillation; CABG: Coronary artery bypass graft; PWPT: P wave peak time.

95% CI: 1.053-1.316, p=0.004), and advanced IAB (OR=8.470, 95% CI: 2.074-34.589, p=0.003) were strong independent predictors of POAF after CABG surgery (Table 3).

In ROC analysis, a PWPT-V1 >41.5 (AUC=0.806, 95% CI: 0.751-0.861, p<0.001) was found to be an independent predictor for the development of POAF after CABG surgery, with 79% sensitivity and 73% specificity. Additionally, age >66.5 years (AUC=0.653, 95% CI: 0.586-0.721, p<0.001) was identified as another independent predictor, with 59% sensitivity and 63% specificity (Figure 2).

DISCUSSION

This comprehensive study investigated the relationship between CABG surgery and POAF. The most important finding in this study was that PWPT-V1, an ECG parameter, was an independent predictor of POAF.

In the past, AF was not considered a significant complication after heart surgery. However, a study has revealed that POAF affects mortality and morbidity.[10] In a study conducted with CABG patients, patients with POAF were examined. A prolonged need for ventilation and longer stays in the intensive care unit and hospital were observed in patients with POAF.[11] It has also been revealed that POAF is associated with an increased risk of mortality and stroke in the long term.[12]

Since it is understood that POAF developing after cardiac surgery can lead to significant complications, it becomes important to identify patients at high risk for AF. For this purpose, conduct comprehensive studies on POAF have been conducted.

Some factors may lead to the development of POAF. A study found a relationship between hypoxemia and POAF.[13] In another study, a relationship was found between different surgical techniques and POAF.[14] The multitude of risk factors that can lead to AF can lead to the development of POAF. In a meta-analysis with 36,834 participants, advanced age, increased left atrium diameter, low ejection fraction, chronic obstructive pulmonary disease, hypertension, myocardial infarction, and diabetes were found to be associated with the development of POAF.[15]

In the ECG, the wave associated with atrial depolarization is the P wave. Structural changes and arrhythmias in the atria can cause changes in the P wave. Therefore, studies have examined whether there is a relationship between P-wave changes and POAF. An ECG taken before undergoing surgery is the simplest method that can be used to predict POAF.

In recent studies, the relationship between PWPT, a new ECG parameter, and AF has been examined. In a study conducted with patients in sinus rhythm with acute ischemic stroke, a significant relationship was found between paroxysmal AF detected in Holter ECG and P-wave duration, dispersion, and terminal force in ECGs.[26] In another study on acute ischemic stroke patients, it was examined whether there was a relationship between PWPT and paroxysmal AF, and it was determined that there was a relationship between PWPT and AF.[16] Another study found PWPT-D2 and PWPT-V1 to be strong markers predicting POAF in patients.[17] Unlike our study, it was found that only PWPT-V1 could be associated with POAF. Furthermore, the AUC, sensitivity, and specificity values of PWPT-V1 in our study in the ROC curve analysis were higher compared to the previous study.[17] We did not have information about the coronary lesions of the CABG patients

included in the study. In a study, PWPT-V1 was found to be significantly longer in the multivessel slow flow group than in the single-vessel group.[18] It was stated that these findings may be related to ischemia being affected by a larger myocardial area and multivessel slow flow.[18] The significant results observed in PWPT-V1 in our study may be due to these reasons.

In IAB, the activation time between the atria is longer than normal. Therefore, the P-wave duration of patients with IAB is ≥120 msec.[19] It was demonstrated that IAB may lead to AF.[20] In one study, IAB was found to be a predictor of AF in patients with coronary artery disease and carotid artery disease.[21] Interatrial block is important because it is commonly found in the elderly population and has previously been associated with AF.[22] In a study, it was found that IAB detected the emergence and recurrence of AF.[23] Bachmann's area is the largest interatrial conduction pathway. It is thought that fibrosis in this region may lead to IAB.[21] The fact that IAB was statistically significant in our study can be explained by this mechanism.

Age is an independent risk factor for the development of AF.[24] It is estimated that AF observed in elderly patients in the European Union will be more than twice as common after 50 years.[25] With this study, we determined the relationship between age and AF and found that one of the most important risk factors for POAF is advanced age.

Atrial fibrillation is a high-risk disease group in terms of ischemic events. Therefore, cerebrovascular events may occur more frequently in these patients. This may explain the higher incidence of cerebrovascular events in the AF group in our study.

The most important limitation of the study was the retrospective design. Lack of sufficient knowledge about the surgical techniques applied was also a significant limitation since the surgical techniques applied may have affected PWPT-V1 values. The data on the anesthetic drugs given to patients before surgery were also absent. The anesthetic agents given may also have influenced PWPT-V1 values. Multicenter, prospective, randomized controlled studies are needed to better understand whether this parameter is predictive of POAF.

In conclusion, PWPT-V1 can predict the development of POAF in patients undergoing CABG. Utilizing this parameter, necessary prophylactic treatments can be performed in these patients before surgery, reducing mortality and morbidity.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, design, control/supervision, analysis and/or interpretation, literature review, writing the article, critical review, materials: İ.K., E.K.; Data collection and/or processing: İ.K.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Anderson E, Dyke C, Levy JH. Anticoagulation strategies for the management of postoperative atrial fibrillation. Clin Lab Med 2014;34:537-61. doi: 10.1016/j.cll.2014.06.012.
2. D'Agostino RS, Jacobs JP, Badhwar V, Fernandez FG, Paone G, Wormuth DW, et al. The society of thoracic surgeons adult cardiac surgery database: 2018 update on outcomes and quality. Ann Thorac Surg 2018;105:15-23. doi: 10.1016/j.athoracsur.2017.10.035.
3. Greenberg JW, Lancaster TS, Schuessler RB, Melby SJ. Postoperative atrial fibrillation following cardiac surgery: A persistent complication. Eur J Cardiothorac Surg 2017;52:665-72. doi: 10.1093/ejcts/ezx039.
4. LaPar DJ, Speir AM, Crosby IK, Fonner E Jr, Brown M, Rich JB, et al. Postoperative atrial fibrillation significantly increases mortality, hospital readmission, and hospital costs. Ann Thorac Surg 2014;98:527-33. doi: 10.1016/j.athoracsur.2014.03.039.
5. Ahlsson A, Fengsrud E, Bodin L, Englund A. Postoperative atrial fibrillation in patients undergoing aortocoronary bypass surgery carries an eightfold risk of future atrial fibrillation and a doubled cardiovascular mortality. Eur J Cardiothorac Surg 2010;37:1353-9. doi: 10.1016/j.ejcts.2009.12.033.
6. Villareal RP, Hariharan R, Liu BC, Kar B, Lee VV, Elayda M, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol 2004;43:742-8. doi: 10.1016/j.jacc.2003.11.023.
7. Lee SH, Kang DR, Uhm JS, Shim J, Sung JH, Kim JY, et al. New-onset atrial fibrillation predicts long-term newly developed atrial fibrillation after coronary artery bypass graft. Am Heart J 2014;167:593-600.e1. doi: 10.1016/j.ahj.2013.12.010.

8. Wong JK, Lobato RL, Pinesett A, Maxwell BG, Mora-Mangano CT, Perez MV. P-wave characteristics on routine preoperative electrocardiogram improve prediction of new-onset postoperative atrial fibrillation in cardiac surgery. J Cardiothorac Vasc Anesth 2014;28:1497-504. doi: 10.1053/j.jvca.2014.04.034.
9. Yıldırım E, Günay N, Bayam E, Keskin M, Ozturkeri B, Selcuk M. Relationship between paroxysmal atrial fibrillation and a novel electrocardiographic parameter P wave peak time. J Electrocardiol 2019;57:81-6. doi: 10.1016/j.jelectrocard.2019.09.006.
10. Stamou SC, Dangas G, Hill PC, Pfister AJ, Dullum MK, Boyce SW, et al. Atrial fibrillation after beating heart surgery. Am J Cardiol 2000;86:64-7. doi: 10.1016/s0002-9149(00)00829-8.
11. Ghurram A, Krishna N, Bhaskaran R, Kumaraswamy N, Jayant A, Varma PK. Patients who develop post-operative atrial fibrillation have reduced survival after off-pump coronary artery bypass grafting. Indian J Thorac Cardiovasc Surg 2020;36:6-13. doi: 10.1007/s12055-019-00844-9.
12. Kosmidou I, Stone GW. New-onset atrial fibrillation after PCI and CABG for left main disease: Insights from the EXCEL trial and additional studies. Curr Opin Cardiol 2018;33:660-4. doi: 10.1097/HCO.0000000000000557.
13. Wahr JA, Parks R, Boisvert D, Comunale M, Fabian J, Ramsay J, et al. Preoperative serum potassium levels and perioperative outcomes in cardiac surgery patients. Multicenter Study of Perioperative Ischemia Research Group. JAMA 1999;281:2203-10. doi: 10.1001/jama.281.23.2203.
14. Zaman AG, Archbold RA, Helft G, Paul EA, Curzen NP, Mills PG. Atrial fibrillation after coronary artery bypass surgery: A model for preoperative risk stratification. Circulation 2000;101:1403-8. doi: 10.1161/01.cir.101.12.1403.
15. Yamashita K, Hu N, Ranjan R, Selzman CH, Dosdall DJ. Clinical risk factors for postoperative atrial fibrillation among patients after cardiac surgery. Thorac Cardiovasc Surg 2019;67:107-16. doi: 10.1055/s-0038-1667065.
16. Öz A, Cinar T, Kızılto Güler C, Efe SÇ, Emre U, Karabağ T, et al. Novel electrocardiography parameter for paroxysmal atrial fibrillation in acute ischaemic stroke patients: P wave peak time. Postgrad Med J 2020;96:584-8. doi: 10.1136/postgradmedj-2020-137540.
17. Zengin A, Karataş MB, Çanga Y, Pay L, Eren S, Çalık AN, et al. A novel electrocardiographic parameter for the prediction of atrial fibrillation after coronary artery bypass graft surgery "P wave peak time". Ir J Med Sci 2022;191:2579-85. doi: 10.1007/s11845-021-02894-8.
18. Aslan B, Işık F, Akyüz A, İnci Ü, Karadeniz M. Prolonged P wave peak time may be a sign of LV diastolic dysfunction in the coronary slow flow phenomenon. Int J Clin Pract 2022;2022:4626701. doi: 10.1155/2022/4626701.
19. Bayés de Luna A, Platonov P, Cosio FG, Cygankiewicz I, Pastore C, Baranowski R, et al. Interatrial blocks. A separate entity from left atrial enlargement: A consensus report. J Electrocardiol 2012;45:445-51. doi: 10.1016/j.jelectrocard.2012.06.029.
20. Tse G, Wong CW, Gong M, Wong WT, Bazoukis G, Wong SH, et al. Predictive value of inter-atrial block for new onset or recurrent atrial fibrillation: A systematic review and meta-analysis. Int J Cardiol 2018;250:152-6. doi: 10.1016/j.ijcard.2017.09.176.
21. Alexander B, Baranchuk A, Haseeb S, van Rooy H, Kuchtaruk A, Hopman W, et al. Interatrial block predicts atrial fibrillation in patients with carotid and coronary artery disease. J Thorac Dis 2018;10:4328-34. doi: 10.21037/jtd.2018.06.53.
22. Martínez-Sellés M. Prevalence and incidence of interatrial block in global population and in different clinical situations. J Geriatr Cardiol 2017;14:158-60. doi: 10.11909/j.issn.1671-5411.2017.03.006.
23. Baranchuk A, Enriquez A, Antiperovitch P, Alexander B, Çinier G. Advanced interatrial block as a key marker for atrial fibrillation recurrence: Bayés' syndrome. J Geriatr Cardiol 2017;14:169-73. doi: 10.11909/j.issn.1671-5411.2017.03.005.
24. Zathar Z, Karunatilleke A, Fawzy AM, Lip GYH. Atrial fibrillation in older people: Concepts and controversies. Front Med (Lausanne) 2019;6:175. doi: 10.3389/fmed.2019.00175.
25. Krijthe BP, Kunst A, Benjamin EJ, Lip GY, Franco OH, Hofman A, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. Eur Heart J 2013;34:2746-51. doi: 10.1093/eurheartj/eht280.
26. Şenöz O, Yurdam FS. Clues on electrocardiography to predict the presence of paroxysmal atrial fibrillation in patients with acute ischemic stroke: A propensity score-matched study. Cardiovasc Surg Int 2022;9:36-42. doi: 10.5606/e-cvsi.2022.1231.

Cardiovasc Surg Int 2024;11(3):177-182
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1721
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Relationship between prognostic nutritional index and contrast-induced nephropathy in patients presenting with acute coronary syndrome

Yusuf Demir

Department of Cardiology, İzmir Bakırçay University, İzmir, Türkiye

Received: August 24, 2024 ***Accepted:*** August 30, 2024 ***Published online:*** September 16, 2024

ABSTRACT

Objectives: This study aimed to evaluate malnutrition with the prognostic nutritional index (PNI) and investigate its association with contrast-induced nephropathy (CIN).

Patients and methods: The retrospective cohort study was conducted with 162 acute coronary syndrome (ACS) patients (113 males, 49 females; mean age: 58.6±12.6 years; range, 26 to 92 years) admitted between Novomber 2016 and September 2017. The patients were divided into two groups according to laboratory, angiographic, demographic, and echocardiographic parameters: those with CIN (n=16) and those without CIN (n=146). The data were obtained from the hospital system, and patients with complete parameters were included in the study. The PNI score was computed by multiplying the total lymphocyte count (mm^3) by 0.005 and adding it to 10 times the serum albumin (g/dL).

Results: Twenty-one (12.9%) of the patients had non-end-stage renal failure before the procedure, and the development of CIN was significantly higher in those with baseline renal dysfunction (50% *vs.* 8.9%, p<0.001). The PNI was significantly lower in the group that developed CIN (43.5±5.5 *vs.* 50.4±8.7, p=0.002). In-hospital mortality occurred in six (3.7%) of 162 patients who underwent PCI due to myocardial infarction. The mortality rate was significantly higher in the CIN group (18.8% *vs.* 2.1%, p=0.01). In the receiver operating characteristic analysis, a PNI <46 had 69% sensitivity and 75% specificity (area under the curve=0.76, 95% confidence interval 0.646-0.879, p=0.001) for determining CIN.

Conclusion: In conclusion, this study demonstrated that PNI, a marker of nutritional status, may be a reliable predictor of contrast nephropathy in patients presenting with ACS.

Keywords: Acute coronary syndrome, contrast-induced nephropathy, prognostic nutritional index.

Acute coronary syndrome (ACS) is a significant contributor to mortality, with a steady rise in occurrence despite advancements in therapy, such as percutaneous coronary intervention (PCI).[1] Therefore, it is necessary to identify high-risk patients based on their modifiable risk factors and use suitable therapies to enhance their prognosis. Malnutrition is an escalating worldwide health problem linked to adverse consequences of several illnesses.[2] The correlation between malnutrition and a poor outcome in cardiovascular disease has been demonstrated.[3,4] Nevertheless, there is a lack of studies investigating the correlation between malnutrition and contrast-induced nephropathy (CIN) in patients with ACS. Hence, this study aimed to examine the impact of the prognostic nutritional index (PNI) on the development of CIN in individuals who presented with ACS.

PATIENTS AND METHODS

The retrospective cohort study included 162 consecutive patients (113 males, 49 females; mean age: 58.6±12.6 years; range, 26 to 92 years) with ACS patients without end-stage renal disease and were admitted to the cardiology clinic of the Çiğli Training and Research Hospital between Novomber 2016 and September 2017. Patients with end-stage

Corresponding author: Yusuf Demir, MD. İzmir Bakırçay Üniversitesi Kardiyoloji Anabilim Dalı, 35665 Menemen, İzmir, Türkiye
E-mail: yusufdemir2502@gmail.com

Citation:
Demir Y. Relationship between prognostic nutritional index and contrast-induced nephropathy in patients presenting with acute coronary syndrome. Cardiovasc Surg Int 2024;11(3):177-182. doi: 10.5606/e-cvsi.2024.1721.

renal disease and those receiving hemodialysis were excluded from the study. Percutaneous coronary intervention was carried out in accordance with the treatment recommendations, based on the judgment of the attending physician. A written informed consent was obtained from each patient. The study protocol was approved by the İzmir Bakırçay University Ethics Committee (date: 08.03.2023 no: 2023/905). The study was conducted in accordance with the principles of the Declaration of Helsinki. Since the study did not include details on the exact kind of PCI therapy, the interventional cardiologists made the decision to perform predilatation, utilize intravascular ultrasound, and choose a particular type of drug-eluting stent. Patients were divided into two groups: those who developed CIN after the operations and those who did not develop CIN. Laboratory and echocardiographic data of the patients were obtained from the hospital information system.

The PNI score was calculated by multiplying the total lymphocyte count (mm^3) by 0.005 and adding it to 10 times the serum albumin (g/dL).[5]

Table 1
Baseline characteristics of patients according to CIN development

	CIN + (n=16)			CIN – (n=146)			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			72.4±8.9			57.1±12.1	<0.001
Sex							
Male	6	37.5		107	73.3		0.007
Hypertension	15	93.8		95	65.1		0.02
Diabetes mellitus	10	62.5		36	24.7		0.003
Smoking	3	18.8		66	45.2		0.06
Hypercholesterolemia	16	100		138	94.5		1
Chronic renal failure	8	50		13	8.9		<0.001
CVD history	2	12.5		4	2.7		0.1
Prior CAD	8	50		54	37.2		0.32
Chronic heart failure	3	18.8		9	6.2		0.1
Multivessel disease	7	43.8		74	50.7		0.59
LVEF (%)			37.8±12.1			45.5±9.6	0.004
Received medication							
Statin	14	87.5		136	93.2		0.33
ACE-i/ARB	6	37.5		89	61		0.07
BB	13	81.3		122	83.6		0.73
MI type							
Anterior MI	9	56.3		55	37.7		
Inferior MI	5	31.3		57	39		0.32
Other MI	2	12.5		34	23.3		
Killip classification							
Killip Class I	5	31.3		115	78.8		
Killip Class II	6	37.5		23	15.8		<0.001
Killip Class III and IV	5	31.3		8	5.5		
In-hospital mortality	3	18.8		3	2.1		0.01

CIN: Contrast induced nephropathy; SD: Standard deviation; CVD: Cerebrovascular diseases; CAD: Coronary artery disease; LVEF: Left ventricular ejection fraction; ACE-i: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin II receptor blocker; BB: Beta blocker; MI: Myocardial infarction.

Contrast-induced nephropathy was defined as the impairment of kidney function, measured as either a 25% increase in serum creatinine from baseline or a 0.5 mg/dL (44 μmol/L) increase in absolute serum creatinine value, within 48 to 72 h after intravenous contrast administration.

Statistical analysis

Data were evaluated in IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The distribution of variables was evaluated with the Kolmogorov-Smirnov test, the homogeneity of variance was evaluated with the Levene test, and all continuous variables presented normal distribution. Data determined by measurement were given as mean ± standard deviation (SD) for those with normal distribution. The unpaired t-test was used in the analysis of these data. Categorical data were shown as absolute and relative frequencies, and the chi-square test or Fisher exact test was used, as appropriate. Variables were analyzed at a 95% confidence interval, and a p-value <0.05 was considered statistically significant. Receiver operating characteristic analysis was used, and the area under the curve was calculated.

RESULTS

Contrast-induced nephropathy developed in 16 (10%) of the patients. Sixty-four (40%) of the patients had anterior myocardial infarction (MI), 62 (38%) had inferior MI, and 36 (22%) had MI involving other walls. The majority of patients (74%) who underwent primary PCI were in the Killip Class I. Twenty-one (12.9%) of the patients had non-end-stage renal failure before the procedure, and the development of CIN was significantly higher in those with baseline renal dysfunction (50% *vs.* 8.9%, p<0.001). Development of CIN was significantly higher in the female sex and older age (p=0.007 and p<0.001, respectively). Rate of diabetes mellitus and hypertension was higher in the CIN group, whereas the mean left ventricular ejection fraction value was lower in the CIN group (Table 1).

Table 2
Baseline laboratory parameters on admission of patients according to CIN development

	CIN + (n=16)	CIN – (n=146)	
Variables	Mean±SD	Mean±SD	*p*
Creatinine (mg/dL)	1.45±0.5	1.11±1.1	0.2
eGFR (mL/min/1.73 m^2)	50.6±26.2	83.6±28.4	<0.001
Fasting blood glucose (mg/dL)	150.5±57.9	123.3±50.5	0.04
Total cholesterol (mg/dL)	190.7±67.3	187.5±42.6	0.79
HDL-cholesterol (mg/dL)	40.1±7.7	39.1±11.1	0.74
LDL-cholesterol (mg/d)	115.6±56.7	114.9±39.9	0.95
Plasma triglycerides (mg/dL)	169.4±74.1	174.1±92.9	0.85
Sodium (mEq/L)	138.4±4.5	138.8±3.3	0.66
Potassium (mEq/L)	4.2±1.1	4.3±0.5	0.71
White blood cell count (×10^9/L)	13.11±6.1	12.1±4.13	0.35
Lymphocyte count (×10^9/L)	1.76±0.57	2.36±1.24	0.06
Neutrophil count (×10^9/L)	9.83±5.25	8.35±3.67	0.14
Hemoglobin (g/DL)	12.3±2.1	13.4±2.1	0.03
Hematocrit (%)	34.3±8.7	39.9±5.7	0.001
Platelet count (×10^9/L)	259.6±59.7	257.5±73.1	0.916
Albumin (g/dL)	3.46±0.4	3.85±0.57	0.009
PNI	43.5±5.5	50.4±8.7	0.002

CIN: Contrast induced nephropathy; SD: Standard deviation; eGFR: Estimated glomerular filtration rate; HDL: High density lipoprotein; LDL: Low density lipoprotein; PNI: Prognostic nutritional index.

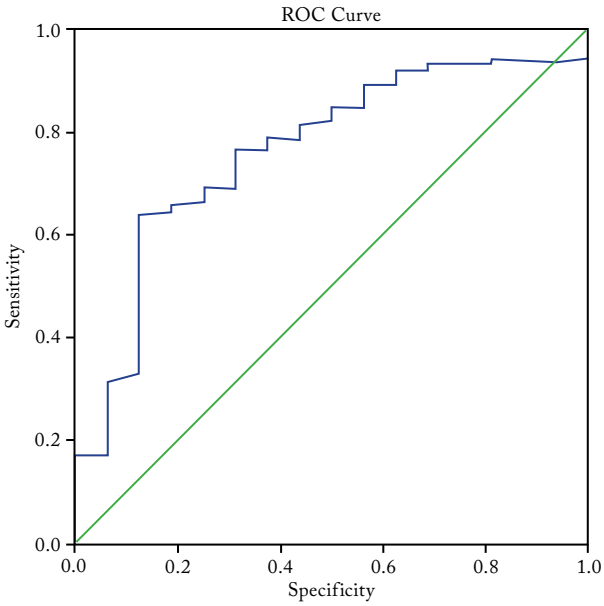


Figure 1. Receiver operating characteristic curve of PNI for predicting the development of CIN.

ROC: Receiver operating characteristic; PNI: Prognostic nutritional index; CIN: Contrast-induced nephropathy.

The PNI was significantly lower in the group that developed CIN (43.5±5.5 *vs.* 50.4±8.7, p=0.002). Furthermore, the rate of high fasting blood sugar and low hemoglobin and low hematocrit levels were significantly higher in the CIN group (p<0.05; Table 2).

In-hospital mortality occurred in six (3.7%) of 162 patients who underwent PCI due to MI. The mortality rate was significantly higher in the CIN group (18.8% *vs.* 2.1%, p=0.01).

In the receiver operating characteristic analysis (Figure 1), a PNI <46 had 69% sensitivity and 75% specificity (area under the curve=0.76, 95% confidence interval 0.646-0.879, p=0.001) for determining CIN.

DISCUSSION

The study assessed nutritional status using the PNI method and found that those with low PNI scores had significantly lower nutritional status and a higher incidence of CIN. Coronary angiography and PCI depend on the use of iodinated intravascular contrast to observe blood vessels and chambers. Although there have been improvements in imaging and interventional procedures, the use of iodinated contrast still has the potential to cause contrast-induced acute kidney damage in some high-risk individuals.[6] This disorder has a complicated pathogenesis, with a prevalence reaching up to 30%, and is linked to increased rates of both short-term and long-term illness and death.[7,8]

Considering the clinical situation and features of the patient, intravenous hydration should be taken into account as a component of the treatment for ACS patients with a low estimated glomerular filtration rate who are scheduled for invasive management. This is done to reduce the likelihood of CIN.[8-12] In our study, patients with ACS were analyzed. In these patients, it is recommended to use less contrast, administer high-dose statin in the early period, and provide intravenous hydration. Contrast-induced nephropathy is usually transient in these patients, but when dialysis is required, it can significantly impair long-term outcomes. Therefore, predicting which patients may develop CIN is important for post-PCI treatment decisions.

Prior research has shown a correlation between malnutrition and an increased susceptibility to contrast-associated acute kidney injury during PCI.[3] Hypoalbuminemia raises cardiovascular risk primarily via the reduction of albumin's antioxidant, oncotic pressure-maintaining, and antithrombotic abilities.[13] Decreased absolute lymphocyte numbers imply impaired immunological responses caused by malnutrition.[14] Malnutrition scores have the potential to aid in the categorization of risk and evaluation of prognosis.

In 1984, Onodera et al.[13] evaluated the nutritional and immunological condition of cancer patients who were having gastrointestinal surgery. In recent years, PNI has established recognition as a unique prognostic marker for several illnesses, including diabetic nephropathy, heart failure, and coronavirus disease 2019.[15-24] To our knowledge, this is the first study in the literature investigating the relationship between nutritional status and the development of contrast nephropathy in patients with ACS.

This study had several limitations, the primary one being its retrospective and single-center design. Additionally, the PNI's ability to predict nutritional status was similarly restricted. There may be variations in nutritional indices among various ethnic communities. As the PNI was generated using the original reference values, we did not have information about the changes in the nutritional values of

the patients. Prospective studies are necessary to determine the effect of dietary status on CIN in individuals with ACS.

In conclusion, this study demonstrated that PNI, a marker of nutritional status, may be a reliable predictor of contrast nephropathy in patients presenting with ACS. A low PNI score indicates an inadequate nutritional status, which is thought to accelerate inflammatory processes and lead to acute kidney injury.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest: The author declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The author received no financial support for the research and/or authorship of this article.

REFERENCES

1. Szummer K, Jernberg T, Wallentin L. From early pharmacology to recent pharmacology interventions in acute coronary syndromes: JACC state-of-the-art review. J Am Coll Cardiol 2019;74:1618-36. doi: 10.1016/j.jacc.2019.03.531.
2. Ni W, Guo K, Shi S, Cheng L, Zhou Y, Zhang F, et al. Prevalence and prognostic value of malnutrition in patients with acute coronary syndrome and chronic kidney disease. Front Nutr 2023;10:1187672. doi: 10.3389/fnut.2023.1187672.
3. Chen L, Zhang S, Luo M, He C, You Z, Zhang L, et al. Assessing the predictive value of different nutritional indexes for contrast-associated acute kidney injury in patients undergoing percutaneous coronary intervention. Circ J 2024;88:902-10. doi: 10.1253/circj.CJ-23-0479.
4. Teker Açıkel ME, Korkut AK. Impact of Controlling Nutritional Status Score (CONUT) and Prognostic Nutritional Index (PIN) on patients undergoing coronary artery bypass graft surgery. Heart Surg Forum 2019;22:E294-7. doi: 10.1532/hsf.2493.
5. Pinato DJ, North BV, Sharma R. A novel, externally validated inflammation-based prognostic algorithm in hepatocellular carcinoma: The Prognostic Nutritional Index (PNI). Br J Cancer 2012;106:1439-45. doi: 10.1038/bjc.2012.92.
6. McCullough PA, Choi JP, Feghali GA, Schussler JM, Stoler RM, Vallabahn RC, et al. Contrast-induced acute kidney injury. J Am Coll Cardiol 2016;68:1465-73. doi: 10.1016/j.jacc.2016.05.099.
7. Marenzi G, Cosentino N, Bartorelli AL. Acute kidney injury in patients with acute coronary syndromes. Heart 2015;101:1778-85. doi: 10.1136/heartjnl-2015-307773.
8. Szummer K, Lundman P, Jacobson SH, Schön S, Lindbäck J, Stenestrand U, et al. Relation between renal function, presentation, use of therapies and in-hospital complications in acute coronary syndrome: Data from the SWEDEHEART register. J Intern Med 2010;268:40-9. doi: 10.1111/j.1365-2796.2009.02204.x.
9. Neumann FJ, Sousa-Uva M. 'Ten commandments' for the 2018 ESC/EACTS guidelines on myocardial revascularization. Eur Heart J 2019;40:79-80. doi: 10.1093/eurheartj/ehy855.
10. Kume K, Yasuoka Y, Adachi H, Noda Y, Hattori S, Araki R, et al. Impact of contrast-induced acute kidney injury on outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Cardiovasc Revasc Med 2013;14:253-7. doi: 10.1016/j.carrev.2013.07.009.
11. Davenport MS, Perazella MA, Yee J, Dillman JR, Fine D, McDonald RJ, et al. Use of intravenous iodinated contrast media in patients with kidney disease: Consensus statements from the American College of Radiology and the National Kidney Foundation. Kidney Med 2020;2:85-93. doi: 10.1016/j.xkme.2020.01.001.
12. Schweiger MJ, Chambers CE, Davidson CJ, Blankenship J, Bhalla NP, Block PC, et al. Prevention of contrast induced nephropathy: Recommendations for the high risk patient undergoing cardiovascular procedures. Catheter Cardiovasc Interv 2007;69:135-40. doi: 10.1002/ccd.20964.
13. Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nihon Geka Gakkai Zasshi. 1984;85:1001-5.
14. Zencirkiran Agus H, Kahraman S. Prognostic nutritional index predicts one-year outcome in heart failure with preserved ejection fraction. Acta Cardiol 2020;75:450-5. doi: 10.1080/00015385.2019.1661139.
15. Zhang J, Xiao X, Wu Y, Yang J, Zou Y, Zhao Y, et al. Prognostic nutritional index as a predictor of diabetic nephropathy progression. Nutrients 2022;14:3634. doi: 10.3390/nu14173634.
16. Barutcu Atas D, Tugcu M, Asicioglu E, Velioglu A, Arikan H, Koc M, et al. Prognostic nutritional index is a predictor of mortality in elderly patients with chronic kidney disease. Int Urol Nephrol 2022;54:1155-62. doi: 10.1007/s11255-021-03002-6.
17. Al-Shami I, Hourani HMA, Alkhatib B. The use of Prognostic Nutritional Index (PNI) and selected inflammatory indicators for predicting malnutrition in COVID-19 patients: A retrospective study. J Infect Public Health 2023;16:280-5. doi: 10.1016/j.jiph.2022.12.018.
18. Chen QJ, Qu HJ, Li DZ, Li XM, Zhu JJ, Xiang Y, et al. Prognostic nutritional index predicts clinical outcome in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Sci Rep 2017;7:3285. doi: 10.1038/s41598-017-03364-x.
19. Boyraz B, Ibisoglu E, Aslan B. The prognostic value of the Nutritional Prognostic Index (NPI) and Controlling Nutritional status (CONUT) scoring systems in non-ST elevated myocardial infarction patients over 65 years of age. Aging Clin Exp Res 2022;34:555-62. doi: 10.1007/s40520-021-02039-y.

20. Keskin M, Hayıroğlu MI, Keskin T, Kaya A, Tatlısu MA, Altay S, et al. A novel and useful predictive indicator of prognosis in ST-segment elevation myocardial infarction, the prognostic nutritional index. Nutr Metab Cardiovasc Dis 2017;27:438-46. doi: 10.1016/j.numecd.2017.01.005.
21. Kurtul A, Gok M, Esenboga K. Prognostic nutritional index predicts contrast-associated acute kidney injury in patients with ST-Segment elevation myocardial infarction. Acta Cardiol Sin 2021;37:496-503. doi: 10.6515/ACS.202109_37(5).20210413A.
22. Manolis AA, Manolis TA, Melita H, Mikhailidis DP, Manolis AS. Low serum albumin: A neglected predictor in patients with cardiovascular disease. Eur J Intern Med 2022;102:24-39. doi: 10.1016/j.ejim.2022.05.004.
23. Fock RA, Blatt SL, Beutler B, Pereira J, Tsujita M, de Barros FE, et al. Study of lymphocyte subpopulations in bone marrow in a model of protein-energy malnutrition. Nutrition 2010;26:1021-8. doi: 10.1016/j.nut.2009.08.026.
24. Güzel T, Avcı E, Kırış T, Arık B, Arslan B, İldırımlı K, et al. Effect of the prognostic nutrition index on long-term outcomes in unprotected left main coronary artery revascularization. Kardiologiia 2023;63:73-9. doi: 10.18087/cardio.2023.11.n2367.

Cardiovasc Surg Int 2024;11(3):183-192
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1694
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Comparison of inflammatory biomarkers between peripheral artery disease patients and healthy individuals

Ahmet Deniz Kaya[1], Esma Nur Metin Kaya[2], İhsan Alur[3]

[1]Department of Cardiovascular Surgery, Bursa Yüksek İhtisas Trainig and Research Hospital, Bursa, Türkiye
[2]Department of Anesthesiology and Reanimation, Bursa Gürsu Cüneyt Yıldız State Hospital, Bursa, Türkiye
[3]Department of Cardiovascular Surgery, Private Egekent Hospital, Denizli, Türkiye

Received: June 12, 2024 ***Accepted:*** August 29, 2024 ***Published online:*** September 16, 2024

ABSTRACT

Objectives: This study aimed to compare inflammatory markers such as fibrinogen, C-reactive protein, and white blood cell count between patients with peripheral artery disease (PAD) and healthy individuals and investigate whether there is a relationship between low-grade inflammation and PAD.

Patients and methods: This case-control study was conducted with 162 individuals (107 males, 55 females; mean age: 52.5±13.7 years; range, 24 to 87) between January 2023 to January 2024. Eighty-seven of these participants were diagnosed with PAD by lower extremity color Doppler ultrasonography and computed tomography angiography, and the remaining 75 were healthy individuals. Biochemical results of patients and control groups were examined.

Results: Comparing the groups, statistical significance ($p<0.05$) was found according to sex, age, hypertension, diabetes mellitus, smoking, blood glucose levels, blood creatinine levels, estimated glomerular filtration rate, high-density lipoprotein, triglyceride, fibrinogen, white blood cell count, and C-reactive protein levels. In the group of PAD patients, male sex, hypertension, diabetes mellitus, and smoking were more prevalent, along with higher levels of glucose, creatinine, triglyceride, fibrinogen, white blood cell count, and C-reactive protein.

Conclusion: Inflammation biomarkers, such as fibrinogen and C-reactive protein, were found to be significantly higher in the PAD group, indicating that the low-grade inflammation hypothesis may play a role in PAD. Large-scale, prospective, randomized controlled studies on this subject are needed.

Keywords: C-reactive protein, fibrinogen, low-grade inflammation, peripheral artery disease, white blood cells.

Peripheral artery disease (PAD) occurs due to atherosclerosis, which causes stenosis or constriction in the main arteries feeding the lower extremity. Peripheral artery disease includes arterial stenosis or occlusion caused by atheromatous plaques, thrombosis, arterial inflammation, arterial dilation/aneurysm, or external pressure.[1] Development of PAD is closely associated with classical cardiovascular risk factors such as diabetes mellitus (DM), dyslipidemia, smoking, hypertension (HT), and advanced age.[1] Endothelial dysfunction is one of the earliest anomalies in the development of atherosclerosis.[2,3] Inflammation is an immune system reaction that helps defends the host by repairing damaged tissues and eliminating toxic agents. If this reaction becomes chronic and continues at a low grade, it can cause increased toxic activity of immune cells and tissue damage.[4] Low-grade inflammation is defined by increased levels of C-reactive protein (CRP) in the blood. C-reactive protein is one of the main biomarkers of inflammation in the body. The higher the level of CRP measured in the blood, the more inflammation there is in the body. Low-grade inflammation can be defined by CRP levels of 3 to 10 mg/L in the blood.[5,6] Low-grade inflammation causes changes in the homeostasis of the organism and eases the onset of chronic diseases such as DM, atherosclerosis,

Corresponding author: Ahmet Deniz Kaya, MD. Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Kalp ve Damar Cerrahisi Kliniği, 16310 Yıldırım, Bursa, Türkiye.
E-mail: drahmetdenizkaya@gmail.com

Citation:
Kaya AD, Metin Kaya EN, Alur İ. Comparison of inflammatory biomarkers between peripheral artery disease patients and healthy individuals. Cardiovasc Surg Int 2024;11(3):183-192. doi: 10.5606/e-cvsi.2024.1694.

heart failure, PAD, obesity, metabolic syndrome, polycystic ovary syndrome, depression, periodontitis, osteoarthritis, and cancer.[5,6] Inflammation, besides atherosclerosis, can have a major role in the progression of PAD. The increase in inflammatory biomarkers can predict low-grade inflammation. These patients can be diagnosed and treated before disease reaches severe grades. Furthermore, preventing and treating low-grade inflammation in this group of patients can stop or slow down the progression of the disease. Yener et al.[7] found that neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio were high in patients with type D lesions according to the TASC (Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease) classification in PAD. They suggested that inflammation may play a role in the development of atherosclerosis in atherosclerotic PAD. The present study aimed to compare the levels of inflammatory biomarkers such as CRP, fibrinogen, and white blood cell (WBC) count in patients with PAD and healthy individuals.

PATIENTS AND METHODS

This case-control study was conducted with 162 individuals (107 males, 55 females; mean age: 52.5±13.7 years; range, 24 to 87) at the Ağrı Training and Research Hospital between January 2023 to January 2024. Eighty-seven of the participants were diagnosed with PAD, and the remaining 75 were healthy individuals. Biochemical results of both groups were examined. Having symptoms resembling PAD and existence of known cardiovascular risk factors were the inclusion criteria for the patient group. The exclusion criteria were age under 18 years, morbid obesity, cancer, and chronic disease such as heart failure, kidney failure, liver failure, and rheumatologic disease. These patients were not included in the study since the inflammation present in chronic diseases increases inflammatory markers. Age, sex, DM, HT, dyslipidemia, smoking, fasting blood glucose level, creatinine, estimated glomerular filtration rate (eGFR), total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride, fibrinogen, and CRP levels and WBC, monocyte, lymphocyte, and platelet counts were recorded. Diabetes mellitus, HT, and dyslipidemia were diagnosed according to relevant guidelines.[8-10] A written informed consent was obtained from each patient. The study protocol was approved by the Ağrı İbrahim Çeçen University, Ethics Committee (date: 29.03.2024, no: E-98270). The study was conducted in accordance with the principles of the Declaration of Helsinki. Peripheral artery disease was diagnosed by lower extremity color Doppler ultrasonography or computed tomography angiography.

Statistical analysis

A power analysis was calculated according to creatinine levels using G*Power version 3.1.9.7 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). A power of 87% was found according to n1=75 (0.82±0.34), n_2=87 (1.16±0.83), alpha=0.05, and effect size (d)=0.49.

Data were analyzed using IBM SPSS version 27.0 (IBM Corp., Armonk, NY, USA) and MedCalc version 15.8 (MedCalc Software, Ostend, Belgium). While evaluating the data, in addition to descriptive statistical methods (frequency, percentage, mean, standard deviation, median, minimum-maximum, and interquartile range), the chi-square test was used to compare qualitative data. The suitability of the data for normal distribution was evaluated with the Kolmogorov-Smirnov test, skewness-kurtosis, and graphical methods (histograms, Q-Q plots, stem-and-leaf plots, and boxplots). In this study, for the evaluation of normally distributed quantitative data, the independent samples t-test was used. For the evaluation of data that did not show normal distribution, the Mann-Whitney U test was used. Receiver operating characteristic curves were used to determine the distinctiveness of the variables, and binary logistic regression was used to determine risk ratios. The level of statistical significance was set at $p<0.05$.

RESULTS

In comparisons made according to groups; it was found that there was a statistically significant difference ($p<0.05$) between the groups in terms of sex, age, HT, DM, smoking, fasting blood glucose, creatinine, eGFR, HDL, triglyceride, fibrinogen, and CRP levels and WBC count (Table 1).

In the PAD group, it was found that the male sex, HT, DM, and smoking rates were higher, along with older age and higher levels of fasting blood glucose, creatinine, triglyceride, fibrinogen, WBCs, and CRP (Table 2). There was no statistically significant difference between the groups in terms of other

variables (p>0.05). Variables that were considered to be more clinically significant and did not have a high correlation between the variables that showed differences in pairwise comparisons between groups (sex, age, HT, DM, smoking, glucose, creatinine, eGFR, HDL, triglyceride, fibrinogen, WBCs, monocytes, lymphocytes, platelets, and CRP) were included in the model. The backward stepwise method was used in the analysis, and the model was terminated at the ninth step. In this model, approximately 87% of the dependent variable (PAD group) could be explained (Nagelkerke R^2=0.866). According to this model, there was a statistically significant relationship between PAD status and sex, age, glucose, creatinine, fibrinogen, monocytes, platelets, and CRP (p<0.05; Table 3).

Peripheral Artery Disease (PAD) is approximately 21.52 times more prevalent in men. It is 1.07 times more common in individuals with higher age, 1.03 times more common in those with elevated glucose levels, and 0.34 times more frequent in those with increased creatinine levels. PAD is also 1.02 times more likely in individuals with higher fibrinogen levels, 1764.11 times more prevalent in those with elevated monocyte counts, 1.01 times

Table 1
Demographic characteristics of the study participants

	n	%	Mean±SD	Median	Min-Max
Age (year)			52.5±13.7	53.0	24.0-87.0
Sex					
Male	107	66.0			
Female	55	34.0			
Group					
Control group	75	46.3			
PAD group	87	53.7			
Hypertension					
Present	129	79.6			
Absent	33	20.4			
Diabetes mellitus					
Present	120	74.1			
Absent	42	25.9			
Smoking					
Present	136	83.4			
Absent	27	16.6			
Glucose (mg/dL)			123.5±61.3	97.8	66.0-348.0
Creatinine (mg/dL)			1.0±0.7	0.9	0.5-6.1
Estimated glomerular filtration rate			89.4±22.8	93.5	9.0-140.0
Cholesterol (mg/dL)			180.9±90.1	178.5	33.6-1.145.0
Low-density lipoprotein (mg/dL)			117.3±30.0	115.7	59.0-197.1
High-density lipoprotein (mg/dL)			44.8±9.7	44.0	22.5-75.9
Triglyceride (mg/dL)			171.7±155.8	132.8	46.0-1.620.4
Fibrinogen			394.1±109.2	392.0	129.3-784.0
White blood cell count (10^9\L)			7.5±2.3	7.4	0.0-14.9
Monocyte (10^9\L)			0.5±0.2	0.5	0.2-1.6
Lymphocyte (10^9\L)			2.5±1.2	2.2	0.8-8.0
Platelet (10^9\L)			302.1±130.9	267.5	140.0-869.0
C-reactive protein (mg/L)			7.2±9.7	4.8	0.2-78.0

SD: Standard deviation; PAD: Peripheral artery disease; Group K: Control group; Group H: Patient group.

Table 2
Comparisons between groups

	Control group (n=75)					PAD group (n=87)					
	n	%	Mean±SD	Median	Q1-Q3	n	%	Mean±SD	Median	Q1-Q3	*p*
Age (year)			43.81±12.63					59.99±9.53			**<0.001**b
Sex											**<0.001**a
Male	34	45.3				73	83.9				
Female	41	54.7				14	16.1				
Hypertension											**<0.001**a
Present	74	98.7				55	63.2				
Absent	1	1.3				32	36.8				
Diabetes mellitus											**<0.001**a
Present	74	98.7				46	52.9				
Absent	1	1.3				41	47.1				
Smoking											**0.020**a
Present	68	90.7				67	77.0				
Absent	7	9.3				20	23.0				
Glucose (mg/dL)			95.61±20.73					147.50±73.47			**<0.001**b
Creatinine (mg/dL)				0.79	0.65-0.92				1.02	0.79-1.18	**<0.001**c
eGFR			101.77±18.10					78.78±21.11			**<0.001**b
Cholesterol (mg/dL)				168.60	140.10-201.30				182.30	137.20-209.70	0.265c
LDL (mg/dL)			116.42±28.21					117.97±31.66			0.745b
HDL (mg/dL)			47.19±10.37					42.66±8.54			**0.003**b
Triglyceride (mg/dL)				117.20	80.00-146.00				161.60	98.70-243.40	**<0.001**c
Fibrinogen			314.57±70.71					462.58±88.09			**<0.001**b
WBC (10^9\L)			6.95±2.08					7.96±2.30			**0.004**b
Monocyte (10^9\L)			0.41±0.12					0.55±0.21			**<0.001**b
Lymphocyte (10^9\L)			2.15±0.50					2.82±1.57			**<0.001**b
Platelet (10^9\L)			266.01±51.43					333.20±166.39			**0.001**b
C-reactive protein (mg/L)				2.30	1.24-4.91				7.21	3.74-9.43	**<0.001**c

SD: Standard deviation; Q: Quartiles; eGFR: Estimated glomerular filtration rate; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; WBC: White blood cell count; Group K: Control group; Group H: Patient group; a: Chi-Square test; b: Independent Samples t test; c: Mann-Whitney U test.

Table 3
Analysis with logistic regression

	Univariate logistic regression analysis						Multivariate logistic regression analysis					
Risk factor	B	SE	Wald	OR	95% CI	*p**	B	SE	Wald	OR	95% CI	*p**
Age	0.127	0.020	40.147	1.14	1.09-1.18	<0.001	0.071	0.033	4.677	1.07	1.01-1.14	0.031
Sex	1.839	0.373	24.333	6.29	3.03-13.05	<0.001	3.069	0.973	9.958	21.52	3.20-144.79	0.002
Glucose (mg/dL)	0.029	0.007	17.162	1.03	1.02-1.04	<0.001	0.026	0.011	5.728	1.03	1.00-1.05	0.017
Creatinine (mg/dL)	2.434	0.666	13.366	11.40	3.09-42.04	<0.001	-1.073	0.452	5.627	0.34	0.14-0.83	0.018
Fibrinogen	0.024	0.003	48.135	1.02	1.02-1.03	<0.001	0.022	0.005	17.272	1.02	1.01-1.03	<0.001
Monocyte (10^9\L)	7.091	1.516	21.883	1200.97	61.56-23.431.15	<0.001	7.475	3.609	4.291	1764.11	1.50-2.080.519.22	0.038
Platelet (10^9\L)	0.005	0.002	8.773	1.01	1.00-1.01	0.003	0.010	0.005	4.288	1.01	1.00-1.02	0.038
CRP (mg/L)	0.266	0.056	22.498	1.30	1.17-1.46	<0.001	0.250	0.116	4.595	1.28	1.02-1.61	0.032
Hypertension	3.762	1.031	13.318	43.05	5.71-324.79	<0.001	--	--	--	--	--	--
DM	4.189	1.029	16.560	65.96	8.77-495.99	<0.001	--	--	--	--	--	--
Smoking	1.065	0.472	5.094	2.90	1.15-7.31	0.024	--	--	--	--	--	--
eGFR	-0.066	0.012	31.385	0.94	0.92-0.96	<0.001	--	--	--	--	--	--
HDL (mg/dL)	-0.051	0.018	8.340	0.95	0.92-0.98	0.004	--	--	--	--	--	--
Triglyceride (mg/dL)	0.005	0.002	7.747	1.01	1.00-1.01	0.005	--	--	--	--	--	--
WBC (10^9\L)	0.214	0.078	7.507	1.24	1.06-1.44	0.006	--	--	--	--	--	--
Lymphocyte (10^9\L)	0.603	0.192	9.835	1.83	1.25-2.67	0.002	--	--	--	--	--	--

SE: Standard error; OR: Odds ratio; CI: Confidence interval; CRP: C-reactive protein; DM: Diabetes mellitus; eGFR: Estimated glomerular filtration rate; HDL: High-density lipoprotein; WBC: White blood cell count; * Binary logistic regression (It is given only for the variables remaining on the model.) Nagelkerke R^2=0.866; Variable(s) removed on step 2: smoking; Step 3: WBC (10^9\L); Step 4: eGFR; Step 5: Hypertension; Step 6: HDL (mg/dL); Step 7: Lymphovyte (10^9\L); Step 8: Triglyceride (mg/dL); Step 9: DM.

Table 4
Real and predicted values according to the created model

	Predicted group		Accuracy
	Control group	PAD group	%
Real group			
Control group	71	4	94.7
PAD group	5	82	94.3
Correctly classified cases (%)			94.4

more common in those with higher platelet counts, and 1.28 times more frequent in individuals with elevated CRP levels (Table 3). A prediction table was created according to the model. Eighty-two of 87 patients (94.3%) with PAD were predicted correctly, and 71 of 75 patients (94.7%) without PAD were predicted correctly. The overall accuracy rate was found to be 94.4% (Table 4). Variables that were considered to be more clinically significant and did not have a high correlation between the variables that showed differences in pairwise comparisons between groups (fibrinogen, WBC count, and CRP) were included in the model. The backward stepwise method was used in the analysis, and the model was finalized at the second step. Approximately 67% of the dependent variable (PAD group) could be explained in this model (Nagelkerke R^2=0.665). According to this model, there was a statistically significant relationship between PAD status and fibrinogen and CRP values ($p<0.05$; Figures 1-5). Those with high fibrinogen values were approximately 1.02 times more likely to have PAD than those without, and those with high CRP values were approximately 1.18 times more likely to have PAD than those without (Table 5). A prediction table was created according to the created model. Eighty of 87 patients (92.0%) with PAD were predicted correctly, while 69 of 75 patients (92.0%) without PAD were predicted correctly. The overall accuracy rate was found to be 92.0% (Table 6).

As a result of the evaluations conducted using ROC analysis on the variables found to be different in pairwise comparisons. The cutoff points of different variables were as follows: fasting blood glucose, >110 mg/dL (area under the curve [AUC]=0.741, 95% confidence interval [CI]: 0.667-0.807, $p<0.001$); creatinine, >0.94 (AUC=0.731, 95% CI: 0.656-0.798, $p<0.001$);

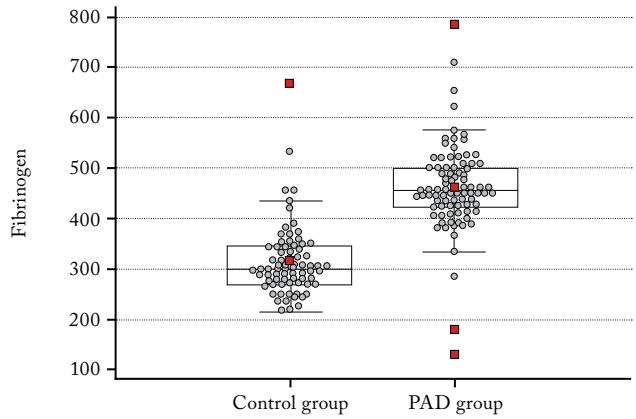


Figure 1. The range of distribution of fibrinogen values in the control and patient groups.

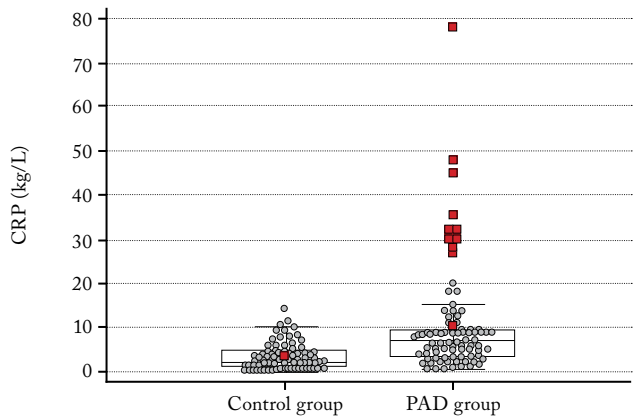


Figure 2. The range of distribution of CRP values in the study groups.

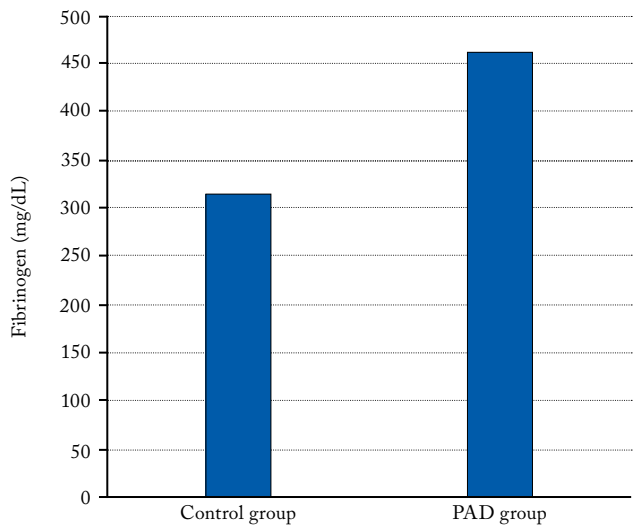


Figure 3. Fibrinogen blood levels in the patient and control groups.

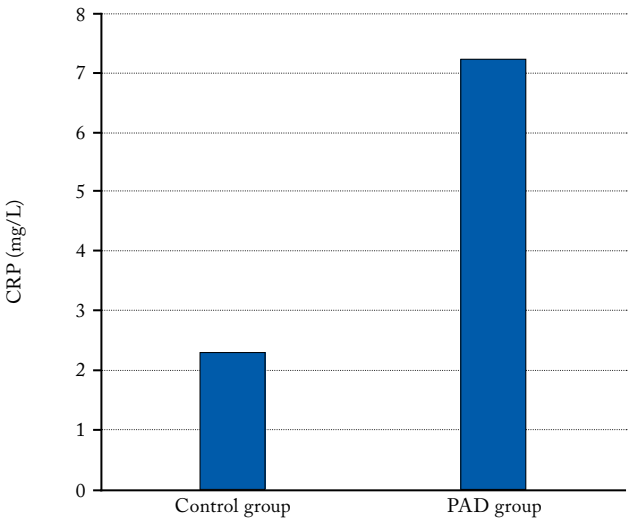


Figure 4. C-reactive protein blood levels in the patient and control groups.
CRP: C-reactive protein.

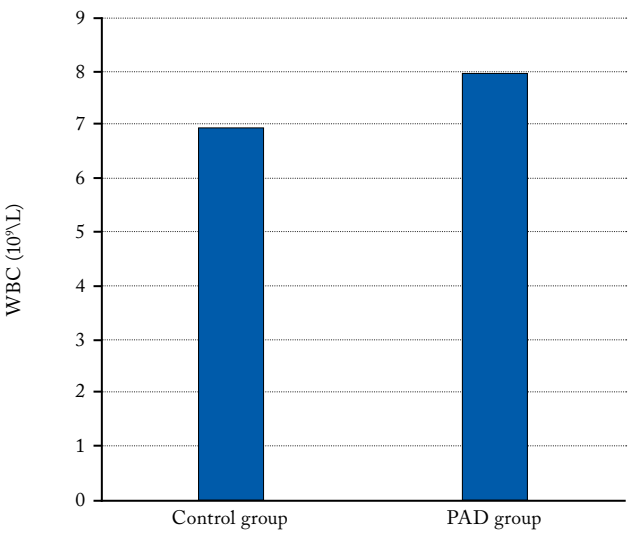


Figure 5. White blood cell count blood levels in the patient and control groups.
WBC: White blood cell count.

eGFR, ≤83 (AUC=0.803, 95% CI: 0.733-0.861, p<0.001); HDL, ≤43.8 (AUC=0.620, 95% CI: 0.540-0.695, p=0.007); triglycerides, >154.4 (AUC=0.661, 95% CI: 0.583-0.734, p<0.001); fibrinogen, >373 (AUC=0.923, 95% CI: 0.871-0.959, p<0.001); monocytes, >0.51 (AUC=0.740, 95% CI: 0.665-0.805, p<0.001); and CRP, >4.76 (AUC=0.781, 95% CI: 0.709-0.842, p<0.001) (Table 7).

Table 5
Evaluations with logistic regression

	Univariate logistic regression analysis						Multivariate logistic regression analysis					
Risk factor	B	SE	Wald	OR	95% CI	*p**	B	SE	Wald	OR	95% CI	*p**
Fibrinogen	0.024	0.003	48.135	1.02	1.02-1.03	0.000	0.021	0.003	37.758	1.02	1.01-1.03	0.000
CRP (mg/L)	0.266	0.056	22.498	1.30	1.17-1.46	0.000	0.169	0.071	5.663	1.18	1.03-1.36	0.017
WBC (10^9\L)	0.214	0.078	7.507	1.24	1.06-1.44	0.006	-	-	-	-	-	-

SE: Standard error; OR: Odds ratio; CI: Confidence interval; CRP: C-reactive protein; WBC: White blood cell count; * Binary logistic regression (It is given only for the variables remaining on the model), Nagelkerke R^2=0,665, Variable(s) removed on step 2: WBC (10^9\L).

Table 6
Real and predicted values according to the created model

	Predicted group		Accuracy
	Control group	PAD group	%
Real group			
Control group	69	6	92.0
PAD group	7	80	92.0
Correctly classified cases (%)			92.0

DISCUSSION

Our findings demonstrated a statistically significant difference in inflammation biomarkers, such as fibrinogen, CRP, and WBC count, in the PAD group compared to the control group. Proposed mechanisms by which low-grade inflammation may affect atherogenesis include increased foam cell formation via monocyte accumulation and LDL cholesterol deposition in the arterial wall.[11,12] Low-grade inflammation has been associated with an increased risk of cardiovascular events and cardiovascular mortality in various populations.[13] In a study conducted in acute myocardial infarction patients with and without DM, high-sensitivity CRP (hsCRP) was shown to predict in-hospital outcomes and two-year mortality.[14] It has also been shown that reducing low-grade inflammation in patients with coronary artery disease with or without type 2 DM reduces the residual risk of cardiovascular events.[13] In our study, the rate of DM in the PAH group was 47.1%. This finding is statistically significant (p<0.001) and is compatible with the literature (Table 2). One study reported a bidirectional relationship between DM and periodontitis, with hyperglycemic individuals having a higher prevalence of periodontitis compared to normoglycemic individuals. It has been suggested that low-grade inflammation and periodontitis increase the levels of proinflammatory mediators in the serum, which may lead to insulin resistance and diabetes.[15] It has been reported that DM and insulin resistance also trigger low-grade inflammation, and systemic inflammation is a risk factor for cardiovascular diseases, including PAD.[5,6]

One study demonstrated that HT is associated with lower-grade systemic inflammation indices in

Table 7
Receiver operating characteristic analysis

	AUC	95% CI	Cut off	Sensitivity	Specificity	Youden index	+PV	–PV	*p**
Glucose (mg/dL)	0.741	0.667-0.807	>110	55.2	85.3	0.405	81.4	62.1	**<0.001**
Creatinine (mg/dL)	0.731	0.656-0.798	>0.94	60.9	82.7	0.436	80.3	64.6	**<0.001**
eGFR	0.803	0.733-0.861	≤83	56.3	93.3	0.497	90.7	64.8	**<0.001**
HDL (mg/dL)	0.620	0.540-0.695	≤43.8	60.9	64.0	0.249	66.3	58.5	**0.007**
Triglyceride (mg/dL)	0.661	0.583-0.734	>154.4	56.3	81.3	0.377	77.8	61.6	**<0.001**
Fibrinogen	0.923	0.871-0.959	>373	94.3	89.3	0.836	91.1	93.1	**<0.001**
WBC (10^9\L)	0.641	0.562-0.714	>7.72	59.8	74.7	0.344	73.2	61.5	**0.002**
Monocyte (10^9\L)	0.740	0.665-0.805	>0.51	51.7	85.3	0.371	80.4	60.4	**<0.001**
Lymphocyte (10^9\L)	0.597	0.518-0.674	>2.74	36.8	92.0	0.288	84.2	55.6	**0.031**
Platelet (10^9\L)	0.575	0.495-0.653	>324	41.4	93.3	0.347	87.8	57.9	**0.104**
CRP (mg/L)	0.781	0.709-0.842	>4.76	72.4	74.7	0.471	76.8	70.0	**<0.001**
Monocyte/HDL ratio	0.743	0.668-0.808	>0.0106	65.5	70.7	0.362	72.2	63.9	**<0.001**
Monocytet/LDL ratio	0.673	0.595-0.744	>0.0039	63.2	64.0	0.272	67.1	60.0	**<0.001**

AUC: Under the curve; CI: Confidence interval; PV: Predictive value; * ROC curve analysis.

hypertrophic cardiomyopathy patients and that the adverse effect of HT in hypertrophic cardiomyopathy patients is a result of systemic effects rather than changes in cardiac function since left ventricular systolic and diastolic dysfunction measurements did not differ between hypertensive and normotensive patients.[16] In a review, it was stated that low-grade inflammation plays an important role in the relationship between the immune system and angiotensin II-induced HT.[17] It has been emphasized that monocyte/macrophage cells play an important role in vascular inflammation and interaction with the arterial wall throughout the progression of HT.[17] In our study, hypertension is statistically absent in 36% of patients with PAD ($p<0.001$; Table 2). One of the risk factors for PAH is dyslipidemia.[1] The risk of early atherosclerotic cardiovascular disease dramatically increases in patients with lipid disorders.[8] Recent studies have shown a definite link between systemic low-grade inflammation and obesity and dyslipidemia, with both disorders being associated with endothelial dysfunction/activation, a proinflammatory and prothrombotic state of the endothelium leading to the infiltration of leukocytes into the arterial wall.[18-20] In our study, the average triglyceride value in the PAD group was 161.60 mg/dL (98.70-243.40 mg/dL), with statistical significance ($p<0.001$; Table 2). Smoking, one of the other risk factors of PAD, is one of the most important preventable factors causing this disease.[1] Cigarette smoke extracts activate the NLRP3 inflammasome via reactive oxygen species, resulting in the downstream release of interleukin (IL)-1 beta, IL-18, and other inflammatory factors, leading to functional changes such as autophagy, pyrolysis, and apoptosis in endothelial cells.[19-21] According to our findings, the rate of smokers in the PAD group was 23% and this results was compatible with the literature (Table 2). In their study investigating the effect of physical activity on inflammation in PAD patients, Christofaro et al.[22] found that high hsCRP values were associated with inflammation and that hsCRP values significantly decreased in patients who engaged in regular physical activity. Jacobs et al.,[23] in their study on patients with metabolic syndrome, investigated CRP, IL-6, sVCAM-1 (soluble vascular cell adhesion molecule-1), sICAM-1 (soluble intercellular adhesion molecule-1), and serum amyloid A levels. They found a partial association between metabolic syndrome and the prevalence of coronary artery disease and PAD severity, suggesting that this relationship was mediated by low-grade inflammation. In our study, the mean fibrinogen 462.58±88.09 mg/dL and mean CRP 7.21±9.7 (3.74-9.43) mg/L values were high and were statistically significant ($p<0.001$). We observed other noteworthy findings in this study. For example, the mean monocyte and lymphocyte values were higher in the PAD group (0.55±0.21 and 2.82±1.57, respectively), with statistical significance ($p<0.001$). Barhoumi et al.[17] demonstrated that monocyte activation plays a role in vascular inflammation and low-grade inflammation.

This study had several limitations, including a small sample size and a retrospective design. Additionally, it would have been more valuable if other inflammatory biomarkers, such as tumor necrosis factor-alpha and IL-6, had been analyzed in this study.

In conclusion, inflammatory biomarkers such as fibrinogen, CRP, and WBC count were found to be statistically significant in the PAD group, indicating that the low-grade inflammation hypothesis may play a role in PAD. If the role of low-grade inflammation in PAD is proven in future large-scale, prospective, randomized controlled trials, anti-inflammatory treatment modalities may be incorporated into PAD treatment.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Study design, overwiew: A.D.K.; Writing and references: E.N.M.K.; Statistics: İ.A.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Wang W, Zhao T, Geng K, Yuan G, Chen Y, Xu Y. Smoking and the pathophysiology of peripheral artery disease. Front Cardiovasc Med 2021;8:704106. doi: 10.3389/fcvm.2021.704106.
2. Gimbrone MA Jr, García-Cardeña G. Endothelial cell dysfunction and the pathobiology of atherosclerosis. Circ Res 2016;118:620-36. doi: 10.1161/CIRCRESAHA.115.306301.
3. Donato AJ, Morgan RG, Walker AE, Lesniewski LA. Cellular and molecular biology of aging endothelial cells. J Mol Cell Cardiol 2015;89:122-35. doi: 10.1016/j.yjmcc.2015.01.021.

4. Alur İ. Low-grade inflammation: A familiar factor in cardiovascular diseases. JACC Basic Transl Sci 2023;8:1475. doi: 10.1016/j.jacbts.2023.09.010.
5. Tristan Asensi M, Napoletano A, Sofi F, Dinu M. Low-grade inflammation and ultra-processed foods consumption: A review. Nutrients 2023;15:1546. doi: 10.3390/nu15061546.
6. Cecoro G, Annunziata M, Iuorio MT, Nastri L, Guida L. Periodontitis, low-grade inflammation and systemic health: A scoping review. Medicina (Kaunas) 2020;56:272. doi: 10.3390/medicina56060272.
7. Yener AU, Cicek OF, Cicek MC, Ozkan T, Korkmaz K, Yener O, et al. Does a basic blood test tell the location of peripheral arterial lesions? Acta Medica Mediterranea 2015;31:377.
8. Handelsman Y, Bloomgarden ZT, Grunberger G, Umpierrez G, Zimmerman RS, Bailey TS, et al. American Association of Clinical Endocrinologists and American College of Endocrinology--Clinical practice guidelines for developing a diabetes mellitus comprehensive care plan--2015. Endocr Pract 2015;21:413-37.
9. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: The task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2013;34:2159-219. doi: 10.1093/eurheartj/eht151.
10. National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143-421.
11. Torzewski M, Rist C, Mortensen RF, Zwaka TP, Bienek M, Waltenberger J, et al. C-reactive protein in the arterial intima: Role of C-reactive protein receptor-dependent monocyte recruitment in atherogenesis. Arterioscler Thromb Vasc Biol 2000;20:2094-9. doi: 10.1161/01.atv.20.9.2094.
12. Zwaka TP, Hombach V, Torzewski J. C-reactive protein-mediated low density lipoprotein uptake by macrophages: implications for atherosclerosis. Circulation 2001;103:1194-7. doi: 10.1161/01.cir.103.9.1194.
13. Sharif S, Van der Graaf Y, Cramer MJ, Kapelle LJ, de Borst GJ, Visseren FLJ, et al. Low-grade inflammation as a risk factor for cardiovascular events and all-cause mortality in patients with type 2 diabetes. Cardiovasc Diabetol 2021;20:220. doi: 10.1186/s12933-021-01409-0.
14. Lucci C, Cosentino N, Genovese S, Campodonico J, Milazzo V, De Metrio M, et al. Prognostic impact of admission high-sensitivity C-reactive protein in acute myocardial infarction patients with and without diabetes mellitus. Cardiovasc Diabetol 2020;19:183. doi: 10.1186/s12933-020-01157-7.
15. Sima C, Glogauer M. Diabetes mellitus and periodontal diseases. Curr Diab Rep 2013;13:445-52. doi: 10.1007/s11892-013-0367-y.
16. Zach DK, Schwegel N, Santner V, Winkelbauer L, Hoeller V, Kolesnik E, et al. Low-grade systemic inflammation and left ventricular dysfunction in hypertensive compared to non-hypertensive hypertrophic cardiomyopathy. Int J Cardiol 2024;399:131661. doi: 10.1016/j.ijcard.2023.131661.
17. Barhoumi T, Todryk S. Role of monocytes/macrophages in renin-angiotensin system-induced hypertension and end organ damage. Front Physiol 2023;14:1199934. doi: 10.3389/fphys.2023.1199934.
18. Domingo E, Marques P, Francisco V, Piqueras L, Sanz MJ. Targeting systemic inflammation in metabolic disorders. A therapeutic candidate for the prevention of cardiovascular diseases? Pharmacol Res 2024;200:107058. doi: 10.1016/j.phrs.2024.107058.
19. Ismaeel A, Brumberg RS, Kirk JS, Papoutsi E, Farmer PJ, Bohannon WT, et al. Oxidative stress and arterial dysfunction in peripheral artery disease. Antioxidants (Basel) 2018;7:145. doi: 10.3390/antiox7100145.
20. Wu X, Zhang H, Qi W, Zhang Y, Li J, Li Z, et al. Nicotine promotes atherosclerosis via ROS-NLRP3-mediated endothelial cell pyroptosis. Cell Death Dis 2018;9:171. doi: 10.1038/s41419-017-0257-3.
21. Wang X, Bian Y, Zhang R, Liu X, Ni L, Ma B, et al. Melatonin alleviates cigarette smoke-induced endothelial cell pyroptosis through inhibiting ROS/NLRP3 axis. Biochem Biophys Res Commun 2019;519:402-8. doi: 10.1016/j.bbrc.2019.09.005.
22. Christofaro DGD, Ritti-Dias RM, Tebar WR, Werneck AO, Bittencourt MS, Cucato GG, et al. Are C-reactive protein concentrations affected by smoking status and physical activity levels? A longitudinal study. PLoS One 2023;18:e0293453. doi: 10.1371/journal.pone.0293453.
23. Jacobs M, van Greevenbroek MM, van der Kallen CJ, Ferreira I, Blaak EE, Feskens EJ, et al. Low-grade inflammation can partly explain the association between the metabolic syndrome and either coronary artery disease or severity of peripheral arterial disease: The CODAM study. Eur J Clin Invest 2009;39:437-44. doi: 10.1111/j.1365-2362.2009.02129.x.

Cardiovasc Surg Int 2024;11(3):193-201
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1647
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Aortic angle in predicting aortic regurgitation after transcatheter aortic valve implantation

Tolga Onuk, Fuat Polat, Barış Yaylak

Department of Cardiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Türkiye

Received: March 05, 2024 ***Accepted:*** September 16, 2024 ***Published online:*** October 17, 2024

ABSTRACT

Objectives: The primary aim of the study was to evaluate the effect of the aortic angle on aortic regurgitation after transcatheter aortic valve implantation (TAVI), while secondary objectives involved exploring correlations between the aortic angle and various clinical and demographic factors.

Patients and methods: The single-center observational study included 105 patients (55 females, 50 males; mean age: 78.8±6.7 years; range, 70 to 92 years) who underwent TAVI between October 2019 and September 2023. Comprehensive preprocedural evaluations were conducted, including echocardiography and computed tomography. Evolut R self-expandable supra-annular valves were used in the procedures.

Results: Hypertension (85.7%) and atrial fibrillation (78.2%) were the most common comorbidities, and 14.3% of patients exhibited moderate aortic regurgitation before TAVI. The mean aortic angle was 46.8±10.6° before the procedure. In receiver operating characteristic analysis, the aortic angle affecting aortic regurgitation after TAVI was determined as 49.5°. After TAVI, significant reductions in pulmonary artery pressures and aortic regurgitation prevalence were observed. Aortic regurgitation decreased in 38.1% of patients, remained unchanged in 47.6% of patients, and increased in 14.3% of patients. A weak linear relationship (R^2=0.011) was observed between aortic insufficiency and the aortic angle.

Conclusion: The study showed that an aortic angle of 49.5° can be used to predict aortic regurgitation after TAVI. However, a weak linear correlation was detected between the aortic angle and aortic regurgitation.

Keywords: Aortic angle, aortic valve insufficiency, computed tomography, echocardiography, transcatheter aortic valve replacement.

Aortic stenosis (AS) refers to the narrowing of the aortic valve opening, restricting blood flow from the left ventricle to the aorta. This condition impedes efficient blood circulation and imposes pressure on the heart, potentially leading to symptoms such as chest pain, shortness of breath, and, ultimately, heart failure.[1,2] The most common cause of AS is progressive calcification and stiffening of the valve leaflets, predominantly affecting older individuals.[3]

Epidemiologically, AS represents a prevalent valvular heart disease, particularly in aging populations. Its prevalence escalates with age, and it is estimated that around 2 to 9% of individuals over 65 years exhibit some degree of AS.[4-6] As life expectancy rises, AS incidence is expected to surge, necessitating effective treatment strategies.[7]

Transcatheter aortic valve implantation (TAVI) involves inserting a prosthetic valve via catheter-based techniques, often through the femoral artery, and positioning it within the native aortic valve. This minimally invasive procedure allows for shorter recovery times and reduced complications.[8] Transcatheter aortic valve implantation utilization has increased due to technological advancements and acceptance as a viable AS treatment.[9,10]

Corresponding author: Tolga Onuk, MD. Dr. Siyami Ersek Göğüs Kalp ve Damar Cerrahisi Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, 34668 Üsküdar, İstanbul, Türkiye.
E-mail: tolgaonuk77@gmail.com

Citation:
Onuk T, Polat F, Yaylak B. Aortic angle in predicting aortic regurgitation after transcatheter aortic valve implantation. Cardiovasc Surg Int 2024;11(3):193-201. doi: 10.5606/e-cvsi.2024.1647.

While TAVI has revolutionized AS management, complications include vascular issues, bleeding, stroke, conduction abnormalities, and aortic regurgitation (AR).[11,12] Factors influencing AR after TAVI include anatomical considerations, valve sizing, and procedural techniques.[13,14] Moderate to severe AR can lead to heart failure and increased morbidity.[15]

Research into aortic valve anatomy and its impact on TAVI outcomes is evolving, with studies exploring aortic annulus dimensions, calcification, and angles.[16] The aortic angle, measured by computed tomography, refers to the angle between the horizontal and aortic annular planes in the coronal section. A greater angle may indicate higher risk for complications.[17,18]

This study aimed to investigate the correlation between the aortic angle and AR following TAVI in patients without advanced annular calcification, using self-expandable supra-annular valves, and offer insights into a specific TAVI subset, potentially refining prognostic information for this cohort.

PATIENTS AND METHODS

This observational study was conducted with 105 patients (55 females, 50 males; mean age: 78.8±6.7 years; range, 70 to 92 years) who underwent TAVI at the Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital between October 2019 and September 2023. Patients with symptomatic severe AS were presented to a TAVI council consisting of cardiologists and cardiovascular surgeons. According to the council's decision, patients who were recommended TAVI and underwent the procedure in the same hospital were included in the study. The inclusion criteria were established as nonemergency TAVI and the presence of complete preprocedure, postprocedure, and predischarge data. The exclusion criteria encompassed active malignancy, bleeding disorders, selection of an entry site other than transfemoral, patients with bicuspid aortic valves, advanced annular calcification, and severe aortic insufficiency. The study protocol was approved by the İstanbul Yeni Yüzyıl University Ethics Committee (decision date: 04.03.2024, no: 2024/03-1234). Written informed consent was acquired from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographic data, comorbidities, and baseline characteristics were collected from electronic medical records. Preprocedural evaluations encompassed echocardiography, computed tomography, and the documentation of various cardiac parameters and anatomical measurements. All TAVI procedures were performed by experienced interventional cardiologists using the Medtronic Evolut R system self-expandable supra-annular valve (Medtronic, Minneapolis, MN, USA) Valve sizing (26, 29, or 34 mm) was determined based on individual patient anatomy. Pre- and postdilatation techniques were applied as clinically indicated.

Patients underwent meticulous predischarge assessments, including echocardiography and measurement of cardiac parameters. Follow-up evaluations aimed to compare pre-TAVI and post-TAVI values, assessing changes in left ventricular function, aortic gradients, pulmonary artery pressures, and the presence of aortic insufficiency.

The primary outcome was the impact of the aortic angle on AR. Secondary outcomes were the exploration of clinical and demographic factors that may influence variations in the aortic angle.

Statistical analysis

Statistical analysis was performed using IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize patient characteristics and baseline measurements. Continuous variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR). Paired t-tests or nonparametric tests were utilized to compare pre- and postprocedural values. Spearman correlation analyses were conducted to explore associations between variables. Receiver operating characteristic (ROC) analysis was employed to determine cutoff values for aortic angles affecting AR. A p-value <0.05 was considered statistically significant.

RESULTS

The prevalent comorbidities identified were hypertension (85.7%) and atrial fibrillation (75.2%). Concomitant coronary artery disease was present in 71.4% of the patient population. The median EuroSCORE II value for these patients was 4.2 (IQR, 3.2-4.8).

In the preprocedural echocardiographic assessments, the mean left ventricular ejection fraction (EF) was 48.1±14.1, the mean systolic pulmonary

Table 1
Clinical and demographic characteristics

	n	%	Mean±SD	IQR	25th-75th Percentiles
Patient characteristics					
Age (year)			78.8±6.7		
Sex					
Male	50	47.6			
Body mass index (kg/m²)			28.2±5.1		
Dyslipidemia (%)	50	47.6			
Diabetes mellitus (%)	45	42.9			
Hypertension (%)	90	85.7			
Atrial fibrillation (%)	79	75.2			
History of CAD (%)	75	71.4			
EuroSCORE II				4.2	3.2-4.8
Echocardiographic measurements					
Left ventricular ejection fraction (%)			48.1±14.1		
Interventricular septum thickness (mm)			13.8±2.7		
Posterior wall thickness (mm)			12.6±1.7		
LVEDD (mm)			47±11.5		
LVESD (mm)			32.8±6.5		
Systolic pulmonary artery pressure (mmHg)			43.8±10.3		
Mean aortic gradient (mmHg)			42.8±15.8		
Moderate to severe mitral regurgitation (%)	45	42.8			
Moderate to severe tricuspid regurgitation (%)	35	33.3			
Moderate aortic regurgitation (%)	15	14.3			
Computed tomography measurements					
LVOT diameter (mm)			24.6±2.2		
Aortic annulus diameter (mm)			24.2±1.4		
Left coronary sinus Valsalva diameter (mm)			31.4±2.4		
Right coronary sinus Valsalva diameter (mm)			28.5±2.3		
Non-coronary sinus Valsalva diameter (mm)			31.0±3.0		
Sinus Valsalva height (mm)			23.0±1.8		
LMCA height (mm)			14.4±3.0		
Right coronary artery height (mm)			18.2±3.2		
Moderate leaflet calcification (%)	35	33.3			
Aortic angle (°)			46.8±10.6		
Procedure-related measurements					
Valve size (%)					
26 mm	20	19.0			
29 mm	65	62.0			
34 mm	20	19.0			
Pre-dilatation (%)					
18 mm	5	4.8			
20 mm	30	28.6			
22 mm	5	4.8			
23 mm	10	9.5			
Post-dilatation (%)					
23 mm	20	19.0			
25 mm	30	28.6			
26 mm	5	4.8			
Permanent pacemaker (%)	10	9.5			
Postoperative moderate to severe aortic regurgitation	10	9.5			

SD: Standard deviation; IQR: Interquartile range; CAD: Coronary artery disease; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; LVOT: Left ventricular outflow diametern; LMCA: Left main coronary artery.

artery pressure was 43.8±10.3 mmHg, and the mean aortic gradient was 42.8±10.3 mmHg. Notably, 15 (14.3%) patients exhibited moderate to severe AR. The most common valve disease that was more than mild was mitral regurgitation (42.8%; Table 1).

In the preprocedural computed tomography evaluations, the mean left ventricular outflow tract diameter was 24.6±2.2, the mean aortic annulus diameter was 24.2±1.4, the mean left main coronary height was 14.4±3.0, and the mean right coronary height was 18.2±3.2. The sinus of Valsalva diameter, encompassing all three sinuses, yielded a mean measurement of 30.3±2.0. Notably, one-third of the patients exhibited moderate leaflet calcification. The degree of leaflet calcification was assessed using computed tomography, with mild calcification defined as scattered, thin calcifications covering less than 10% of the leaflet area, moderate calcification characterized by thicker calcifications covering 10 to 30% of the leaflet area, and severe calcification involving extensive, dense calcifications covering more than 30% of the leaflet area. Furthermore, the mean aortic angle was 46.8±10.6° (Table 1).

Evolut R self-expandable supra-annular 26-mm valves were used in 19%, 29-mm valves were used in 62%, and 34-mm valves were used in 19%. Predilatation was applied to 47.6% of the patients, and postdilatation was applied to 52.4%. A permanent pacemaker was needed after the procedure in 10 (9.5%) patients, and moderate AR was observed in 10 (9.5%) patients (Table 1).

The study compared pre-TAVI and predischarge echocardiographic parameters. As anticipated, a significant reduction was evident in the mean and peak aortic gradients before discharge (mean postprocedural gradient: 7.5±4.3 mmHg; peak aortic gradient: 14.9±7.7 mmHg; p<0.001). There was no significant difference between the mean EF (48.1±14.1%), left ventricular end-diastolic diameter (LVEDD; 47±11.5 mm), and left ventricular end-systolic diameter (LVESD; 32.8±6.5 mm) before TAVI and the mean EF (49.8±12.3%), LVEDD (48.6±5.3 mm), and LVESD (31.3±6.1 mm) before discharge. A significant decrease was noted in the systolic pulmonary artery pressure before discharge compared to preoperative levels (preoperative: 43.8±10.3; predischarge: 39.6±8.7; p=0.046). Additionally, the prevalence of moderate or higher AR decreased after valve implantation (preoperative: 14.3%; post-TAVI: 11.4%; p=0.033; Table 2).

Patient characteristics affecting the aortic angle were evaluated with Spearman correlation analysis. A positive correlation was observed between interventricular septum thickness, ascending aorta

Table 2
Comparison of preoperative and postoperative echocardiographic measurements

Echocardiographic measurements	Preoperative Mean±SD	Postoperative Mean±SD	*p*
Left ventricular ejection fraction (%) (Prior to TAVI-Prior to discharge)	48.1±14.1	49.8±12.3	0.052
Mean aortic gradient (mmHg) (Prior to TAVI-Prior to discharge)	42.8±15.8	7.5±4.3	<0.001
Peak aortic gradient (mmHg) (Prior to TAVI-Prior to discharge)	66.8±22.4	14.9±7.7	<0.001
LVEDD (mm) (Prior to TAVI-Prior to discharge)	47.0±11.5	48.6± 5.3	0.161
LVESD (mm) (Prior to TAVI-Prior to discharge)	32.8±6.4	31.3±6.1	0.156
sPAP (mmHg) (Prior to TAVI-Prior to discharge)	43.8±10.3	39.6±8.7	0.046
Moderate to severe AR (%) (Prior to TAVI-After TAVI)	%14.3	%11.4	0.033

SD: Standard deviation; TAVI: Transcatheter aortic valve implantation; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; sPAP: Systolic pulmonary artery pressure; AR: Aortic regurgitation.

Table 3
Clinical characteristics affecting the aortic angle

	Aortic angle	
	Correlation coefficient	*p*
Age	–0.109	0.266
Sex		
Male	0.155	0.114
Body mass index	0.235	0.135
EuroSCORE II	0.084	0.396
Left ventricular ejection fraction (%)	–0.194	0.047
IVS	0.205	0.036
LVEDD	0.072	0.467
Mean aortic gradient	0.172	0.356
Moderate to severe AR	0.235	0.089
LVOT diameter	–0.301	0.002
Aortic annulus diameter	–0.350	0.001
Ascendant aorta diameter	0.280	0.004
Left coronary sinus Valsalva diameter	–0.188	0.055
Right coronary sinus Valsalva diameter	–0.169	0.084
Non-coronary sinus Valsalva diameter	–0.554	0.001
Sinus Valsalva height	–0.225	0.021
LMCA height	–0.157	0.110
RCA height	–0.410	0.001
Moderate to severe leaflet calcification	0.176	0.073

AR: Aortic regurgitation; IVS: Interventricular septum thickness; LVEDD: Left ventricular end-diastolic diameter; AR: Aortic regurgitation; LVOT: Left ventricular outflow diameter; LMCA: Left main coronary artery; RCA: Right coronary artery.

diameter, and aortic angle (p=0.036 and p=0.004, respectively). A negative correlation was observed between EF, left ventricular outflow tract diameter, aortic annulus diameter, noncoronary cuspid sinus Valsalva diameter, sinus Valsalva height, right coronary artery height, and aortic angle (p=0.047, p=0.002, p=0.001, p=0.001, p=0.021, and p=0.001, respectively; Table 3).

A ROC analysis was performed to determine the cutoff value for the aortic angle affecting the AR after TAVI (before postdilatation). An aortic angle of 49.5° was determined as the cutoff value for the development of AR after TAVI, with 56% sensitivity and 50% specificity (area under the curve: 0.653; Figure 1).

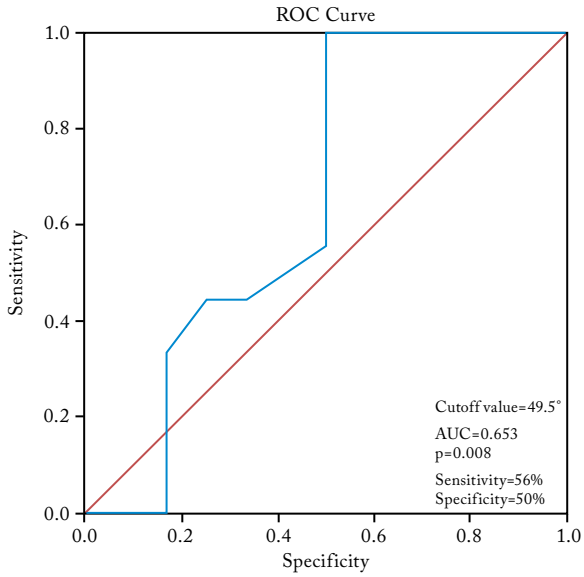
Moderate AR was observed in 12 patients after TAVI (before postdilatation). Of the patients who developed moderate AR before postdilatation, the aortic angle was above 49.5° in 10 (Figure 2).

The change in AR after TAVI (before discharge) compared to before TAVI was examined in all patients. At least one-degree decrease in AR was observed in 40 (38.1%) patients, the same level was observed in 50 (47.6%) patients, and an increase in AR was observed in 15 (14.3%) patients (Figure 3).

When post-TAVI (before postdilatation) AR was divided into none, mild, and moderate, a weak linear relationship was detected between AR and the aortic angle (R^2=0.011; Figure 4).

DISCUSSION

The management of severe AS has evolved significantly, with TAVI emerging as a less invasive



Area AUC				
Test results variable(s): Aortic angle				
Area	SE[a]	Asymptotic sig.[b]	Asymptotic 95% CI	
0.653	0.055	0.008	Lover bound	Upper bound

The test result variable(s): Aortic angle has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. a: Under the nonparametric assumption; b: The effect being studied does not exist (if p value >0.05).

Figure 1. ROC analysis of the effect of the aortic angle on AR after TAVI.

AUC: Area under the curve; ROC: Receiver operating characteristic; AR: Aortic regurgitation; TAVI: Transcatheter aortic valve implantation; SE: Standard error; CI: Confidence interval.

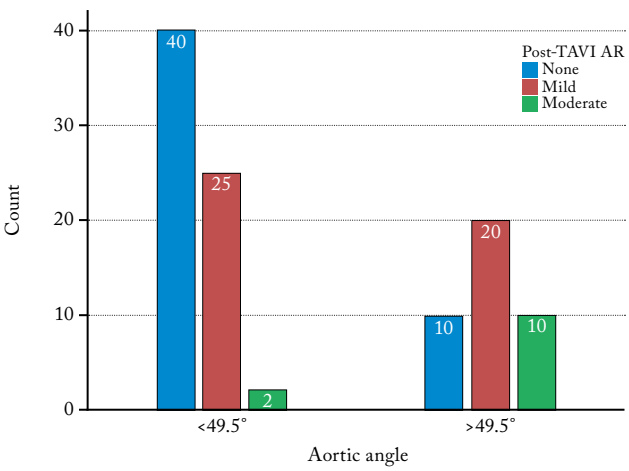


Figure 2. The graphical representation of the AR observed in patients according to the cutoff value of the aortic angle determined according to ROC analysis with a column chart.

AR: Aortic regurgitation; ROC: Receiver operating characteristic.

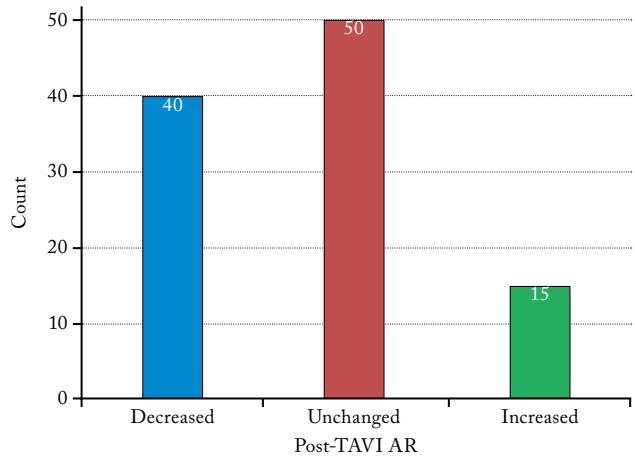


Figure 3. The graphical representation of the change in AR in the echocardiography performed after TAVI (before discharge) compared to before TAVI with a bar graph.

TAVI: Transcatheter aortic valve implantation; AR: Aortic regurgitation.

alternative to surgical aortic valve replacement. However, complications after TAVI, notably AR, remain a concern. This observational study delves into the predictive role of the aortic angle in post-TAVI AR and explores its correlations with various clinical and demographic factors, shedding light on the significance of this anatomical parameter in TAVI outcomes.

In line with our investigation, Roule et al.[19] demonstrated an association between increased angulation between the ascending aorta and the left ventricle long axis and higher rates of AR after TAVI, independent of other potential correlations. Conversely, conflicting findings emerged from other studies. One study suggested that an aortic angle ≥48° did not impact procedural success or in-hospital outcomes and recommended against considering it when determining valve selection.[20] Another study indicated that the aortic angle influenced procedural success in balloon-expandable valves but had no effect on self-expandable valves.[21]

Our study aligns with prior research, confirming the significance of the aortic angle in predicting AR following TAVI. The identified cutoff angle of 49.5° holds merit in assessing risk and forecasting outcomes for TAVI patients. Notably, our study reveals a correlation between higher aortic angles and the development of moderate AR after TAVI, albeit with a weak linear relationship. These insights underscore the importance of thorough preprocedural evaluations,

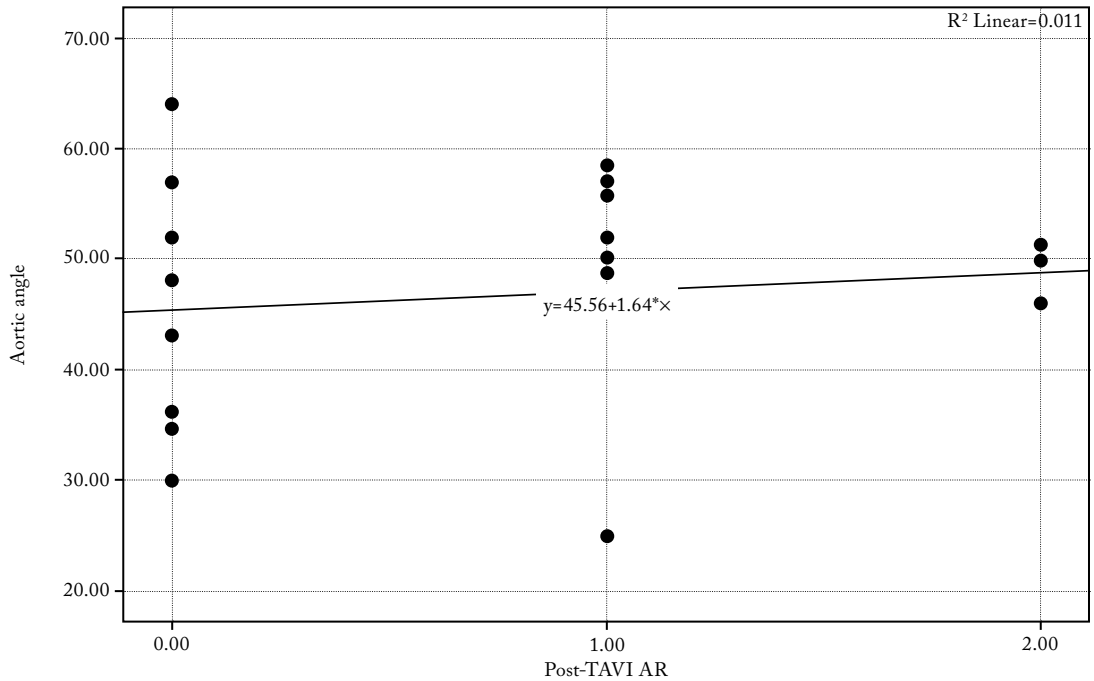


Figure 4. The graphical representation of the linear relationship between aortic insufficiency and the aortic angle after TAVI (before postdilation) with a scatter plot graph.
TAVI: Transcatheter aortic valve implantation; AR: Aortic regurgitation.

emphasizing the necessity of meticulous assessment of aortic anatomy to anticipate and manage post-TAVI complications effectively.

Our investigation into patient characteristics influencing the aortic angle revealed potential predictors for post-TAVI outcomes. Positive correlations with interventricular septum thickness and ascending aorta diameter, alongside negative correlations with parameters such as EF, left ventricular outflow tract diameter, aortic annulus diameter, and sinus of Valsalva dimensions, provide nuanced insights into anatomical factors influencing the aortic angle. These correlations offer the potential for risk stratification and personalized approaches in TAVI procedures.

Although there is a lack of studies investigating specific associations between the aortic angle and interventricular septal hypertrophy, the study by Yoshitani et al.[22] indicated that surgical aortic valve replacement was more effective in improving functional impairment in the presence of interventricular septal hypertrophy in AS patients compared to TAVR. Additionally, sharper angulation of the aortic arch has been linked to late AR after arterial switch surgery for ascending aortic dilatation and transposition of the great arteries.[23] This highlights the diverse impact of aortic geometry on various cardiac conditions.

A decrease in left ventricular EF can remodel the left ventricle, resulting in a leftward shift and a flatter appearance at the apex. This alteration in shape helps elucidate the negative relationship between an increased aortic angle and EF.

Our study's focus on patients without advanced annular calcification, utilizing Evolut R self-expandable supra-annular valves, characterizes a distinct subset of TAVI patients. This focused approach provides unique insights into this subset, potentially facilitating more refined prognostic assessments for this subgroup.

The observed improvements in aortic gradients, pulmonary artery pressures, and the reduction in moderate or higher AR after TAVI underscore the procedure's efficacy in managing valvular pathologies.[24] These improvements highlight the clinical benefits and success of TAVI in relieving symptomatic burden among patients with severe AS.

Our study aimed to identify the primary risk factors contributing to aortic insufficiency following TAVI procedures, with a particular focus on the aortic angle. One of the significant findings was the association between an increased aortic angle and a higher incidence of aortic insufficiency. To ensure a more accurate assessment of this relationship, patients with bicuspid aortic valves were excluded from our study. This exclusion was critical in eliminating a well-known confounding factor that could independently affect the outcomes. We acknowledge that aortic insufficiency is multifactorial, and other potential risk factors such as leaflet calcification extent, annular dimensions, bicuspid aortic valves, and overall valve morphology could play crucial roles. Our findings emphasize the need for future studies to incorporate a broader evaluation of these additional risk factors. A comprehensive analysis that includes various anatomical and procedural factors will provide a more holistic understanding of the determinants of aortic insufficiency after TAVI.

This study had several limitations that warrant consideration. The study's single-center observational design and limited sample size might constrain the generalizability of the findings. Additionally, potential confounders not accounted for in the analysis, incomplete medical records, and retrospective data collection could introduce bias due to missing information. While correlations were established, determining causation necessitates further prospective investigations encompassing comprehensive multifactorial analyses.

In conclusion, this study highlights the pivotal role of the aortic angle in predicting AR after TAVI, establishing a crucial threshold at 49.5°. Investigating correlations between the aortic angle and patient characteristics revealed potential predictors for post-TAVI outcomes, offering avenues for further exploration. The observed improvements in aortic gradients, pulmonary artery pressures, and decreased prevalence of moderate or higher AR after TAVI underscore the procedure's efficacy in managing valvular pathologies. While a weak linear correlation between AR and the aortic angle was noted, the study emphasizes the significance of meticulous preprocedural assessments for predicting and managing complications.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conceived of the presented idea: T.O., F.P. Developed the theory and performed the computations: F.P.; Verified the analytical methods: B.Y.; Supervised the findings of this work: T.O., B.Y. All authors discussed the results and contributed to the final manuscript.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Généreux P, Stone GW, O'Gara PT, Marquis-Gravel G, Redfors B, Giustino G, et al. Natural history, diagnostic approaches, and therapeutic strategies for patients with asymptomatic severe aortic stenosis. J Am Coll Cardiol 2016;67:2263-88. doi: 10.1016/j.jacc.2016.02.057.
2. Gottlieb M, Long B, Koyfman A. Evaluation and management of aortic stenosis for the emergency clinician: An evidence-based review of the literature. J Emerg Med 2018;55:34-41. doi: 10.1016/j.jemermed.2018.01.026.
3. Bhatia N, Basra SS, Skolnick AH, Wenger NK. Aortic valve disease in the older adult. J Geriatr Cardiol 2016;13:941-4. doi: 10.11909/j.issn.1671-5411.2016.12.004.
4. Rana M. Aortic valve stenosis: Diagnostic approaches and recommendations of the 2021 ESC/EACTS guidelines for the management of valvular heart disease -a review of the literature. Cardiol Cardiovasc Med 2022;6:315-24. doi: 10.26502/fccm.92920267.
5. Osnabrugge RL, Mylotte D, Head SJ, Van Mieghem NM, Nkomo VT, LeReun CM, et al. Aortic stenosis in the elderly: Disease prevalence and number of candidates for transcatheter aortic valve replacement: A meta-analysis and modeling study. J Am Coll Cardiol 2013;62:1002-12. doi: 10.1016/j.jacc.2013.05.015.
6. Carità P, Coppola G, Novo G, Caccamo G, Guglielmo M, Balasus F, et al. Aortic stenosis: Insights on pathogenesis and clinical implications. J Geriatr Cardiol 2016;13:489-98. doi: 10.11909/j.issn.1671-5411.2016.06.001.
7. Kanwar A, Thaden JJ, Nkomo VT. Management of patients with aortic valve stenosis. Mayo Clin Proc 2018;93:488-508. doi: 10.1016/j.mayocp.2018.01.020.
8. Kalogeropoulos AS, Redwood SR, Allen CJ, Hurrell H, Chehab O, Rajani R, et al. A 20-year journey in transcatheter aortic valve implantation: Evolution to current eminence. Front Cardiovasc Med 2022;9:971762. doi: 10.3389/fcvm.2022.971762.
9. Panayiotides IM, Nikolaides E. Transcatheter Aortic Valve Implantation (TAVI): Is it time for this intervention to be applied in a lower risk population? Clin Med Insights Cardiol 2014;8:93-102. doi: 10.4137/CMC.S19217.
10. Voigtländer L, Seiffert M. Expanding TAVI to low and intermediate risk patients. Front Cardiovasc Med 2018;5:92. doi: 10.3389/fcvm.2018.00092.

11. van Ginkel DJ, Brouwer J, van Hemert ND, Kraaijeveld AO, Rensing BJWM, Swaans MJ, et al. Major threats to early safety after transcatheter aortic valve implantation in a contemporary cohort of real-world patients. Neth Heart J 2021;29:632-42. doi: 10.1007/s12471-021-01638-8.
12. Laborde JC, Brecker SJ, Roy D, Jahangiri M. Complications at the time of transcatheter aortic valve implantation. Methodist Debakey Cardiovasc J 2012;8:38-41. doi: 10.14797/mdcj-8-2-38.
13. Stähli BE, Maier W, Corti R, Lüscher TF, Jenni R, Tanner FC. Aortic regurgitation after transcatheter aortic valve implantation: Mechanisms and implications. Cardiovasc Diagn Ther 2013;3:15-22. doi: 10.3978/j.issn.2223-3652.2013.02.01.
14. Collas VM, Paelinck BP, Rodrigus IE, Vrints CJ, Bosmans JM. Aortic regurgitation after Transcatheter Aortic Valve Implantation (TAVI) - Angiographic, echocardiographic and hemodynamic assessment in relation to one year outcome. Int J Cardiol 2015;194:13-20. doi: 10.1016/j.ijcard.2015.05.015.
15. Dujardin KS, Enriquez-Sarano M, Schaff HV, Bailey KR, Seward JB, Tajik AJ. Mortality and morbidity of aortic regurgitation in clinical practice. A long-term follow-up study. Circulation 1999;99:1851-7. doi: 10.1161/01.cir.99.14.1851.
16. Schoenhagen P, Hausleiter J, Achenbach S, Desai MY, Tuzcu EM. Computed tomography in the evaluation for Transcatheter Aortic Valve Implantation (TAVI). Cardiovasc Diagn Ther 2011;1:44-56. doi: 10.3978/j.issn.2223-3652.2011.08.01.
17. Randhawa A, Gupta T, Singh P, Aggarwal A, Sahni D. Description of the aortic root anatomy in relation to transcatheter aortic valve implantation. Cardiovasc Pathol 2019;40:19-23. doi: 10.1016/j.carpath.2019.01.005.
18. Gorla R, De Marco F, Garatti A, Bianchi G, Popolo Rubbio A, Acerbi E, et al. Impact of aortic angle on transcatheter aortic valve implantation outcome with Evolut-R, Portico, and Acurate-NEO. Catheter Cardiovasc Interv 2021;97:E135-45. doi: 10.1002/ccd.28957.
19. Roule V, Placente A, Sabatier R, Bignon M, Saplacan V, Ivascau C, et al. Angles between the aortic root and the left ventricle assessed by MDCT are associated with the risk of aortic regurgitation after transcatheter aortic valve replacement. Heart Vessels 2018;33:58-65. doi: 10.1007/s00380-017-1032-1.
20. Medranda GA, Musallam A, Zhang C, Rappaport H, Gallino PE, Case BC, et al. The impact of aortic angulation on contemporary transcatheter aortic valve replacement outcomes. JACC Cardiovasc Interv 2021;14:1209-15. doi: 10.1016/j.jcin.2021.03.027.
21. Abramowitz Y, Maeno Y, Chakravarty T, Kazuno Y, Takahashi N, Kawamori H, et al. Aortic angulation attenuates procedural success following self-expandable but not balloon-expandable TAVR. JACC Cardiovasc Imaging 2016;9:964-72. doi: 10.1016/j.jcmg.2016.02.030.
22. Yoshitani H, Isotani A, Song JK, Shirai S, Umeda H, Jang JY, et al. Surgical as opposed to transcatheter aortic valve replacement improves basal interventricular septal hypertrophy. Circ J 2018;82:2887-95. doi: 10.1253/circj.CJ-18-0390.
23. Agnoletti G, Ou P, Celermajer DS, Boudjemline Y, Marini D, Bonnet D, et al. Acute angulation of the aortic arch predisposes a patient to ascending aortic dilatation and aortic regurgitation late after the arterial switch operation for transposition of the great arteries. J Thorac Cardiovasc Surg 2008;135:568-72. doi: 10.1016/j.jtcvs.2007.10.020.
24. Radhoe SP, Veenis JF, Van Mieghem NM, Brugts JJ. The effect of transcatheter aortic valve implantation on pulmonary artery pressures in a patient suffering from chronic heart failure: A case report. Eur Heart J Case Rep 2021;5:ytab112. doi: 10.1093/ehjcr/ytab112.

Cardiovasc Surg Int 2024;11(3):202-209
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1711
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Effectiveness of remote endarterectomy in superficial femoral artery occlusion

Burak Koçak[1], Bülent Mert[2], Sinan Güzel[3], Kamil Boyacıoğlu[2]

[1]Department of Cardiovascular Surgery, Niğde Training and Research Hospital, Niğde, Türkiye
[2]Department of Cardiovascular Surgery, Bağcılar Training and Research Hospital, İstanbul, Türkiye
[3]Department of Cardiovascular Surgery, Dörtyol Public Hospital, Hatay, Türkiye

Received: July 23, 2024 ***Accepted:*** October 04, 2024 ***Published online:*** October 17, 2024

ABSTRACT

Objectives: The study aimed to evaluate the one-year patency rates of patients who underwent remote endarterectomy (RE) and compare them with femoral-popliteal bypass (FPB) surgery.

Patients and methods: The single-center observational study included 48 consecutive patients (46 males, 2 females; mean age: 60.0±6.1 years; range, 48 to 73 years) who underwent RE (n=24) or FPB surgery (n=24), which was performed solely for peripheral artery disease, between January 2017 and January 2022. Demographic and clinical data of the patients and data related to the procedures and follow-up were obtained from hospital records, and the evaluations were performed retrospectively. The exclusion criteria were defined as being under 18 years of age and undergoing FPB following trauma.

Results: While 21 (87.5%) of the patients who underwent RE had a lesion in the popliteal artery, none of the patients who underwent FPB had a popliteal artery lesion. The one-year patency rate in patients who underwent RE and FPB was 73.9% and 62.5%, respectively. Although the Global Limb Anatomical Staging System scores of patients who underwent RE were more advanced, patency rates were found to be higher. The number of patients who underwent RE and required revascularization within the first week was five (21.7%), and all of these procedures were performed endovascularly. In the FPB group, the number of patients requiring revascularization was two (8.3%), and embolectomy was performed in these patients.

Conclusion: Remote endarterectomy may be a good option in patients who have long-segment lesions, in those who previously underwent FPB surgery, in patients who require repeated intragraft embolectomy revisions, in those with limited access for endovascular procedures, in patients with graft infections, and in those who cannot use prosthetic materials.

Keywords: Femoropopliteal bypass, peripheral artery disease, remote endarterectomy.

The occlusion of the superficial femoral artery (SFA) is a common and debilitating condition, often associated with peripheral artery disease.[1] Patients with SFA occlusion frequently experience reduced blood flow to the lower extremities, leading to symptoms such as claudication, pain at rest, and impaired mobility.[2] While endovascular techniques, such as angioplasty and stenting, have gained prominence in the management of SFA occlusions, a surgical alternative known as remote endarterectomy (RE) has emerged as a compelling approach.

Remote endarterectomy, originally developed as a less invasive alternative to femoral-popliteal bypass (FPB) surgery, allows for the removal of the atherosclerotic plaque and restoration of blood flow through a small incision in a remote location of the artery. Nowadays, the role of endovascular interventional methods increases in the treatment of SFA stenosis or occlusion.[3] The segment most commonly treated with endovascular interventions is the femoropopliteal arterial segment.[4] As researchers and clinicians seek to refine and expand the scope of RE, it is vital to examine the effectiveness of this procedure in addressing SFA occlusions and its potential benefits over alternative treatment options.

Corresponding author: Burak Koçak, MD. Niğde Eğitim ve Araştırma Hastanesi, Kalp ve Damar Cerrahisi Kliniği, 51100 Niğde, Türkiye.
E-mail: dr.burakkocak@hotmail.com

Citation:
Koçak B, Mert B, Güzel S, Boyacıoğlu K. Effectiveness of remote endarterectomy in superficial femoral artery occlusion. Cardiovasc Surg Int 2024;11(3):202-209. doi: 10.5606/e-cvsi.2024.1711.

This study aimed to explore the current state of knowledge regarding RE in the context of SFA occlusion. By examining existing research, clinical outcomes, and patient experience, we endeavored to assess the efficacy of RE as a treatment modality for this challenging condition. This exploration sought to determine whether RE represents a promising avenue for improving outcomes in individuals suffering from SFA occlusion, potentially offering enhanced symptom relief, increased quality of life, and improved long-term vascular health.

PATIENTS AND METHODS

A total of 48 patients (46 males, 2 females; mean age: 60.0±6.1 years; range, 48 to 73 years) who underwent either RE (n=24) or FPB surgery (n=24) at the Bağcılar Training and Research Hospital, Department of Cardiovascular Surgery between January 1, 2017, and January 1, 2022 were included in the observational study. The exclusion criteria were as follows: patients under the age of 18 years and patients who underwent FPB for revascularization following trauma. Evaluations were conducted retrospectively. The primary endpoint of the study was to assess the one-year patency rate of RE. Additionally, its association with diabetes mellitus, the lipid panel (low-density lipoprotein, high-density lipoprotein, and total cholesterol), smoking status, age, sex, hypertension, and discharge medication were evaluated. In patients who underwent femoropopliteal procedures, saphenous vein grafts (SVGs) were never used; PTFE (polytetrafluoroethylene) grafts were used in all patients. The one-year patency of RE and FPB, which was performed solely due to peripheral artery disease, was compared. Demographic and clinical data of patients and variables related to the procedure and follow-up were obtained from hospital records. The study protocol was approved by the Bağcılar Training and Research Hospital Ethics Committee (date: 16.11.2022, no: 2022/11/04/025). Written informed consent was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

One-year patency was defined as the result of computed tomography angiography (CTA) or duplex ultrasonography (DUS) assessments performed at the one-year follow-up for all patients. Revision was defined as endovascular treatments and embolectomy procedures performed with the purpose of revascularization. Restenosis was defined as stenosis of more than 50% that did not lead to total SFA occlusion within the first seven days postoperatively. The target INR (international normalized ratio) for patients prescribed a vitamin K antagonist (VKA) at discharge was 2-3 mg/dL. Procedure success was defined as achieving complete patency during RE without extravasation during the operation. Performing distal and proximal anastomoses without complications was considered a successful FPB surgery. Concomitant lesion was defined as lesions classified up to less than 50% stenosis due to extensive calcification in the External iliac artery (EIA), common femoral artery (CFA), profunda femoral artery (PFA), or popliteal artery (PopA) that did not lead total occlusion. Additional surgery was defined as revision operations performed in case of restenosis, hematoma development, or bleeding using endovascular or open surgical methods. Values above the reference range of 1.00 mg /dL, determined by the central laboratory for creatinine levels, were classified as renal dysfunction.

Surgical procedure

Remote endarterectomy is generally performed in hybrid operating rooms; however, we conducted the procedure in the angiography unit within our available resources. An incision was made in the femoral region on the lesion side of the patient. After turning the CFA, SFA, and PFA with tapes, it was ensured that an adequate field of view was obtained, and heparinization was performed with heparin sodium administered at 5,000 IU. The activated clotting time (ACT) measurement was performed to achieve a target value >200.

After making an arteriotomy with a longitudinal incision of approximately 5 cm, the plaque was visualized, freed, and completely cut vertically from the middle. Endarterectomy was performed on both arteriotomy sites. A Martin dissector (LeMaitre, Burlington, USA) was passed around the plaque. The plaque was dissected from all sides of the vessel, and then using a Vollmar ring dissector (LeMaitre, Burlington, USA), the plaque was completely freed up to the area where preoperative measurements were taken and marked. Subsequently, the most distal part of the measured and freed region was cut using a MollRing cutting transection device (LeMaitre, Burlington, USA), and the plaque was

removed in one piece. Immediately afterward, a 6F sheath was stabilized from the arteriotomy site, and imaging was performed using digital subtraction angiography. The residual lesion remaining in the distal SFA region was retrieved using the EndoHelix Retrieval device (LeMaitre, Burlington, USA). After the residual lesion was removed, another digital subtraction angiography image was taken, and if focal stenotic foci were observed, balloon angioplasty was performed as needed.

In cases where complete patency was achieved without any complications, the arteriotomy site was closed by primary closure, with a Dacron graft or SVG depending on the diameter of the artery, using 5-0 sutures. Following hemostasis control, one Hemovac drain was inserted, and the procedure was successfully concluded.

Postdischarge medication

All patients received low-molecular-weight heparin (LMWH) after discharge. Nineteen patients who underwent RE were discharged with LMWH, acetylsalicylic acid (ASA), and VKA, while three patients were given clopidogrel treatment instead of VKA. Two patients were discharged with only LMWH and ASA due to the risk of bleeding.

In the group that underwent FPB, 16 patients were given LMWH, ASA, and clopidogrel, while six patients were given VKA instead of clopidogrel. Two patients were discharged with only LMWH and ASA due to the risk of bleeding.

When deciding on medication after discharge, parameters such as the antithrombotic and anticoagulant drugs used by patients before the operation, the presence of coronary artery and carotid artery diseases, atrial fibrillation, and comorbidities were evaluated.

Statistical analysis

Data were analyzed using IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics (number, percentage, mean ± standard deviation (SD), minimum, and maximum) of the data were provided in the study. As the first step in data analysis, the normality assumption was checked with the Shapiro-Wilk test. When the normality assumption was met, the independent sample t-test was used to examine the difference in means of two independent groups, and when the assumption was not met, the Mann-Whitney U test was conducted. In cases where the normality assumption was met, a paired t-test was used to examine the difference in means of two dependent groups, and in cases where the assumption was not met, the Wilcoxon signed-rank test was used. A p-value <0.05 was considered statistically significant.

RESULTS

Thirteen (54.2%) patients who underwent RE and nine (37.5%) patients who underwent FPB were diabetic. Demographic characteristics were similar for the groups (Table 1). There was no mortality in the study.

All patients included in the study had long-segment SFA lesions and were classified with the femoropopliteal Global Limb Anatomical Staging System (GLASS). According to GLASS scores, 18 (75%) patients who underwent RE were evaluated as Stage 3, and six (25%) were evaluated as Stage 4. Among patients who underwent FPB surgery, 20 (83.3%) were evaluated as Stage 2, and four (16.7%) were evaluated as Stage 3 (Table 2). There was also a statistically significant difference in lesion lengths according to the type of surgery ($p<0.05$). Lesions in RE were found to be longer than lesions in FPB surgery (Table 3).

In the RE and FPB groups respectively, according to the Rutherford category, nine (37.5%) and four (16.7%) patients had mild claudication, six (25%) and nine (37.5%) patients had moderate claudication, five (20.8%) and six (25%) patients had severe claudication, and three (12.5%) and five (20.8%) patients had rest pain. There was only one (4.2%) patient with minor tissue loss in the RE group.

Procedural success was achieved in 95.8% and 100% of cases in the RE and FPB groups, respectively. Among the patients who underwent RE and required revascularization within the first week, five (21.7%) underwent endovascular procedures. Two (8.3%) of patients who underwent FPB and required revascularization underwent embolectomy procedures.

Dacron grafts were used in four (16.7%) patients who underwent RE, and SVG patches were used

Table 1
Demographic and clinical characteristics by type of operation

	RE group		FPB group		Total	
	n	%	n	%	n	%
Sex						
Male	23	95.8	23	95.8	46	95.8
Female	1	4.2	1	4.2	2	4.2
Operation side						
Right	12	50.0	10	41.7	22	45.8
Left	12	50.0	14	58.3	26	54.2
DM	13	54.2	9	37.5	22	45.8
Hypertension	11	45.8	16	66.7	27	56.3
Smoking	17	70.8	16	66.7	33	68.8
Additional lesion						
CFA	19	79.2	12	50.0	31	64.6
EIA	4	16.7	1	4.2	5	10.4
SFA	24	100.0	24	100.0	48	100.0
PopA	21	87.5	0	0.0	21	43.8
Endovascular revision	5	21.7	0	0.0	5	10.4
Arteriotomi closure						
Dacron graft	4	16.7	0	0.0	4	8.3
SVG	11	45.8	0	0.0	11	22.9
Primary	8	33.3	0	0.0	8	16.7
PTFE interposition	1	4.2	0	0.0	1	2.1
VKA	19	79.2	6	25.0	25	52.1
Discharge medication						
CPD	3	12.5	16	66.7	19	39.6
ASA (single)	2	8.3	2	8.3	4	8.3
LMWH (single)	0	0.0	0	0.0	0	0.0
One-year patency	17	73.9	15	62.5	32	68.1
Follow-up evaluation						
DUS	10	41.7	17	70.8	27	56.2
CTA	14	58.3	7	29.2	21	43.8
Renal dysfunction	8	33.3	5	20.8	13	27.1

DM: Diabetes mellitus; CFA: Common femoral artery; EIA: External iliac artery; SFA: Superficial femoral artery; PopA: Popliteal artery; SVG: Saphenous vein graft; PTFE: Polytetrafluoroethylene; VKA: Vitamin K antagonist; CPD: Clopidogrel; ASA: Acetyl salicylic acid; LMWH: Low molecular weight heparin; DUS: Duplex Ultrasonography; CTA: Computed tomography angiography.

in 11 (45.8%). In this group, arterial integrity was achieved in eight (33.3%) patients using the primary closure method, while PTFE interposition was used in one (4.2%) patient (Table 1). No wound infection was reported.

In our study, it was found that RE was most frequent procedure when the additional lesion areas were PFA, CFA, and EIA ($p<0.05$). Lesion length was found to be longer in RE compared to FPB surgery ($p<0.05$; Table 3).

When the one-year patency of all patients was examined, 32 (68.1%) were found to have patent arteries. Postdischarge follow-ups for these patients were conducted using DUS in 27 (56.2%) and CTA in 21 (43.8%) (Additional Table 1). The mean preoperative ankle-brachial index was 0.49±0.10, and the mean postoperative ankle-brachial index was 0.86±0.08 (Table 4). The relationship between preoperative and postoperative ABI values and patency is also illustrated in Additional Table 2.

Table 2
Staging according to the type of operation

	RE group		FPB group		Total	
	n	%	n	%	n	%
Preoperative Rutherford category						
Mild claudication	9	37.5	4	16.7	13	27.1
Moderate claudication	6	25.0	9	37.5	15	31.3
Severe claudication	5	20.8	6	25.0	11	22.9
Rest pain	3	12.5	5	20.8	8	16.7
Minor tissue loss	1	4.2	0	0.0	1	2.1
Preoperative GLASS stage						
Stage 2	0	0.0	20	83.3	20	41.7
Stage 3	18	75.0	4	16.7	22	45.8
Stage 4	6	25.0	0	0.0	6	12.5
One-year Rutherford category						
Asymptomatic	13	54.2	11	45.8	24	50.0
Mild claudication	2	8.3	4	16.7	6	12.5
Moderate claudication	5	20.8	1	4.2	6	12.5
Severe claudication	4	16.7	7	29.2	11	22.9
Rest pain	0	0.0	1	4.2	1	2.1

GLASS: Global Limb Anatomical Staging System.

Table 3
Comparison of mean lesion lengths according to operation type

	Operation type	Mean±SD	Rank average	Test statistics	*p*
Lesion length	RE	26.17±2.39	35.23	30.50**	<0.0001*
	FPB	16.29±4.50	13.77		

SD: Standard deviation; RE: Remote endarterectomy; FPB: Femoral-popliteal bypass; * p<0.05; ** One-sample Wilcoxon signed-rank test.

Table 4
Variables related to operations

	Mean±SD	Min-Max
RE		
Age (year)	60.0±6.1	48-73
Preoperative ABI	0.49±0.10	0.31-0.67
Postoperative ABI	0.86±0.08	0.71-1.00
HDL-C	36.79±8.19	20-51
LDL-C	120.50±44.99	52-222
Creatinine	0.96±0.23	0.63-1.62
HbA1c	7.28±1.92	5.60-14
Total		
Age	60.29±11.35	23-91
Preop ABI	0.48±0.11	0.23-0.70
Postop ABI	0.87±0.09	0.67-1.00
HDL-C	41.10±10.66	20-79
LDL-C	121.02±37.82	52-222
Creatinine	0.91±0.24	0.56-1.75
HbA1c	6.88±1.66	5-14

SD: Standard deviation; ABI: Ankle-brachial index; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; HbA1c: Hemoglobin A1c.

A statistically significant relationship was found between the patency status observed one year after surgery and the type of medication at discharge ($p<0.05$). When the data was examined, it was observed that all patients discharged with VKAs had patent grafts ($p<0.05$). While VKA was mostly prescribed to patients who underwent RE at discharge, clopidogrel was mostly given to patients who underwent FPB surgery ($p>0.05$) (Table 5).

When the relationship between the one-year patency of FPB patients and preoperative creatinine values was examined, it was observed that the graft was mostly occluded in patients with renal dysfunction ($p<0.05$). All patients were evaluated, and no significant relationship was found between renal dysfunction and one-year patency.

Diabetes mellitus is a well-known factor that may affect the success rates of surgical procedures.[5] Statistically significant relationships were not obtained between diabetes mellitus, sex, age, surgical side,

Table 5
Associations and cross-tabulation between patency status at one-year and demographic and clinical characteristics for all patients

	Patency status						
	Occluded			Patent			
	n	%	Variety (%)	n	%	Variety (%)	*p*
Sex							0.546
Male	16	34.8	100.0	30	65.2	93.8	
Female	0	0.0	0.0	2	100.0	6.3	
Operation side							0.888
Right	7	31.8	43.8	15	68.2	46.9	
Left	9	34.6	56.3	17	65.4	53.1	
Diabetes mellitus	8	36.4	50.0	14	63.6	43.8	0.682
Hypertension	11	40.7	68.8	16	59.3	50.0	0.217
Smoking	11	33.3	68.8	22	66.7	68.8	1.000
Additional lesion							0.931
CFA	11	35.5	68.8	20	64.5	62.5	
EIA	2	40.0	12.5	3	60.0	9.4	
SFA	16	33.3	100.0	32	66.7	100.0	
PopA	15	33.3	93.8	30	66.7	93.8	
Endovascular revision	2	40.0	12.5	3	60.0	9.4	0.829
Discharge medication							0.190
VKA	6	24.0	37.5	19	76.0	59.4	
CPD	10	47.6	62.5	11	52.4	34.4	
ASA (single)	1	25.0	6.3	3	75.0	9.4	

CFA: Common femoral artery; EIA: External iliac artery; SFA: Superficial femoral artery; PopA: Popliteal artery; VKA: Vitamin K antagonist; CPD: Clopidogrel; ASA: Acetyl salicylic acid.

hypertension status, smoking, one-year patency rate, and the type of surgery (p>0.05).

DISCUSSION

The importance of peripheral artery diseases in terms of mortality and morbidity is increasing.[6] Early diagnosis, treatment, and management of this disease, particularly in light of preventive medicine principles, are of great importance.

Remote endarterectomy is a good choice in long segment lesions, where the success rate of endovascular intervention is low, in redo patients who previously underwent FPB surgery, and in patients with graft infection.

The contributions of RE to the medical literature include offering a minimally invasive approach that accelerates recovery and reduces the risk of complications.[7] This technique results in reduced pain and faster recovery compared to open surgical methods, leading to shorter hospital stays. Additionally, studies on the long-term outcomes of RE provide valuable data for clinical applications.[8] Overall, these contributions enhance the understanding of this technique for both surgeons and patients, further enriching the clinical knowledge base.

As a result of examining the one-year primary patency rates, when the GLASS stage of the patients who underwent RE and FPB surgery were evaluated, although the stage of the RE group was more advanced, the one-year primary patency rate of the patients who underwent this operation was higher, which is important for the preferability of this method in suitable patients. In the study by Martin et al.,[9] it was observed that the patency rate was 70.0% at the 30-month follow-up of patients who underwent RE. In another study, it was observed that the one-year primary patency rate was 60.0%.[10] In the study by Gabrielli et al.,[11] the patency rate was found to be 76.5% at the 24-month follow-up.

In the study by Gisbertz et al.[12] comparing RE and FPB surgery, one-year patency rates were found

to be 61.0% and 73.0% for RE and FPB, respectively. In our study, the one-year patency rate was 73.9% in patients who underwent RE.

Antoniou et al.[10] found the RE success rate to be 94.0% in their study. In another study, the success rate was found to be 79.0%.[13] Our success rate was 95.8%. Karathanos et al.[14] reported the technical success as 100.0% in a study of 12 patients who underwent RE. While the mortality rate was 8.0% (n=1) in the same study, no mortality was observed in our study.

Gabrielli et al.[11] reported that the prevalence of diabetes mellitus, hypertension, and smoking was 45.0%, 68.0%, and 71.0% in the RE group, respectively. In the same study, the rate of renal dysfunction, limited to an upper creatinine value of <1.5 mg/dL, was found to be 14.0%. In our study, eight RE and five FPB patients with creatinine values above the specified reference range had chronic kidney disease and did not receive preoperative dialysis. None of the patients required dialysis or progressed to chronic renal failure after the operation.

In the study conducted by Rahman and Özkısacık,[15] the one-year patency rates of patients with lower extremity peripheral artery disease who underwent endovascular procedures were reported to be similar to the rates in our study.

The study had some limitations. The individual risk factors of the patients, the lack of standardization of the discharge medication due to the medications they previously used and comorbid diseases, and the fact that the GLASS scores of the patients who underwent RE and FPB surgery were not similar were among the limitations. The inability to standardize between DUS and CTA due to patient-specific comorbidities and renal dysfunction in patient follow-up could also be considered a limitation.

In conclusion, remote endarterectomy method may be a good option in patient groups who have long segment lesions, in those who previously underwent FPB surgery, in patients who require repeated intragraft embolectomy revisions, in those with limited access for endovascular procedures, in patients with graft infections, and in those who cannot use prosthetic materials. Further randomized controlled studies with larger samples are needed to support our findings.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, control/supervision: B.K., B.M.; Design, writing the article, data collection and/or processing, references and fundings, other: B.K.; Analysis and/or interpretation, critical review: B.K., K.B.; Literature review, materials: B.K., S.G.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Bozkurt AK. Periferik Arter ve Ven Hastalıkları. Ulusal Tedavi Kılavuzu. İstanbul: Bayçınar Tıbbi Yayıncılık; 2021.
2. Erdinç İ. Single center experience with percutaneous peripheral atherectomy with the use of C-arm scopy for the treatment of lower extremity peripheral artery disease. Cardiovasc Surg Int 2022;9:111-20. doi: 10.5606/e-cvsi.2022.1351
3. Ketenciler S, Gemalmaz H. Effectiveness of directional atherectomy with the drug-coated balloon method for long and heavily calcified superficial femoral artery lesions. Cardiovasc Surg Int 2022;9:89-96. doi: 10.5606/e-cvsi.2022.1339
4. Özpak B, Çayır Çağdaş M. Farklı uzunluklardaki femoropopliteal stent içi restenozun ilaç salgılayan balon ile tedavisi. Turk Gogus Kalp Dama 2020;28:460-6. doi: 10.5606/tgkdc.dergisi.2020.18980
5. Saydam O, Şerefli D, Atay M, Yaprak Engin A. Endovascular treatment versus femoropopliteal bypass surgery for TASC II type C lesions of the superficial femoral artery. Turk J Vasc Surg 2022;31:25-32.
6. Saaya S, Osipova O, Gostev A, Rabtsun A, Starodubtsev V, Cheban A, et al. A prospective randomized trial on endovascular recanalization with stenting versus remote endarterectomy for the superficial femoral artery total occlusive lesions. J Vasc Surg 2022;76:158-64. doi: 10.1016/j.jvs.2022.02.019.
7. Oborin A, Muchamadeev I, Danilov V. Long-term outcome of remote endarterectomy and femoropopliteal bypass in TASC C and D lesions. J Vasc Surg 2022;75:e114.
8. Coppi G, Stringari C, Mottini F, Zaraca F, Perkmann R. Selective use of remote endarterectomy in the present vascular practice. Eur J Vasc Endovasc Surg 2019;58:e782.
9. Martin JD, Hupp JA, Peeler MO, Warble PB. Remote endarterectomy: Lessons learned after more than 100 cases. J Vasc Surg 2006;43:320-6. doi: 10.1016/j.jvs.2005.10.017.
10. Antoniou GA, Koutsias S, Antoniou SA, Giannoukas AD. Remote endarterectomy for long segment superficial femoral artery occlusive disease. A systematic review. Eur J Vasc Endovasc Surg 2008;36:310-8. doi: 10.1016/j.ejvs.2008.04.005.

11. Gabrielli R, Rosati MS, Vitale S, Baciarello G, Siani A, Chiappa R, et al. Randomized controlled trial of remote endarterectomy versus endovascular intervention for TransAtlantic Inter-Society Consensus II D femoropopliteal lesions. J Vasc Surg 2012;56:1598-605. doi: 10.1016/j.jvs.2012.06.081.
12. Gisbertz SS, Ramzan M, Tutein Nolthenius RP, van der Laan L, Overtoom TT, Moll FL, et al. Short-term results of a randomized trial comparing remote endarterectomy and supragenicular bypass surgery for long occlusions of the superficial femoral artery [the REVAS trial]. Eur J Vasc Endovasc Surg 2009;37:68-76. doi: 10.1016/j.ejvs.2008.09.014.
13. Devalia K, Magee TR, Galland RB. Remote superficial femoral endarterectomy: Long-term results. Eur J Vasc Endovasc Surg 2006;31:262-5. doi: 10.1016/j.ejvs.2005.10.019.
14. Karathanos C, Spanos K, Saleptsis V, Antoniou GA, Koutsias S, Giannoukas AD. Single-center experience with remote endarterectomy for the treatment of long-segment superficial femoral artery occlusion: Long-term results. Vasc Endovascular Surg 2015;49:250-5. doi: 10.1177/1538574415617555.
15. Rahman ÖF, Özkısacık EA. Patency and survival in patients undergoing revascularization for peripheral arterial disease. VHS 2024;14:215-23.

Additional Table 1

	Operation type							
	RE			FPB				
	n	%	Group (%)	n	%	Group (%)	Test statistics	*p*
Sex							**	1.000
Male	23	50.0	95.8	23	50.0	95.8		
Female	1	50.0	4.2	1	50.0	4.2		
Operation side							0.336	0.562
Right	12	54.5	50.0	10	45.5	41.7		
Left	12	46.2	50.0	14	53.8	58.3		
Diabetes mellitus	13	59.1	54.2	9	40.9	37.5	1.343	0.247
Hypertension	11	40.7	45.8	16	59.3	66.7	2.116	0.146
Smoking	17	51.5	70.8	16	48.5	66.7	0.097	0.755
Additional lesion							11.759***	**0.038***
CFA	19	61.3	79.2	12	38.7	50.0		
EIA	4	80.0	16.7	1	20.0	4.2		
SFA	24	50.0	100.0	24	50.0	100.0		
PopA	21	46.7	87.5	24	53.3	100.0		
One-year patency	17	53.1	70.8	15	46.9	62.5	0.375	0.540
Follow up evaluation							4.148	**0.042***
DUS	10	37.0	41.7	17	63.0	70.8		
CTA	14	66.7	58.3	7	33.3	29.2		

RE: Remote endarterectomy; FPB: Femoral-popliteal bypass; CFA: Common femoral artery; EIA: External iliac artery; SFA: Superficial femoral artery; PopA: Popliteal artery; DUS: Duplex Ultrasonography; CTA: Computed tomography angiography; * p<0.05; ** Fisher exact test; *** Multiple chi-square test.

Additional Table 2

	One-year patency	Mean±SD	Test statistics	*p*
Preoperative ABI	Occluded	0.45±0.08	–1.530	0.140
	Patent	0.51±0.10		
Postoperative ABI	Occluded	0.83±0.09	–1.263*	0.220
	Patent	0.88±0.07		

SD: Standard deviation; ABI: Ankle-brachial index; p<0.05; * Mann Whitney U test.

Cardiovasc Surg Int 2024;11(3):210-212
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1738
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Case Report Open Access

The fate of mitral homograft valve prosthesis implanted in tricuspid position

Mahsati Akhundova[1], Osman Nuri Tuncer[2], Serkan Ertugay[2], Yüksel Atay[2], Anıl Ziya Apaydın[2]

[1]Department of Cardiovascular Surgery, İzmir Tınaztepe University Private Buca Hospital, İzmir, Türkiye
[2]Department of Cardiovascular Surgery, Ege University Faculty of Medicine, İzmir, Türkiye

Received: September 17, 2024 ***Accepted:*** October 02, 2024 ***Published online:*** October 17, 2024

ABSTRACT

Tricuspid valve surgery is performed less frequently than other heart valve surgeries, and displacement constitutes a very limited portion of these surgeries. Valve selection during the replacement remains controversial. Although bioprosthetic valves are currently the most preferred prostheses, mitral homografts, which are biological materials with proven long-term durability, have also been used for this surgery. Herein, a 35-year-old male patient who underwent tricuspid valve replacement using a mitral homograft with a durability of 18 years was presented. This case highlights the first mitral homograft produced using the country's own resources and implanted in the tricuspid position.

Keywords: Cardiac valve prothesis, homografts, tricuspid valve.

Surgery for the tricuspid valve (TV) is performed less commonly than for other heart valves. When an operation is required, annuloplasty is usually sufficient in most cases. Therefore, replacements are infrequent.

The selection of valve prosthesis for the TV position remains controversial. The need for lifelong anticoagulant therapy and the difficulty of permanent pacemaker implantation are the limitations of mechanical valves. The risk of degeneration is the only concern associated with the use of bioprosthetic prostheses. Therefore the bioprosthetic valves are the most common preferred prostheses for TV replacement (TVR).[1] Homograft is another alternative biological solution owing to its long-term durability; however, its availability is a major limitation.

Herein, we presented a patient who underwent TVR with a mitral homograft. Additionally, this case is worth presenting, as it marks the first mitral homograft successfully implanted in the TV position produced from the country's own resources.

CASE REPORT

A 35-year-old male with symptoms of right-sided heart failure was referred to our clinic. Echocardiography revealed severe tricuspid regurgitation secondary to rheumatic degeneration. The decision to implant a homograft was made because the patient was too young for life-long anticoagulant therapy. Homograft cryopreservation and storage were performed at our institutional homograft bank. It was 33 mm in diameter (measured by a bioprosthetic mitral valve sizer). Tricuspid valve replacement with a mitral homograft was performed using the Doty technique.[2] Additionally, a 33-mm tricuspid ring (Carpentier-Edwards Inc., Irvine, CA, USA) was implanted for annular stabilization. Intraoperative transesophageal echocardiography showed good function of homograft leaflets without any regurgitation. The postoperative course was uneventful.

Corresponding author: Osman Nuri Tuncer, MD. İzmir Tınaztepe Üniversitesi Özel Buca Hastanesi, Kalp ve Damar Cerrahisi Kliniği, 35400 Buca, İzmir, Türkiye.
E-mail: osnutuncer@gmail.com

Citation:
Akhundova M, Tuncer ON, Ertugay S, Atay Y, Apaydın AZ. The fate of mitral homograft valve prosthesis implanted in tricuspid position. Cardiovasc Surg Int 2024;11(3):210-212. doi: 10.5606/e-cvsi.2024.1738.

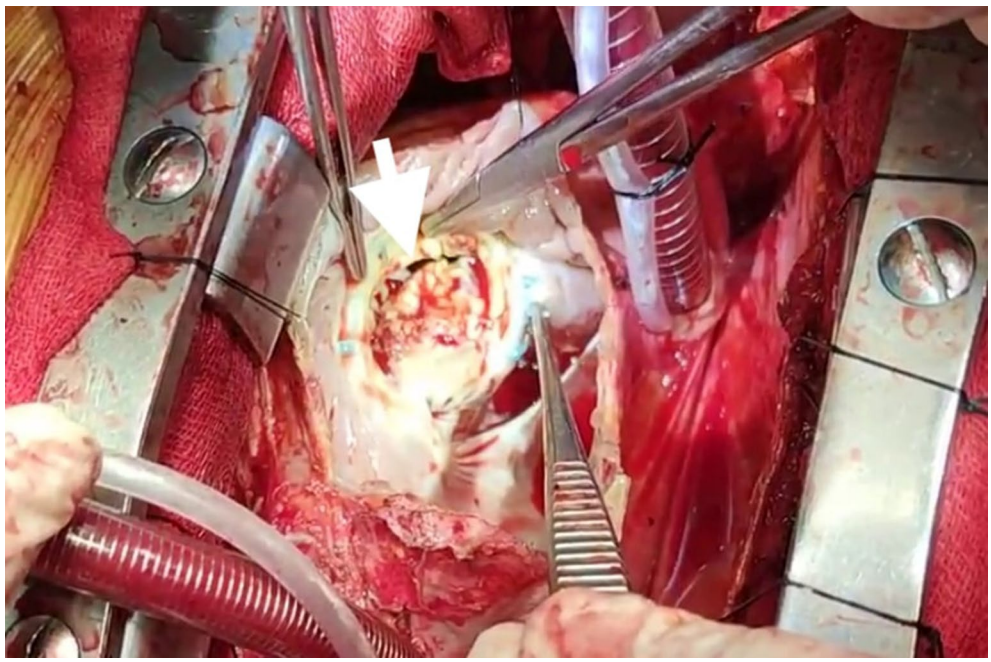


Figure 1. The picture shows a mitral homograft implanted 18 years ago. Heavy calcification is evident, and the white arrow indicates detachment from the ring that was implanted for stabilization.

The same patient was readmitted at 54 years of age with similar symptoms prior to the index operation. Transthoracic echocardiography revealed a heavily calcified homograft in tricuspid position. Severe tricuspid stenosis was detected (maximum transvalvular gradient: 20 mmHg), and the leaflets were immobile. The tricuspid ring was partially detached from the annulus.

Right atriotomy was performed after aorto-bicaval cannulation. The leaflets of the mitral homograft were heavily calcified. The homograft was dislocated anteriorly from the surrounding ring (Figure 1). The ring was explanted, and the remaining calcifications, which extended to the papillary muscles, were removed after removal of the homograft tissue. A 29-mm bioprosthetic valve (Pericarbon; Sorin Biomedica Cardio, Spa Saluggia, Italy) was implanted using 2-0 pledgetted sutures. Postoperative transesophageal echocardiography showed a maximum gradient of 3 mmHg and no regurgitation. The patient was discharged on the seventh postoperative day after an uneventful postoperative period. The patient remained in sinus rhythm. A written informed consent was obtained from the patient.

DISCUSSION

Mitral homograft implantation in the tricuspid position was first performed by Pomar et al.[3] They reported satisfactory results of TVR in three patients with right-sided endocarditis. In the following years, similar reports showed that a mitral homograft can be an alternative biological solution for TVR in cases of infective endocarditis or degenerated prothesis.[4]

Mitral homograft implantation in the tricuspid position is preferred, particularly in pediatric patients, due to its growth potential, low thrombogenicity, and resistance to infection. Nozar et al.[5] reported satisfactory results, although the surgery was challenging in two pediatric cases. To date, no significant difference in survival and thrombosis between mitral homografts and other bioprosthetic valves has been observed.

A recent study analyzing outcomes in patients under 20 years of age showed better durability, particularly after 10 years.[6] In our case, the mitral homograft showed a durability of 18 years.

Correct positioning of the leaflets and subvalvular aparatus of the homograft and avoidance of damage to the conduction system are

crucial. Beyond the difficulty of surgical techniques, the most important issue is the limited availability of homograft valves of the desired size and time. Homografts are cost-effective and feasible when the institute has its own bank. The first homograft application in Türkiye was performed at our institution. After the establishment of the country's first tissue bank in 1994, 371 homografts were cryopreserved for 24 years, and only eight of these were mitral homografts.[7] Three mitral homografts were sent to different centers in Türkiye after the presented case.

In conclusion, homografts have not gained widespread use due to procurement issues. Homografts appear to have high biological and clinical benefits owing to their lower thrombogenicity and higher resistance to infection than mechanical or biological prostheses. There are no solid recommendations for their use due to the lack of studies including larger number of patients and long-term follow-up. This case report offers insight into their long-term outcomes.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, analysis and/or interpretation, literature review: M.A., O.N.T.; Design, writing the article: O.N.T., A.Z.A.; Control/supervision, critical review: A.Z.A., Y.A.; Data collection and/or processing: S.E., M.A.; References and fundings: S.E.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Cheng Z, Fang T, Wang D, Guo Y. Tricuspid valve replacement: Mechanical or biological prostheses? A systematic review and meta-analysis. Heart Surg Forum 2021;24:E209-14. doi: 10.1532/hsf.3531.
2. Doty JR, Doty DB. Tricuspid valve replacement. Oper Tech Thorac Cardiovasc Surg 2003;8:193-200.
3. Pomar JL, Mestres CA, Pare JC, Miro JM. Management of persistent tricuspid endocarditis with transplantation of cryopreserved mitral homografts. J Thorac Cardiovasc Surg 1994;107:1460-3.
4. Mestres CA, Miro JM, Pare JC, Pomar JL. Six-year experience with cryopreserved mitral homografts in the treatment of tricuspid valve endocarditis in HIV-infected drug addicts. J Heart Valve Dis 1999;8:575-7.
5. Nozar JV, Anzibar R, Picarelli D, Tambasco J, Leone RW. Mitral homograft replacement of tricuspid valve in children. J Thorac Cardiovasc Surg 2000;120:822-3. doi: 10.1067/mtc.2000.108694.
6. Marathe SP, Bell D, Betts K, Sayed S, Dunne B, Ward C, et al. Homografts versus stentless bioprosthetic valves in the pulmonary position: A multicentre propensity-matched comparison in patients younger than 20 years. Eur J Cardiothorac Surg 2019. doi: 10.1093/ejcts/ezz021.
7. Özbaran M, İsa D, Yüksel M, Hamulu A, Atay Y, Badak İ, ve ark. Aortik homograft kapak replasmam: Klinik sonuçlar. GKD Cer Derg 1994;2:242-247.

Cardiovasc Surg Int 2024;11(3):213-216
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1717
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Case Report Open Access

An interesting case of refractory hypotension and noncardiogenic pulmonary edema after amlodipine overdose

İhsan Alur[1], Gökhan Peker[2], Taner Taşyüz[2], Ahmet Deniz Kaya[3], Osman Kaya[4]

[1]Department of Cardiovascular Surgery, Private Egekent Hospital, Denizli, Türkiye
[2]Department of Anesthesiology and Reanimation, Private Egekent Hospital, Denizli, Türkiye
[3]Department of Cardiovascular Surgery, Ministry of Health, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Türkiye
[4]Department of Anesthesiology and Reanimation, Ministry of Health, Nizip State Hospital, Gaziantep, Türkiye

Received: August 08, 2024 ***Accepted:*** September 16, 2024 ***Published online:*** October 17, 2024

ABSTRACT

Amlodipine is a dihydropyridine calcium channel blocker that acts on intravascular L-type calcium channels. It is most effective on vascular smooth muscle cells and has little effect on cardiac tissue. Its most common use is hypertension, angina, arrhythmias, subarachnoid hemorrhage, migraine, and Raynaud's disease. Amlodipine is preferred because it is used once a day and has minimal side effects on heart rate. However, in case of acute overdose, either accidental or deliberate (e.g., suicide attempts), dangerous side effects may occur and may result in death. Herein, we presented a 34-year-old male patient who ingested 90 tablets of amlodipine 10 mg and was successfully treated.

Keywords: Amlodipine, hemodialysis, hemofiltration, intoxication, overdoze, ultrafiltration.

Amlodipine is a dihydropyridine calcium channel blocker (CCB) that works on intravascular L-type calcium channels. It is most effective on vascular smooth muscle cells and has little impact on cardiac tissue.[1] It is most commonly used to treat hypertension and angina.[2] Amlodipine, unlike other CCBs, has low metabolic clearance and can be administered once daily to maintain an almost constant plasma concentration.[2] However, it has a lengthy half-life of 30 to 60 h and has a protracted impact in acute overdose. It can induce high plasma concentrations that can last for days.[3] Hypotension, acidosis, decreased tissue perfusion, respiratory arrest due to noncardiogenic pulmonary edema, and mortality may ensue in the event of intoxication due to vascular smooth muscle relaxation.[1,2,4] The most frequent therapeutic options for amlodipine acute overdose include gastrointestinal decontamination, fluid resuscitation, intravenous calcium, vasopressor medications, atropine, high-dose insulin euglycemic therapy, and pacemaker implantation.[1-4] Herein, we presented a patient who ingested 90 tablets of amlodipine 10 mg and was effectively treated.

CASE REPORT

A 34-year-old male patient stated taking 90 tablets of amlodipine 10 mg (900 mg in total) over 40 min in an attempt to commit suicide. After ingesting the tablets, he left his house and traveled approximately 2,000 m before passing out. During this time, he noted experiencing dizziness and his pulse slowing down before passing out. The patient was later discovered in a forest on the side of the road and taken to the emergency department. He was monitored at the hospital, and when the patient developed hypotension and anuria 48 h after taking the medications, he was transferred to our hospital due to the absence of a dialysis unit. The patient arrived with signs of pulmonary edema. He appeared

Corresponding author: İhsan Alur, MD. Özel Egekent Hastanesi, Kalp ve Damar Cerrahisi Kliniği, 20125 Merkezefendi, Denizli, Türkiye.
E-mail: alur_i@hotmail.com

Citation:
Alur İ, Peker G, Taşyüz T, Kaya AD, Kaya O. An interesting case of refractory hypotension and noncardiogenic pulmonary edema after amlodipine overdose. Cardiovasc Surg Int 2024;11(3):213-216. doi: 10.5606/e-cvsi.2024.1717.

anxious, restless, agitated, and dyspneic. It was noted that the patient had no history of significant chronic disease or psychiatric disorder and that this was his first suicide attempt. The arterial blood pressure was 80/50 mmHg, and the heart rate was 79 beats per minute. The electrocardiogram revealed sinus rhythm. Bedside transthoracic echocardiography showed a left ventricular systolic function of 60%, with no additional pathological findings. The results of the arterial blood gas examination were as follows: partial pressure of oxygen, 39.4 mmHg; partial pressure of carbon dioxide, 38.1 mmHg; oxygen saturation, 70%; hemoglobin, 11.1 g/dL; hematocrit, 33%; lactate, 7.87 mmol/L; base excess, –13.8 mmol/L. Biochemical analysis revealed a urea of 78 mg/dL, creatinine of 2.44 mg/dL, and blood glucose of 97 mg/dL. A written informed consent was obtained from the patient. The patient was intubated. Due to the hypotensive course, a norepinephrine infusion at 0.4 mcg/kg/min was initiated. Dopamine and dobutamine infusions at 0.5 mcg/kg/min were initiated due to persistent hypotension. The time required for gastrointestinal absorption had passed by the time the patient arrived at the hospital, which was 48 h after ingestion. Therefore, gastric lavage was not performed. Computed tomography of the thorax revealed bilateral lung infiltrates, a ground-glass appearance, and acute respiratory distress syndrome (ARDS) (Figure 1a). Due to low arterial blood pressure, hourly urine output was insufficient; hence, continuous venovenous hemodiafiltration was performed at the bedside. Over six days, a total of 25 L of fluid were taken from the patient. The patient's refractory hypotension persisted for seven days. Later on, respiratory parameters, along with arterial blood pressure and arterial blood gas levels, began to improve. Vasopressors were withdrawn on the eighth day of hospitalization, starting with norepinephrine, followed by dopamine. While oxygen saturation and arterial blood pressure did not change significantly as norepinephrine and dopamine doses were gradually reduced, hemodynamics rapidly deteriorated and oxygen saturation declined when dobutamine dosage was reduced. As a result, dobutamine could only be discontinued on the 12th day due to the patient's hypersensitivity. Furthermore, hourly urine output increased, and venovenous hemodiafiltration was discontinued. After regulated monitoring with continuous positive airway pressure, the patient was extubated on the 10th day of intubation. The ARDS abnormalities were reported to have regressed in the control thorax computed tomography (Figure 1b). On the 13th day of hospitalization, the patient was transferred from the intensive care unit to the general ward. Vital signs were monitored. Arterial blood gas, complete blood count, and biochemistry levels all returned to normal. On the 19th day of his stay, the patient was discharged.

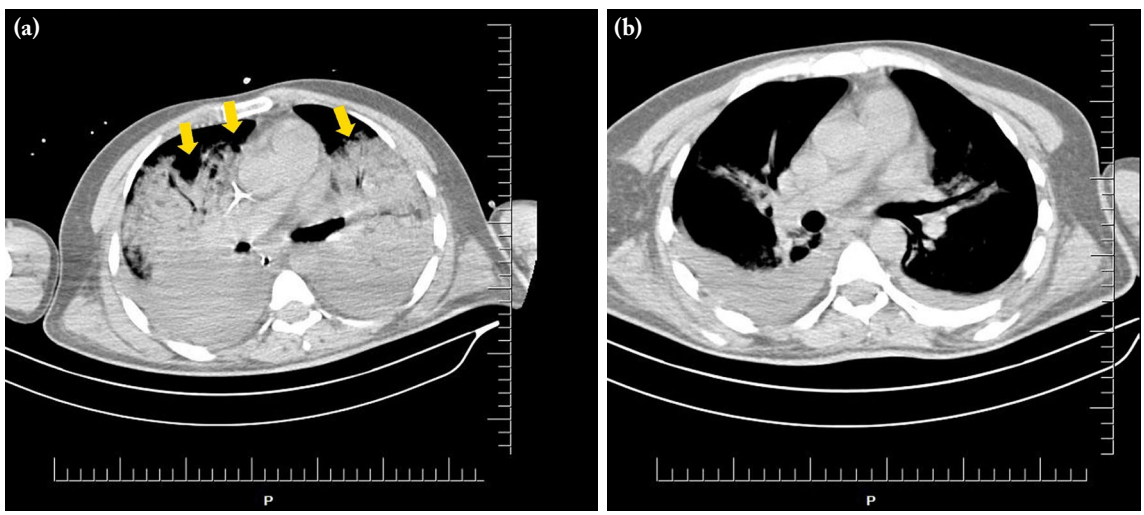


Figure 1. **(a)** Bilateral lung infiltration, ground glass appearance, and ARDS on thorax computed tomography (yellow arrows). **(b)** Control thorax computed tomography shows regression of ARDS findings.
ARDS: Acute respiratory distress syndrome; CT: Computed tomographic.

DISCUSSION

The patient arrived at our hospital 48 h after ingesting the tablets, was extubated after 10 days of intubation, recovered hemodynamically without the need for extracorporeal membrane oxygenation (ECMO), and was discharged, distinguishing this case from similar reports in the literature.

Calcium channels are present in numerous cells throughout the body, including cardiac myocytes, smooth muscle cells, and pancreatic β-cells. Calcium channel blockers inhibit calcium mobilization through each of these channels.[1] The effects of this vascular smooth muscle blockade comprise a drop in blood pressure, dilation of the coronary vascular system, and a decrease in afterload. Impaired inotropy emerges from calcium channel blockade in the cardiac muscles, and heart rate decreases owing to channel blockade in the sinoatrial and atrioventricular nodes.[1] Under normal physiological circumstances, amlodipine is selective for peripheral calcium channels. However, this selectivity is lost in acute overdose, leading to negative cardiac effects such as hypotension and bradycardia.[1] Inotropic support with isoproterenol is beneficial in the treatment of amlodipine-associated bradycardia.[5] Calcium administration and hemodynamic support with vasopressors and inotropes are standard treatments for amlodipine intoxication. Calcium is delivered at supratherapeutic levels as boluses or continuous infusions to overcome calcium channel antagonism.[1] Our patient did not have bradycardia, so isoproterenol was not started; however, intravenous bolus calcium replacement was initiated for its vasopressor effect.

Due to peripheral vasodilation in patients with amlodipine overdose, maintaining intravascular volume balance is critical. Excessive fluid administration to an anuric patient may lead to pulmonary edema. Vasopressor support must be initiated concurrently with volume support.[1-3] In our case, the hypotension proved resistant to inotropic medications. With a maximum blood pressure of 80/50 mmHg, the patient was observed for seven days with high-dose inotropic support and intravenous volume replacement. Due to anuria, continuous venovenous hemodiafiltration was also used at the bedside. As a result, we tried to maintain the arterial blood pressure and avoid hypervolemia to prevent the recurrence of pulmonary edema. Subcutaneous insulin was used to control the patient's blood glucose levels. Patel et al.[6] emphasized that glucagon has an inotropic effect by activating the cardiovascular adenylate cycle and that glucagon therapy and hyperinsulinemia/euglycemia therapy may enhance the direct cardiotropic effect of insulin and improve cardiovascular carbohydrate oxidation, which is often impaired in these patients. Another treatment modality for lipid-soluble drug overdose is intravenous lipid infusions.[6] Since our patients was not hypoglycemic, we did not administer glucagon.

An overdose of CCBs can be fatal, leading to noncardiogenic pulmonary edema and shock. Conventional therapy is insufficient for a severe CCBs overdose. The primary course of therapy for CCB overdose is supportive care, which includes fluid resuscitation. Since the mechanism underlying noncardiogenic pulmonary edema is unclear, mechanical ventilation is typically employed. In patients with severe poisoning, circulatory shock may not react to atropine, glucagon, or calcium, necessitating the use of vasopressors. For CCB poisoning, hyperinsulinemia/euglycemia therapy is preferable over other treatments because it actively transports glucose via insulin, counteracting the intracellular carbohydrate deficiency caused by CCBs. Although there is little use of intravenous lipid emulsion in treating lipophilic drug overdose, intravascular sequestration may enhance cardiac inotropy.[4] If oxygenation values do not improve despite intubation due to ARDS, ECMO support might be initiated. Extracorporeal membrane oxygenation has been shown to be effective until the lung parenchyma tissue recovers functionally.[4] In the study by Yusuke et al.,[7] a 46-year-old male patient intoxicated with 1,210 mg of amlodipine and 936 mg of candesartan was treated with vasopressors, calcium gluconate, and hyperinsulinemia/euglycemia therapy as an intubation and therapeutic protocol. However, the patient's hemodynamic condition deteriorated, and venoarterial ECMO support was initiated on the fifth day. The patient died on the 18th day. Initiating ECMO support earlier may have resulted in a better outcome. Although success was achieved in our case, it can be argued that ECMO support should be rapidly considered for poisoning with 1,000 mg or more.[7] In our case, ECMO support was not required because placing the patient in prone position improved oxygen saturation to roughly 80 to 90%, and respiratory parameters were adequate following intubation. One notable aspect of this case was the

patient's relative sensitivity to dobutamine compared to other vasopressor medications. Although there were no changes in oxygen saturation and arterial blood pressure during the progressive reduction of norepinephrine and dopamine doses, a rapid deterioration in hemodynamics was observed when the dobutamine dose was reduced. Additionally, arterial blood pressure began to decrease, and oxygen saturation dropped below 70%. Consequently, due to the patient's hypersensitivity to dobutamine, it could only be terminated on the 12th day.

In conclusion, the occurrence of refractory hypotension, leading to anuria and subsequent acute renal failure, is a significant issue in cases of amlodipine intoxication. In these patients, it is imperative to initiate vasopressor treatment in conjunction with volume support to rectify the blood pressure. Simultaneously, pulmonary edema may develop in these cases. In the event of the development of pulmonary edema, it is recommended to administer continuous venovenous hemodiafiltration, conventional hemodialysis, or ultrafiltration at the bedside while also ensuring careful monitoring of volume balance.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, writing, control/supervision: İ.A.; Design, data collection and/or processing: G.P.; Literature review: T.T.; Design/analysis and/or interpretation: A.D.K.; Data collection/design: O.K.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Chudow M, Ferguson K. A case of severe, refractory hypotension after amlodipine overdose. Cardiovasc Toxicol 2018;18:192-7. doi: 10.1007/s12012-017-9419-x.
2. Osman AF, Prasad RM, Marein S, O'Brien C. Multi-organ dysfunction as a presentation of calcium channel blocker intoxication. BMJ Case Rep 2022;15:e245711. doi: 10.1136/bcr-2021-245711.
3. Jang DH, Nelson LS, Hoffman RS. Methylene blue in the treatment of refractory shock from an amlodipine overdose. Ann Emerg Med 2011;58:565-7. doi: 10.1016/j.annemergmed.2011.02.025.
4. Siddiqi TA, Hill J, Huckleberry Y, Parthasarathy S. Non-cardiogenic pulmonary edema and life-threatening shock due to calcium channel blocker overdose: A case report and clinical review. Respir Care 2014;59:e15-21. doi: 10.4187/respcare.02244.
5. Ebihara T, Morita M, Kawada M, Amano K, Kato F, Nakata Y. Efficacy of isoproterenol for treating amlodipine overdose resulting in bradycardia. Acute Med Surg 2017;4:353-7. doi: 10.1002/ams2.284.
6. Patel T, Tietze D, Mehta AN. Amlodipine overdose. Proc (Bayl Univ Med Cent) 2013;26:410-1. doi: 10.1080/08998280.2013.11929022.
7. Yusuke M, Hidetoshi Y, Yusuke T, Koji I, Masahito T, Susumu Y, et al. Intoxication with massive doses of amlodipine and candesartan requiring venoarterial extracorporeal membrane oxygenation. Acute Med Surg 2023;10:e878. doi: 10.1002/ams2.878.

Cardiovasc Surg Int 2024;11(3):217-220
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1730
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Case Report Open Access

Could hybrid treatments be an option for abdominal aortic pseudoaneurysms?

Erturk Karaagac, Hasan Iner, Hidayet Onur Selcuk, Muhammed Cagri Yalcin, Levent Yilik

Department of Cardiovascular Surgery, İzmir Katip Çelebi University Faculty of Medicine, İzmir, Türkiye.

Received: September 09, 2024 ***Accepted:*** September 19, 2024 ***Published online:*** October 17, 2024

ABSTRACT

Traumatic pseudoaneurysm of the abdominal aorta is a life-threatening and rare pathology that often occurs after blunt trauma or penetrating injuries. In suprarenal pseudoaneurysms, surgery is complicated by the classic approach, as access to the abdominal aorta is difficult due to the complex anatomy, with a high risk of bleeding. Therefore, hybrid solutions should always be considered in areas with a high risk of spontaneous rupture. In this case report, we presented a successful hybrid surgical option with endovascular aortic stent grafting and visceral debranching in a 20-year-old male patient with an abdominal aortic pseudoaneurysm.

Keywords: Aortic pseudoaneurysm, debranching, endovascular, hybrid treatment, traumatic injury.

Traumatic pseudoaneurysm of the abdominal aorta is a life-threatening and rare pathology that often occurs after trauma.[1] After trauma, the clinical presentation may be asymptomatic, or symptoms may occur due to compression. However, the most feared situation is spontaneous rupture leading to death. Therefore, it should be treated quickly and with the most appropriate approach.

The part of the abdominal aorta where the pseudoaneurysm is located is extremely important for the surgical approach. In suprarenal pseudoaneurysms, the classic approach makes operation more difficult, as access to the abdominal aorta is difficult due to the complex anatomy, with a high risk of bleeding. Therefore, hybrid solutions should always be considered for suprarenal abdominal aortic pseudoaneurysms, where the risk of spontaneous rupture is high.[2]

In this case report, we presented a successful hybrid operation in a patient who was diagnosed with a traumatic abdominal aortic pseudoaneurysm after complaining of abdominal pain on the postoperative Day 14.

CASE REPORT

A 20-year-old male patient underwent urgent surgery by a general surgeon for hemodynamic instability following a gunshot wound to the abdomen. After laparotomy, the retroperitoneum was examined, and although there was a small amount of retroperitoneal bleeding, the vascular structures were found to be intact. The patient, who had been complaining of abdominal pain since postoperative Day 14, underwent computed tomography angiography (CTA). The CTA showed a 77×51×64 mm pseudoaneurysm originating from the abdominal aorta at the level of the celiac trunk (CT) and located in the left lateral retroperitoneum (Figure 1a, b). A written informed consent was obtained from the patient for pseudoaneurysm repair, and the patient was taken for reoperation. Under general anesthesia, the visceral arteries and the right common iliac artery were explored and released. A bypass to relieve the abdominal aorta was created from the right common iliac artery to the CT with an 8-mm Dacron graft. A bypass was then created from the CT graft to the superior mesenteric artery using an 8 mm Dacron graft. After the

Corresponding author: Erturk Karaagac, MD. İzmir Katip Çelebi Üniversitesi Tıp Fakültesi Kalp ve Damar Cerrahisi Anabilim Dalı, 35150 Karabağlar, İzmir, Türkiye.
E-mail: erturkkaraagac@gmail.com

Citation:
Karaagac E, Iner H, Selcuk HO, Yalcin MC, Yilik L. Could hybrid treatments be an option for abdominal aortic pseudoaneurysms? Cardiovasc Surg Int 2024;11(3):217-220. doi: 10.5606/e-cvsi.2024.1730

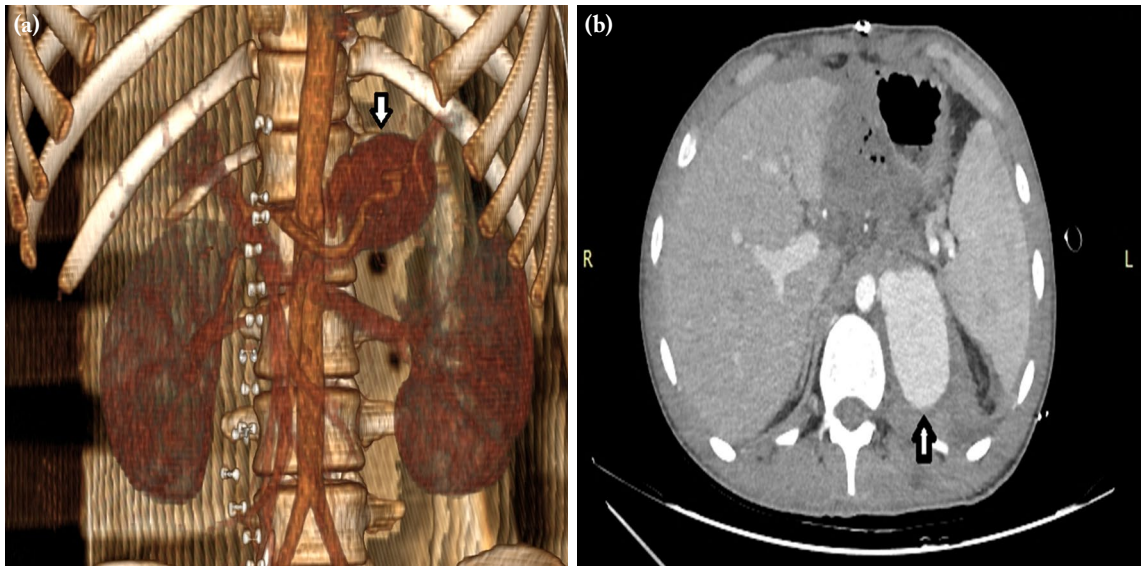


Figure 1. (a, b) Preoperative CTA images of traumatic abdominal aortic pseudoaneurysm at the level of CT. The tip of the white arrow shows aortic pseudoaneurysm.
CTA: Computed tomography angiography; CT: Computed tomography.

visceral debranching procedure, the CT and superior mesenteric artery were ligated. A 20×20×82 mm endovascular aortic stent graft was then placed in the suprarenal region to contain the pseudoaneurysm sac. A control angiography was performed (Figure 2). After hemostasis, the operation was completed. The patient was transferred to the ward two days later. The patient's control CTA (Figure 3a, b) revealed that the pseudoaneurysm sac was thrombosed, and the debranching grafts were patent. The patient was discharged on postoperative Day 10. The patient's follow-up treatment has been continued routinely.

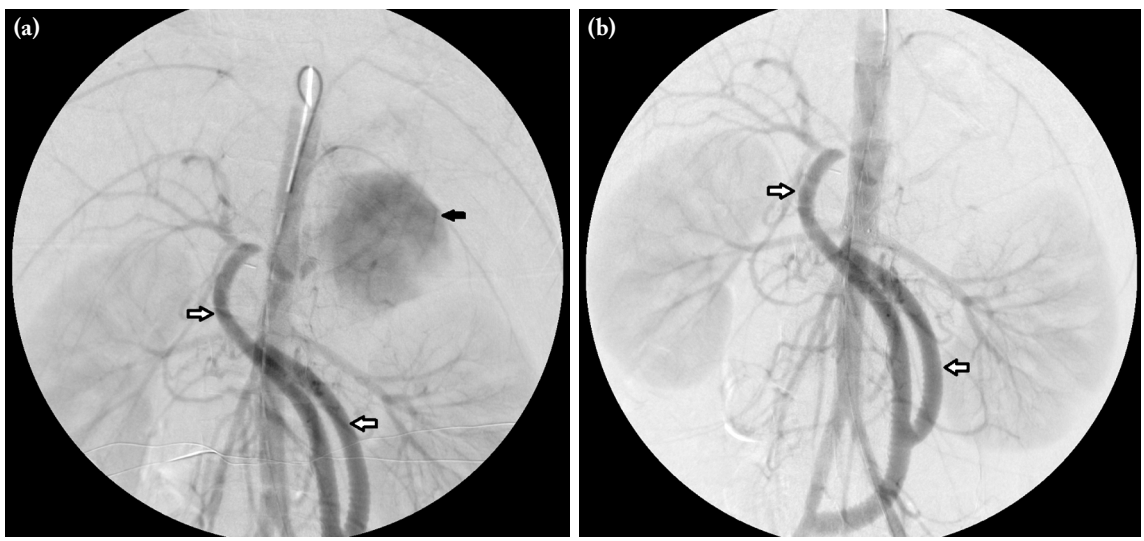


Figure 2. Intraoperative angiographic images of the hybrid procedure. **(a)** Angiographic image of the aortic pseudoaneurysm after visceral debranching. **(b)** Angiographic image of the successful hybrid procedure. The tip of the white arrow shows patent debranching grafts, while the tip of the black arrow shows pseudoaneurysm sac.

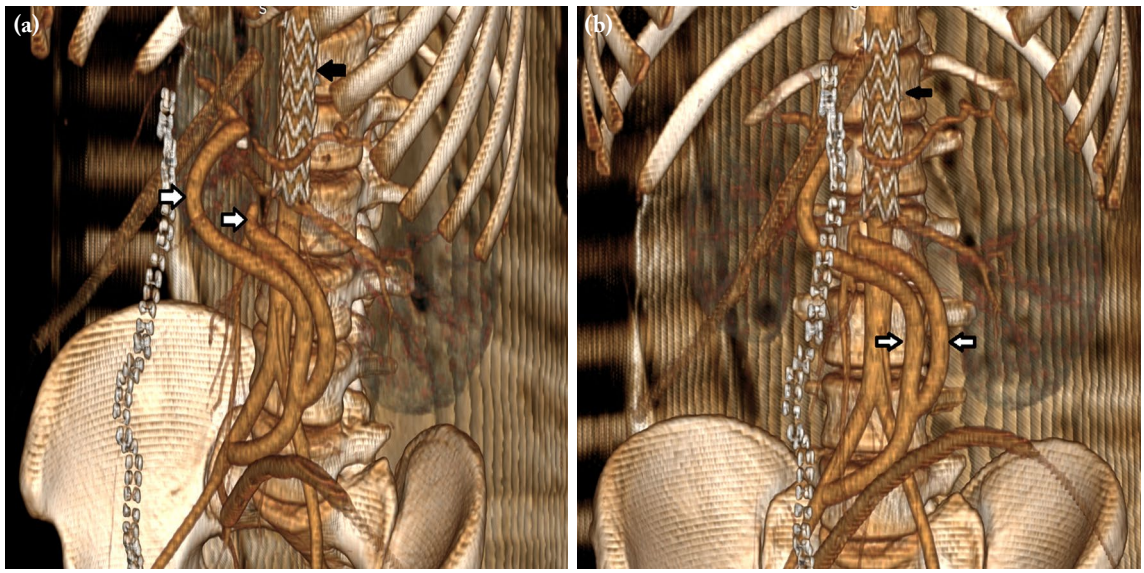


Figure 3. (a, b) Postoperative CTA images of the hybrid procedure. The tip of the white arrow shows patent debranching grafts, while the tip of the black arrow shows endovascular aortic stent graft with no endoleak.
CTA: Computed tomography angiography.

DISCUSSION

Penetrating abdominal aortic injuries still have a high mortality rate despite the rapid intervention of the trauma team. This type of injury may be associated with rupture and massive hemorrhage leading to death, and it is also known to be limited to the development of a pseudoaneurysm due to the retroperitoneal location of the abdominal aorta. Although aortic injury is not clearly recognizable on initial exploration, the presence of retroperitoneal hemorrhage at the time of exploration should raise suspicion. In such cases, it is possible to detect severe and potential pathologies, such as pseudoaneurysm, with CTA during follow-up.[3]

In a pseudoaneurysm that develops due to penetrating abdominal aortic injury, a variety of clinical findings, such as abdominal pain, pulsatile hematoma in the abdomen, bile duct obstruction, and ileus, can be observed.[4] These clinical findings are exacerbated depending on the size of the pseudoaneurysm sac. The time interval between the initial trauma and the onset of clinical symptoms can vary from a few days to years. Although it is difficult to make a diagnosis in the late phase, particularly if there is a suspicion in the early phase, patients should be examined with modern imaging techniques without wasting time. In the initial examination, CTA is preferred due to its high sensitivity in making a diagnosis. Computed tomography angiography not only provides information on the location and size of the lesion but also serves as a guide for surgical planning.

Graft interposition can be performed during open surgical repair of a pseudoaneurysm.[5] In suitable patients, repair with endovascular stent grafts or coil embolization should always be considered. However, hybrid procedures with endovascular aortic stent grafting and debranching may be a solution in cases where open surgery presents high risk due to the location of the pseudoaneurysm and where endovascular treatment alone is not suitable due to the visceral arterial structures.

Open surgical repair of pseudoaneurysms adjacent to visceral arterial structures is associated with a high mortality rate due to the difficulty in controlling the aorta and the risk of massive bleeding. Therefore, the use of various treatment procedures in high-risk cases has come to the fore with the developments in endovascular surgery. In a case series published by Scali et al.,[6] it was found that fenestrated endovascular treatment can also be used in pseudoaneurysm repair. Although pseudoaneurysm treatment is possible with this method, the technical difficulties, the risk of branched stent thrombosis, and the endoleak risk

should not be disregarded. Hybrid treatments offer us an alternative to minimize these risks.[2] In the hybrid treatment, which we preferred in this case, visceral debranching is first performed on the common iliac arteries, which represent a safe area. Afterward, the bypassed arteries are ligated from the aorta, and the hybrid procedure is rapidly completed by inserting the endovascular aortic stent graft. In this way, pseudoaneurysm repair is performed with less risk than open surgical repair, and patency of the visceral arterial structures is guaranteed.

In conclusion, pseudoaneurysms that develop due to penetrating abdominal aortic injury are a life-threatening pathology that can lead to death even before symptoms appear. In case of doubt, the diagnosis should be made using modern imaging techniques, and the optimal treatment protocol tailored to the patient should be determined. It should be kept in mind that hybrid treatment with endovascular aortic stenting and debranching may be the solution in high-risk cases.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conception or design of the experiment(s), or collection and analysis or interpretation of data: E.K., H.I. Drafting the manuscript or revising its intellectual content: E.K., H.I., O.S., M.C.Y.; Approval of the final version of the manuscript to be published: L.Y.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Tucker S Jr, Rowe VL, Rao R, Hood DB, Harrell D, Weaver FA. Treatment options for traumatic pseudoaneurysms of the paravisceral abdominal aorta. Ann Vasc Surg 2005;19:613-8. doi: 10.1007/s10016-005-4652-3.
2. Ma X, Feng Y, Tardzenyuy MA, Qin B, Zhu Q, Akilu W, et al. Debranching abdominal aortic hybrid surgery for aortic diseases involving the visceral arteries. Front Cardiovasc Med 2023;10:1219788. doi: 10.3389/fcvm.2023.1219788.
3. Orguc S, Demirpolat G, Elcin F, Gurgan U. Aorta patolojilerinin değerlendirilmesinde helikal bilgisayarlı tomografi ve 3-D görüntüleme metodlarının tanıya katkısı. Turk Gogus Kalp Dama 1999;7:270-5.
4. Chase CW, Layman TS, Barker DE, Clements JB. Traumatic abdominal aortic pseudoaneurysm causing biliary obstruction: A case report and review of the literature. J Vasc Surg 1997;25:936-40. doi: 10.1016/s0741-5214(97)70226-x.
5. Surer S, Besir Y, Rodoplu O, Tetik O. Giant external iliac artery pseudoaneurysm following percutaneous coronary intervention: A rare case. Cardiovascular Surgery and Interventions 2014;1:35-7. doi: 10.5606/e-cvsi.2014.86
6. Scali ST, Waterman A, Feezor RJ, Martin TD, Hess PJ Jr, Huber TS, et al. Treatment of acute visceral aortic pathology with fenestrated/branched endovascular repair in high-surgical-risk patients. J Vasc Surg 2013;58:56-65.e1. doi: 10.1016/j.jvs.2012.12.043.

Cardiovasc Surg Int 2024;11(3):221-222
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1746
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Letter to the Editor Open Access

Comment on "Analysis of incorrect referrals to the cardiovascular surgery outpatient clinic"

Muhammet Hüseyin Erkan

Department of Cardiovascular Surgery, Konya City Hospital, Konya, Türkiye

Received: September 18, 2024 ***Accepted:*** September 23, 2024 ***Published online:*** October 17, 2024

I read with interest the article titled, "Analysis of incorrect referrals to the cardiovascular surgery outpatient clinic," recently published in Cardiovascular Surgery and Interventions by Rahman and Ayyıldız.[1] The study is an important and timely research in terms of highlighting the inefficiencies of the Central Physician Appointment System (CPAS) in Türkiye and the burden it places on healthcare services.

The data presented in the study clearly show the difficulties in the functioning of the CPAS and the areas where the system can be improved. In this sense, the suggestions are crucial to improving the performance of the system. However, I believe there are some points that should be addressed.

It is an undeniable fact that the number of physicians in our country is insufficient in relation to the population. According to the 2021 OECD (Organisation for Economic Co-operation and Development) data, the number of physicians per 1,000 individuals in our country was 2.2, while the mean was 3.7.[2] On the other hand, considering the number of examinations by specialty, the number of examinations in cardiology was several times higher than in cardiovascular surgery.[3] However, the same ratio was not observed between the number of cardiology specialists and cardiovascular surgery specialists.

Considering that the number of daily appointments provided by the CPAS is the same for all specialists, appointments for the cardiology department are available much later than for the cardiovascular surgery department. Therefore, it should not be overlooked that patients may prefer or be directed to the cardiovascular surgery department to reach the specialist related to the possible cardiac complaints earlier. I believe that if the optimal number of specialists is provided according to the population, the reasons for referrals to the wrong department will be better understood.

In conclusion, the study by Rahman and Ayyıldız provides a valuable starting point by addressing an important problem in the Turkish healthcare system. I look forward to further research in this area and hope that the authors will consider these recommendations in their future work.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest: The author declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The author received no financial support for the research and/or authorship of this article.

REFERENCES

1. Rahman ÖF, Ayyıldız F. Analysis of incorrect referrals to the cardiovascular surgery outpatient clinic. Cardiovasc Surg Int 2024;11:102-7. doi: 10.5606/e-cvsi.2024.1658.
2. OECD, Health at a Glance, Doctors. [Internet] Available at: https://data.oecd.org/healthres/doctors.htm. [Accessed: 17.09.2024]

Corresponding author: Muhammet Hüseyin Erkan, MD. Konya Şehir Hastanesi Kalp ve Damar Cerrahisi Kliniği, 42020 Karatay, Konya, Türkiye.
E-mail: mhuseyinerkan@gmail.com

Citation:
Erkan MH. Comment on "Analysis of incorrect referrals to the cardiovascular surgery outpatient clinic". Cardiovasc Surg Int 2024;11(3):221-222. doi: 10.5606/e-cvsi.2024.1746.

3. Her Branşta İlk 100 Hastane' 2017 Yılı Kamu Hastaneleri Poliklinik, Yatış, Yoğun Bakım, Ameliyat, Acil Servis Ve Doğum Sayıları. [Internet] Available at: https://khgmistatistikdb.saglik.gov.tr/TR,43819/her-branstailk-100-hastane-2017-yili-kamu-hastaneleri-muayene-yatis-yogun-bakim-ameliyat-acil-servis-ve-dogum-sayilari.html. [Accessed: 17.09.2024]