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ORIGINAL ARTICLE

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Cardiovasc Surg Int 2026;13(1):55-60

CARDIOVASCULAR SURGERY AND INTERVENTIONS

Does endovenous radiofrequency ablation cause endothermal heat-induced thrombosis?

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ABSTRACT

Objectives: Endovenous radiofrequency ablation (RFA) is widely used for the treatment of chronic venous disease. However, concerns regarding endothermal heat-induced thrombosis (EHIT) have traditionally led to avoidance of ablation close to the saphenofemoral junction (SFJ). This study aimed to evaluate the incidence of EHIT and early anatomic outcomes following flush RFA at the SFJ.

Patients and methods: This single-center retrospective study included 60 limbs treated with endovenous RFA for great saphenous vein incompetence. Patients with CEAP class C2-C6 and no concomitant deep venous insufficiency were included. Ablation was performed using a standardized technique, and limbs were categorized according to flush strategy as optimal flush (+1 to -2 mm) or flush free (>-2 mm). Duplex ultrasonography was performed on postoperative day 1 to assess EHIT and at 1 month to evaluate early anatomic outcome.

Results: No cases of EHIT were detected (0/60; exact 95% confidence interval, 0-5.96%). At 1 month, complete vein occlusion was observed in 41 limbs (68.3%). Complete occlusion was significantly more frequent in the optimal flush group compared with the flush free group (85.4% *vs.* 31.6%; p<0.001). The likelihood of achieving complete occlusion was higher with optimal flush (risk ratio, 2.70; 95% confidence interval, 1.38-5.30). Early anatomic outcomes did not differ between high-risk and low-risk EHIT subgroups.

Conclusion: Flush endovenous RFA at the SFJ appears to be safe in the short term and is not associated with an increased risk of EHIT. Optimal flush positioning is associated with significantly improved early anatomic outcomes.

Keywords: Endovenous radiofrequency ablation, endothermal heat-induced thrombosis, saphenofemoral junction, chronic venous disease, venous reflux.

Endovenous thermal ablation techniques have become the primary treatment modality for chronic venous disease, replacing conventional surgical ligation and stripping in most clinical settings. Among these techniques, endovenous radiofrequency ablation (RFA) is widely adopted due to its reproducibility, favorable safety profile, and consistent occlusion rates. Despite these advantages, thrombotic complications related to endovenous ablation continue to represent a major clinical concern. In particular, endothermal heat-induced thrombosis (EHIT), defined as thrombus extension from the treated superficial vein into the adjacent deep venous system, has been recognized as a distinct and potentially serious complication of thermal ablation procedures. Although EHIT is often detected incidentally on early postoperative duplex ultrasonography, progression to deep vein thrombosis or pulmonary embolism has been reported, underscoring the need for careful procedural planning and surveillance.[1,2]

Concerns regarding EHIT have traditionally influenced technical strategies during RFA, particularly with respect to the saphenofemoral junction (SFJ). To reduce the perceived risk of thrombus propagation into the common femoral vein, many operators have intentionally avoided ablation close to the SFJ, leaving a proximal untreated segment of the great saphenous vein (GSV). However, residual proximal stumps have been associated with persistent reflux, neovascularization, and late recurrence of varicose veins. Several long-term observational studies have suggested that incomplete proximal treatment may compromise

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durable anatomic success, thereby challenging the rationale of routinely avoiding junction-level ablation.[3,4] Reported EHIT rates after endovenous thermal ablation are generally low, but vary across studies and surveillance protocols, with most contemporary RFA series reporting EHIT in the low single-digit percentage range.[5,6]

With improvements in ultrasound guidance, catheter design, and standardized ablation protocols, flush or near-flush ablation at the SFJ has become technically feasible. This approach aims to eliminate the proximal stump while maintaining procedural safety. Nevertheless, the role of flush positioning remains controversial, particularly in patients considered to be at increased risk for EHIT. While several studies have reported low overall EHIT rates following RFA, most series do not specifically stratify outcomes according to flush distance or stump length. Moreover, data evaluating early anatomic outcomes in relation to flush positioning remain limited. As a result, uncertainty persists regarding whether flush ablation at the SFJ meaningfully improves technical success without increasing thrombotic risk.[5]

The present study was designed to evaluate the short-term safety of flush endovenous RFA at the SFJ, with particular emphasis on the occurrence of EHIT. In addition, early anatomic outcomes were compared between different flush strategies to assess whether optimal flush positioning is associated with improved early vein occlusion without compromising safety.

PATIENTS AND METHODS

Study Design and Patient Selection

This single-center retrospective study evaluated patients who underwent endovenous RFA for GSV incompetence between March 2023 and June 2024. All procedures were unilateral; each patient contributed a single treated limb. Limbs were included if patients had chronic venous disease classified as CEAP C2-C6, demonstrated significant reflux at the SFJ on duplex ultrasonography, and had no evidence of concomitant deep venous insufficiency or prior deep vein thrombosis. Limbs with previous venous interventions involving the SFJ or incomplete follow-up were excluded.

Ethical permission was obtained from the Health Sciences Scientific Research Ethics Committee (Kırşehir) for this study with date 17/09/2024 and number 2024-15/127, and Helsinki Declaration rules were followed to conduct this study. Informed consent forms were obtained from all patients.

Definition of EHIT and Risk Stratification

EHIT was defined as thrombus extension from the treated superficial vein into the adjacent deep venous system, detected by duplex ultrasonography. EHIT surveillance and classification were performed in accordance with established consensus definitions. Patients were categorized into low/standard-risk or high-risk EHIT subgroups based on recognized clinical and anatomic risk factors, including vein diameter, body mass index, and disease severity.[1,2] High-risk EHIT status was defined a priori based on recognized risk factors, including vein diameter thresholds (GSV diameter ≥8 mm and/or SFJ diameter ≥10 mm), additional clinical risk factors (e.g., body mass index ≥30 kg/m², advanced CEAP class (4-6), prior venous thromboembolism/thrombophilia), and unfavorable SFJ anatomy on preoperative duplex (e.g., marked junctional ectasia or large accessory confluence). Patients not meeting these criteria were classified as low/standard risk.

Procedural Technique and Flush Categorization

All procedures were performed using a standardized endovenous RFA technique (ClosureFast™, Medtronic), under ultrasound guidance. Venous access was obtained distally, and the ablation catheter was positioned proximally according to the planned flush strategy. Tumescent anesthesia was administered perivenously along the treated segment. Intraoperative ultrasound measurements and catheter positioning were performed by a single experienced operator using a standardized protocol, with the SFJ plane identified in a consistent longitudinal view. Measurements were recorded at the time of catheter positioning and documented in the operative record.

Catheter positioning was planned to achieve an optimal flush when anatomy and ultrasound visualization allowed safe junction-level placement; a flush-free position (>2 mm distal to the SFJ plane) was used when junctional anatomy or accessory confluence limited reliable near-junction positioning. Measurements were referenced to the SFJ plane (the junctional confluence between the GSV and common femoral vein visualized on ultrasound). Distances distal to the SFJ were recorded as negative values, whereas values at or marginally proximal to the SFJ plane (within the superficial junctional segment) were recorded as positive. The 0-PD distance was defined as the ultrasound-measured distance between the proximal end of the post-ablation closure segment (proximal endpoint of the treated/occluded segment) and the SFJ plane. Limbs were categorized into two groups:

- **Optimal flush:** Catheter tip positioned between +1 mm and -2 mm relative to the SFJ,
- **Flush-free:** Catheter tip positioned >2 mm distal to the SFJ plane (i.e., more than -2 mm).

This categorization was selected to reflect clinically relevant differences in proximal stump length while maintaining procedural reproducibility.[5]

Postoperative Surveillance and Follow-up

POD-1 duplex ultrasonography was performed to detect early EHIT at the SFJ and to guide timely management if present. A planned 1-month duplex assessment was used to evaluate early anatomic outcomes and is consistent with guideline-recommended post-ablation surveillance windows (e.g., 1-4 weeks) for clinical and duplex assessment.[1] Early anatomic outcome was categorized as complete occlusion or partial occlusion (mild or moderate residual reflux).[6]

No routine pharmacologic prophylaxis (UFH/LMWH) was administered solely based on EHIT risk category; anticoagulation was reserved for patients with an established indication. This is stated to facilitate interpretation of thrombotic outcomes.

Study Endpoints

The primary endpoint of the study was the occurrence of EHIT within the early postoperative period. Secondary endpoints included early anatomic outcome at 1 month and comparison of occlusion patterns according to flush strategy and EHIT risk subgroup.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation, and categorical variables as counts and percentages. Baseline characteristics were compared between flush groups using the Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. The incidence of EHIT was reported descriptively with exact 95% confidence intervals. Associations between flush strategy and early anatomic outcome were evaluated using Fisher's exact test, and effect size was expressed as risk ratios with corresponding confidence intervals. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Study Population and Baseline Characteristics

A total of 60 patients (60 treated limbs) were included in the analysis; all procedures were unilateral. The mean patient age was 47.1±14.8 years, and the mean body mass index was 28.3±4.0 kg/m². The mean GSV diameter was 7.1±1.6 mm. Female patients constituted 58.3% of the cohort, and diabetes mellitus was present in 46.7% of patients.

According to CEAP classification, 36 limbs (60.0%) were classified as C2-C3 and 24 limbs (40.0%) as C4-C6. Overall, 26 limbs (43.3%) were categorized as high risk for EHIT.

Based on proximal catheter positioning, 41 limbs (68.3%) were treated using an optimal flush strategy, while 19 limbs (31.7%) were treated using a flush free strategy.

Baseline demographic, clinical, and anatomic characteristics were comparable between the two flush groups. No statistically significant differences were observed with respect to age, body mass index, GSV diameter, sex distribution, diabetes mellitus, CEAP class distribution, or EHIT risk category (all p>0.05) (Table 1).

Procedural Characteristics and Early Follow-up

All procedures were completed successfully using a standardized RFA protocol. Flush positioning was achieved according to the predefined intraoperative ultrasound measurements, allowing clear separation between optimal flush and flush free groups (Figure 1).

All patients underwent duplex ultrasonography on postoperative day 1. No cases of deep vein thrombosis were detected during early postoperative surveillance. A follow-up duplex examination was completed at 1 month in all included limbs, allowing assessment of early anatomic outcomes.

Primary Outcome: EHIT

No cases of EHIT were detected during the early postoperative period. EHIT incidence was 0 of 60 treated limbs, corresponding to an estimated incidence of 0%, with an exact 95% confidence interval ranging from 0% to 5.96%. No cases of deep vein thrombosis were observed on postoperative day 1 or during the 1-month follow-up period.

Secondary Outcome: Early Anatomic Results at 1 Month

At 1-month follow-up, complete occlusion of the treated GSV was observed in 41 of 60 limbs (68.3%). Partial occlusion, defined as the presence of mild or moderate residual reflux, was identified in 19 limbs (31.7%).

When stratified by flush strategy, complete occlusion was significantly more frequent in the optimal flush group than in the flush free group. In the optimal flush group, 35 of 41 limbs (85.4%) demonstrated complete occlusion, compared with 6 of 19 limbs (31.6%) in the flush free group. This difference was statistically significant (Fisher's exact test, p<0.001).

The likelihood of achieving complete occlusion was significantly higher in limbs treated with an optimal flush strategy, with a risk ratio of 2.70 (95% confidence interval, 1.38-5.30).

Table 1. Baseline characteristics of the study cohort according to flush strategy

Characteristics	Overall (n=60)	Optimal flush (+1 to -2 mm) (n=41)	Flush free (>-2 mm) (n=19)	p-value
Age, years	47.1±14.8	47.6±14.7	46.1±15.5	0.7205
BMI, kg/m²	28.3±4.0	28.1±3.7	28.5±4.6	0.8737
GSV diameter, mm	7.1±1.6	7.0±1.8	7.4±1.3	0.1020
Sex, n (%)				0.5831
Female	35 (58.3%)	25 (61.0%)	10 (52.6%)	
Male	25 (41.7%)	16 (39.0%)	9 (47.4%)	
Diabetes mellitus, n (%)	28 (46.7%)	20 (48.8%)	8 (42.1%)	0.7821
CEAP class, n (%)				0.3431
C2-C3	36 (60.0%)	27 (65.9%)	9 (47.4%)	
C4-C6	24 (40.0%)	14 (34.1%)	10 (52.6%)	
High-risk EHIT subgroup, n (%)				1.0000
Low/standard risk	34 (56.7%)	23 (56.1%)	11 (57.9%)	
High risk	26 (43.3%)	18 (43.9%)	8 (42.1%)	

BMI: Body mass index; GSV: Great saphenous vein; EHIT: Endothermal heat-induced thrombosis.

Subgroup Analysis: EHIT Risk Stratification

Early anatomic outcomes were further analyzed according to EHIT risk stratification. No statistically significant difference in complete occlusion rates was observed between limbs categorized as high risk and those categorized as low or standard risk for EHIT. Similarly, EHIT did not occur in either risk subgroup.

Summary of Results

Across the entire cohort, flush endovenous RFA at the SFJ was not associated with the occurrence of EHIT. Optimal flush positioning was associated with a significantly higher rate of early complete vein occlusion, without an increase in thrombotic complications (Figure 2).

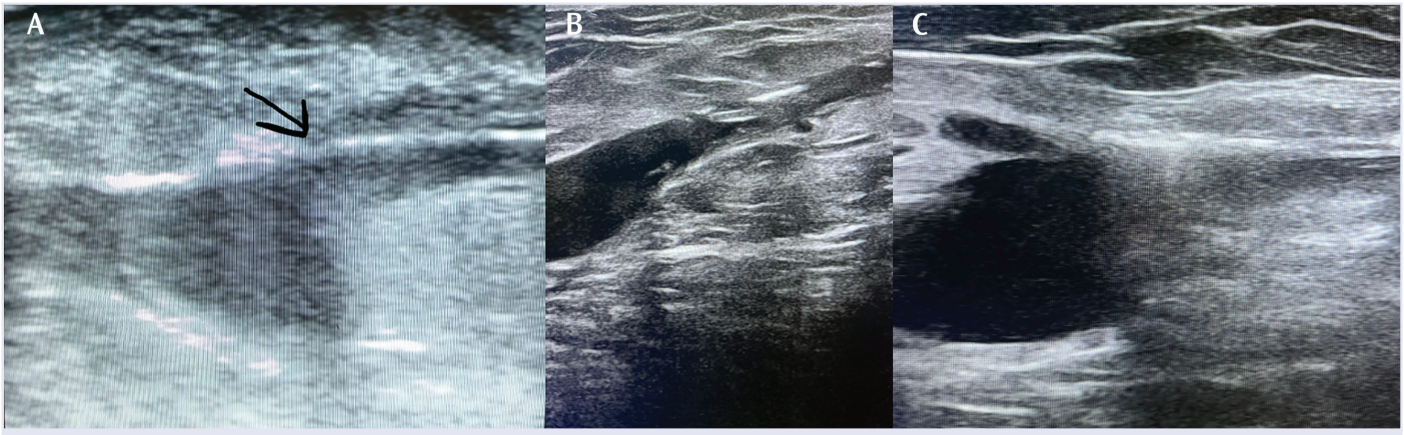

Figure 1. Intraoperative catheter positioning and postoperative saphenofemoral junction imaging. (**A**) Intraoperative ultrasound image demonstrating proximal positioning of the radiofrequency ablation catheter at the saphenofemoral junction (arrow). (**B**) Postoperative duplex ultrasonography image of the saphenofemoral junction showing a 0-PD distance of -5 mm, consistent with a flush-free ablation strategy. (**C**) Postoperative duplex ultrasonography image of the saphenofemoral junction showing a 0-PD distance of -1 mm, consistent with an optimal flush ablation strategy.

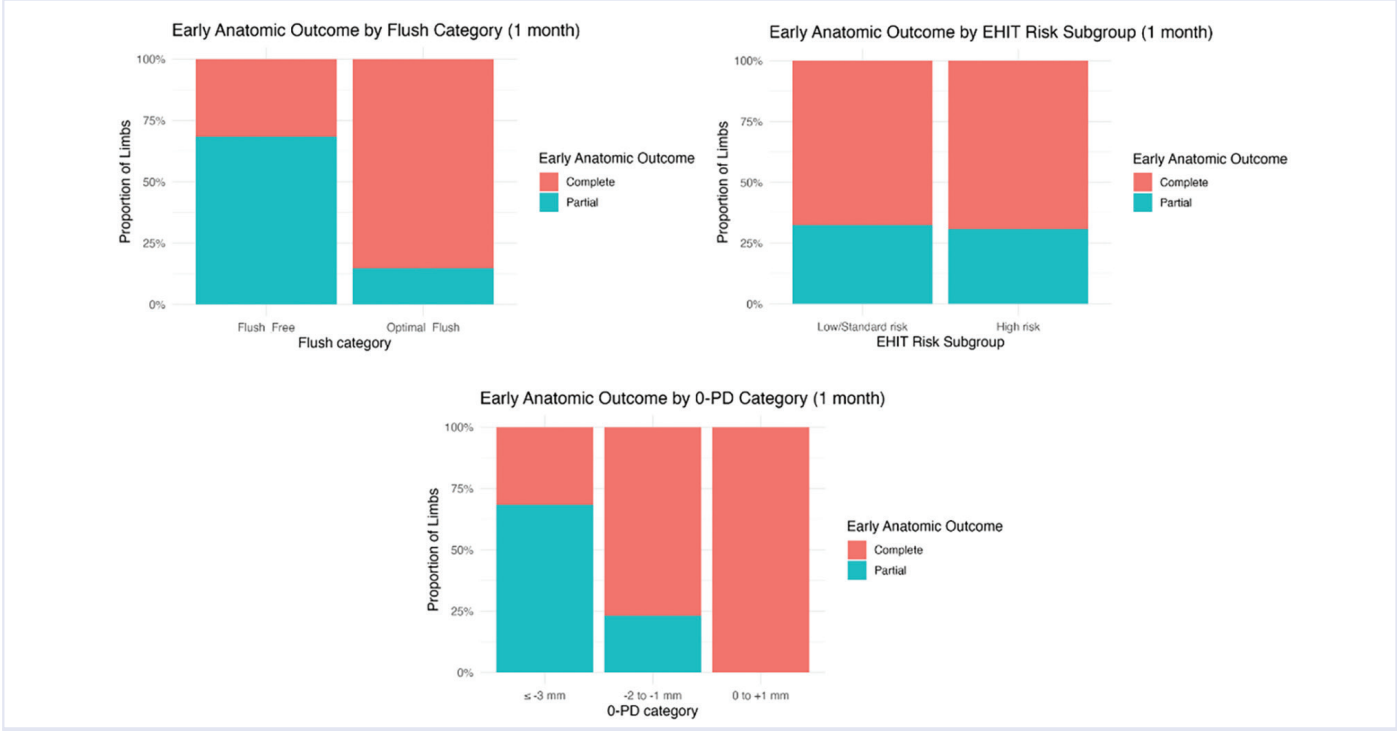

Figure 2. Early anatomic outcomes according to flush strategy, 0-PD distance, and EHIT risk subgroup. Stacked bar plots illustrate early anatomic outcomes at 1 month following endovenous radiofrequency ablation. Early anatomic outcomes stratified by flush strategy, comparing Optimal_Flush and Flush_Free positioning. Early anatomic outcomes stratified by 0-PD distance category (≤-3 mm, -2 to -1 mm, and 0 to +1 mm). Early anatomic outcomes stratified by EHIT risk subgroup (low/standard risk *vs.* high risk). Early anatomic outcome was classified as complete occlusion or partial occlusion (mild or moderate residual reflux). Bar heights represent proportions within each subgroup.
EHIT: Endothermal heat-induced thrombosis.

DISCUSSION

The present study demonstrates that flush endovenous RFA at the SFJ can be performed safely in the short term, without an increased risk of EHIT. In a cohort that included a substantial proportion of patients categorized as high risk for EHIT, no cases of EHIT were detected, and early anatomic outcomes were significantly improved with optimal flush positioning.

Published EHIT rates after RFA vary, with contemporary large-scale series typically reporting overall EHIT in the low single-digit range and severe EHIT being uncommon; therefore, our observed EHIT incidence of 0/60 should be interpreted within the context of limited sample size and the corresponding exact confidence interval.[1,5]

Concerns regarding EHIT have historically shaped technical strategies during endovenous thermal ablation, particularly at the level of the SFJ. EHIT has been recognized as a distinct complication of thermal ablation, characterized by thrombus extension into the deep venous system, with variable clinical significance depending on the degree of extension. Although most EHIT cases are detected incidentally and remain clinically silent, progression to deep vein thrombosis and pulmonary embolism has been reported, reinforcing a conservative approach in junction-level treatment.[1,2]

As a result, many operators have traditionally avoided ablation close to the SFJ, intentionally leaving a proximal untreated segment of the GSV. However, the presence of a residual proximal stump has been implicated in persistent reflux and late recurrence. Long-term surgical and endovenous series have suggested that incomplete proximal treatment may compromise durable anatomic success, challenging the rationale of routinely avoiding the junction.[3,4]

With advances in ultrasound guidance and standardized ablation techniques, flush or near-flush ablation at the SFJ has become technically feasible. Nevertheless, data specifically addressing the safety of flush positioning in relation to EHIT remain limited. Most published RFA series report overall EHIT rates but do not stratify outcomes according to catheter position or stump length. In this context, the absence of EHIT in the present cohort, despite intentional flush positioning and inclusion of high-risk patients, provides supportive evidence that flush RFA at the SFJ does not inherently increase thrombotic risk when performed with careful technique and appropriate surveillance.[5]

Beyond safety, the present study highlights a clinically relevant association between flush strategy and early anatomic outcome. Optimal flush positioning was associated with a significantly higher rate of complete vein occlusion at 1 month, with a nearly threefold increase in the likelihood of achieving complete occlusion compared with a flush-free approach. Importantly, baseline characteristics were comparable between groups, suggesting that this difference reflects a technical effect rather than selection bias. These findings support the concept that minimizing the proximal stump may enhance early technical success without compromising safety. Early complete occlusion at 1 month represents an anatomic surrogate endpoint. The present study did not evaluate symptom scores, venous severity measures, or quality-of-life outcomes, and the short follow-up precludes conclusions regarding long-term durability, recurrence, or clinical benefit. Therefore, the observed association between optimal flush positioning and early occlusion should not be overinterpreted as evidence of improved long-term clinical outcomes.

Subgroup analysis further demonstrated that EHIT risk stratification did not influence early anatomic outcomes, and EHIT did not occur in either risk category. Although the study was not powered to detect rare thrombotic events, this observation suggests that flush positioning may be feasible even in patients considered at increased risk for EHIT, provided that meticulous technique and early duplex surveillance are employed.

Several limitations of this study should be acknowledged. The retrospective design and single-center setting may limit generalizability. Although no EHIT events were observed, the sample size limits our ability to detect rare complications; therefore, low-frequency EHIT events cannot be excluded, as reflected by the exact 95% confidence interval. Nevertheless, the use of standardized procedural techniques, objective duplex-based assessment, and clearly defined flush categories strengthens the internal validity of the findings. Residual tumescent fluid in the early postoperative period may reduce image quality and could potentially influence fine measurements around the junction. Nevertheless, EHIT assessment primarily relied on evaluation of thrombus extension into the deep venous lumen at the SFJ, and all studies were performed by experienced sonographers; this remains a potential limitation. This EHIT risk categorization was a pragmatic, center-based operational definition rather than a formally validated prediction model, which may limit comparability across studies. The observed diabetes prevalence reflects the routine case-mix treated at our center during the study period and was not the result of targeted selection. Laboratory markers related to thrombosis surveillance (e.g., D-dimer) were not routinely collected in this retrospective cohort and therefore could not be analyzed; this represents another limitation. Flush categorization relied on precise millimetric ultrasound measurements and may be operator-dependent. Interobserver variability was not formally assessed; therefore, measurement error around narrow cut-offs could influence group assignment and may limit generalizability.

In conclusion, flush endovenous RFA at the SFJ appears to be safe in the short term and is not associated with an increased risk of EHIT. Optimal flush positioning is associated with significantly improved early anatomic outcomes. Further prospective studies with larger cohorts and longer follow-up are warranted to confirm these findings and to clarify the long-term clinical implications of flush ablation strategies.

Flush endovenous RFA at the SFJ was not associated with EHIT in this cohort; however, given the sample size, rare EHIT events cannot be excluded and the findings should be interpreted with caution. In this study, no EHIT events were observed despite the inclusion of patients with recognized risk factors. Optimal flush positioning was associated with significantly improved early anatomic outcomes, as reflected by higher rates of complete vein occlusion. These findings support the feasibility of flush ablation strategies at the SFJ when performed with careful technique and early duplex surveillance. Further prospective studies with larger patient cohorts and longer follow-up are needed to define the long-term clinical implications of this approach.

Ethics

Ethics Committee Approval: Ethical permission was obtained from the Health Sciences Scientific Research Ethics Committee (Kırşehir) for this study with date 17/09/2024 and number 2024-15/127, and Helsinki Declaration rules were followed to conduct this study.

Informed Consent: Informed consent forms were obtained from all patients.

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Footnotes

This study has been accepted for an oral presentation at the 18th Congress of the Turkish Society of Cardiovascular Surgery, to be held in Antalya on November 21, 2024.

Authorship Contributions

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

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

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REFERENCES

1. De Maeseneer MG, Kakkos SK, Aherne T, Baekgaard N, Black S, Blomgren L, et al. Editor's choice - European Society for Vascular Surgery (ESVS) 2022 clinical practice guidelines on the management of chronic venous disease of the lower limbs. Eur J Vasc Endovasc Surg. 2022;63:184-267. doi:10.1016/j.ejvs.2021.12.024. Erratum in: Eur J Vasc Endovasc Surg. 2022;64:284-5. doi: 10.1016/j.ejvs.2022.05.044.
2. Spinedi L, Stricker H, Keo HH, Staub D, Uthoff H. Feasibility and safety of flush endovenous laser ablation of the great saphenous vein up to the saphenofemoral junction. J Vasc Surg Venous Lymphat Disord. 2020;8:1006-13. doi:10.1016/j.jvsv.2020.01.017.
3. Proebstle TM, Alm BJ, Göckeritz O, Wenzel C, Noppeney T, Lebard C, et al. Five-year results from the prospective European multicentre cohort study on radiofrequency segmental thermal ablation for incompetent great saphenous veins. Br J Surg. 2015;102:212-8. doi:10.1002/bjs.9679.
4. Nelzén O. Reconsidering the endovenous revolution. Br J Surg. 2016;103:939-40. doi:10.1002/bjs.10192.
5. Kedwai BJ, Geiger JT, Lehane DJ, Glocker RJ, Newhall KA, Pitcher GS, et al. Strategies to reduce rates of severe endothermal heat-induced thrombosis following radiofrequency ablation. J Vasc Surg Venous Lymphat Disord. 2024;12:101864. doi: 10.1016/j.jvsv.2024.101864.
6. Kabnick LS, Sadek M, Bjarnason H, Coleman DM, Dillavou ED, Hingorani AP, et al. Classification and treatment of endothermal heat-induced thrombosis: recommendations from the American Venous Forum and the Society for Vascular Surgery. J Vasc Surg Venous Lymphat Disord. 2021;9:6-22. doi: 10.1016/j.jvsv.2020.06.008.

ORIGINAL ARTICLE

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CARDIOVASCULAR SURGERY AND INTERVENTIONS

Comparison of long-term efficacy of lumbar sympathetic interventions in peripheral artery disease

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ABSTRACT

Objectives: The aim of this study is comparing the effectiveness of non-surgical interventional methods in peripheral vascular disease.

Patients and methods: The results of patients who underwent interventional procedures due to Fontaine stage 2-3 peripheral vascular disease in the algology clinic between June 2016 and December 2023 were evaluated. The numeric rating scale (NRS) scores were recorded before the procedure, at 1st month, 6th month and 12th month follow-ups after the procedure. The developing side effects and complications were evaluated.

Results: Thirty-five patients were evaluated in the chemical neurolysis (CN), 32 patients in the radiofrequency thermocoagulation (RFT), 28 patients in the continuous epidural block (CEB), 34 patients in the combined CN and RFT, 38 patients in the combined CN+CEB group. In all groups, NRS scores were significantly lower at 1st and 6th months after the procedure compared to before the procedure ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, respectively). In the combined CN+RFT group, NRS scores were significantly lower at 12th month compared to before the procedure. Catheter migration was observed in 2 patients, but no major complications were recorded.

Conclusion: Combined CN and RFT treatment applied to the sympathetic chain in peripheral vascular disease is an effective and safe method in long-term follow-up.

Keywords: Peripheral arterial ischemia, chemical neurolysis, radiofrequency ablation, continue epidural block.

Ischemic pain is the main symptom of diseases such as peripheral arterial disease and Raynaud phenomenon, which result in inadequate blood flow to the extremities and ischemia.[1] The effective treatment options in critical extremity ischemia are revascularization, bypass, endarterectomy, and endovascular treatments.[2] Surgical sympathectomy is another option for the treatment of ischemic pain and non-healing ulcers.[3] Lumbar sympathectomy is indicated for the treatment of critical extremity ischemia, Buerger disease, thromboembolic events, diabetic ulcers, and diabetic neuropathic pain. Surgical sympathectomy causes too much trauma and tissue damage. Neurolysis of the lumbar sympathetic ganglion is a safe and effective method compared to invasive surgical procedures.[4] Lumbar sympathetic ganglias are located in the paravertebral region from L2 to L5. Lumbar sympathetic ganglia block pruduce vasodilatationby the denervation of sympathetic fibers of the lower extremities. Sympathetic denervation causes increased blood flow and improved circulation. Thermal neurolysis or chemical neurolysis (CN) of the lumbar sympatheticganglia withh radiofrequency thermocoagulation (RFT) is a safe and effective option.[5] There are reports in the literature onusingg combined methods, but there are very few studies. In this study, we aimedto compareg the effectiveness of the methods we applied in peripheral arterial disease (CN, RFT, continuous epidural block [CEB]) and their combinations.

PATIENTS AND METHODS

Ethics, Permission

Our study is a retrospective design based on the collection of data by reviewing the retrospective files. Declaration of Helsinki principles were followed in the study. Approval of the Aydın Adnan Menderes University's Ethics Committee was obtained (approval no: 2024/118,

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date: 10.06.2024). Human ethics and participation approval was obtained from all patients. Written informed consent forms were obtained from all patients.

Patient Selection

The follow-up data of all patients who underwent CN, RFT and CEB and their combinations to the lumbar sympathetic ganglion due to peripheral arterial disease between May 2016 and December 2023 will be examined.

Inclusion Criteria

Patients with Peripheral arterial disease who were Fontaine stage 2-3, who were not suitable for revascularization surgery, endovascular treatments or who were unresponsive to endovascular treatments were included in the study.

Exclusion Criteria

Local infection, pacemaker, mental retardation, coagulopathy, pregnancy, severe liver and kidney dysfunction.

Fontaine stage 1 (asymptomatic patients) was excluded from the study because it would present diagnostic difficulties, and Fontaine stage 4 patients were excluded because the effectiveness of interventional procedures in the advanced stage would not be sufficient.

Patient Evaluation

Patients' demographic and clinical examination findings at admission (gender, age, pain character, neurological examination, Fontaine staging, medications used), NRS scores were recorded.

The patients evaluated for pain intensity with NRS scores (0: No pain; 10: Worst pain).[6]

Patients were staged for peripheral arterial ischemia with Fontaine classification (asymptomatic: Stage I, claudication: Stage II, rest pain: Stage III, ulcers/gangrene, Stage IV).[7]

NRS pain scores, clinical and neurological examination, and developing complication findings will be recorded at the first month follow-up after the procedure. At the end of the 6 and 12 months follow-up, the patients' NRS pain scores were evaluated for developing side effects and complications.

Procedure

The patient was placed in a sterile operating room and the possible lumbar sympathetic ganglion located at the L2 and L4 levels under fluoroscopy guidance in the prone position. Local anesthesia was provided with 2% lidocaine. For CN, the anterior vertebral body was targeted with a 15 cm long 21 gauge Chiba needle. The needle's depth in the lateral, anterior-posterior position was confirmed with fluoroscopy (Figure 1a, b). After confirmation with radiopaque material, 5 mL of a mixture of 0.25% bupivacaine and 6% phenol was applied for each level. For RFT, the anterior part of the L2 and L4 vertebral body was targeted with a 10x10 mm long 10 mm active tip radiofrequency cannula. The depth of the cannula in the lateral, anterior-posterior position was confirmed with fluoroscopy. The final localization of the cannula was tested with radiopaque material after 50 Hz sensory and 2 Hz motor stimuli. After 5 cc of 0.24% bupivacaine was administered, conventional RFT was performed at 85 degrees and 90 seconds. For CEB, an epidural catheter was inserted and fixed using the paramedian interlaminar approach and loss of resistance method (Figure 1c, d). 100 mg of 2% lidocaine was administered through the epidural catheter 4 times a day for 5 days.

Statistical Analysis

SPSS 21.0 statistics program was used to analyze the data of the study. Descriptive analyses were studied using number (n), mean, standard deviation, median, minimum, maximum. Parametric properties of continuous variables in independent groups were studied with Student's t-test. Comparing non-parametric properties of continuous variables in independent groups were studied with Mann-Whitney U test. Continuous variables to normal distribution was investigated with Kolmogorov-Smirnov test. Comparing non-parametric properties of continuous variables in dependent groups were studied with Wilcoxon test. Chi-square test was used to show whether there was a difference between categorical variables in the study. P-value was determined as less than 0.05 to indicate statistical significance.

RESULTS

The clinical and demographic characteristics of the patients are presented in Table 1. Thirty-five patients were evaluated in the CN, 32 patients in the RFT, 28 patients in the CEB, 34 patients in the combined

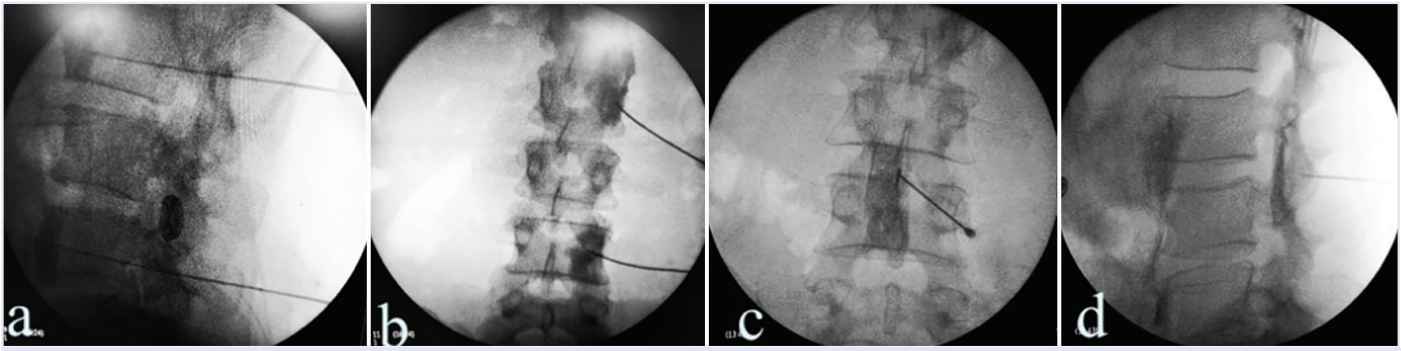

Figure 1. a) Fluoroscopic demonstration of opaque spread in the lateral plane of the needle/cannula placed anterior to the L2 and L4 vertebrae; b) Fluoroscopic demonstration of opaque spread in the anterior-posterior plane of the needle/cannula placed anterior to the L2 and L4 vertebrae; c) Image of epidural catheter placement with the interlaminar method using the paramedian approach from the L3 level and demonstration of contrast medium spread; d) Demonstration of contrast medium spread in the anterior vertebrae and posterior epidural space in combined CEB and CN application.
CEB: Continuous epidural block; CN: Chemical neurolysis.

CN+RFT, 38 patients in the combined CN+CEB group. In all groups, NRS scores were significantly lower at 1st month and 6th month after the procedure compared to before the procedure (p<0.001, p<0.001, p<0.001, p<0.001, p<0.001, respectively) (Table 2).

NRS scores were significantly lower at 12th month in the combined (CN+RFT) group compared to before the procedure (Table 2). Catheter migration was observed in 2 patients, and no major complication was recorded.

Table 1. Comparison of demographic and clinical characteristics of the groups

		CN	RFT	CEB	CN+RFT	CN+CEB	p
Gender (n)	**Female**	8	10	11	10	12	0.06
	Male	27	22	17	24	26	
Age (mean ± SD)		58.3±5.6	56.7±3.3	51.8±9.6	62.2±7.2	59.8±4.5	0.21*
Symptom duration (year)		4.8±2.2	6.3±1.5	7.2±1.4	5.4±2.3	6.5±3.1	0.07
Fontaine stage (n)	**2**	17	14	15	19	20	0.2
	3	18	18	13	15	18	
NRS 0 (mean ± SD)		7.1±0.9	8.3±0.4	7.9±1.6	8.4±0.7	8.2±1.3	0.3**
Drugs (n)	**Gabapentinoid**	14	13	11	10	17	0.1
	SNRI	3	2	6	8	5	
	Opioid	10	10	12	9	11	
	TCA	10	7	11	7	10	
	Anticonvulsant	7	4	4	6	4	

*: Parametric test; **: Non-parametric test; SD: Standard deviation; SNRI: Serotonin-neuradrenaline reuptake inhibitor; TCA: Tricyclic antidepressants; NRS: Numeric rating scale; CEB: Continuous epidural block; CN: Chemical neurolysis; RFT: Radiofrequency thermocoagulation.

Table 2. Comparison of pre-procedure NRS scores with post-procedure scores at 1, 6, 12 months

		NRS 0	NRS 1	NRS 6	NRS 12	p
CN	**Mean**	7.8	3.5	4	7.2	**<0.001**[1,2]
	SD	0.8	1.3	1.5	0.9	
	Median	8	3	4	8	
	Minimum	6	2	1	5	
	Maximum	9	8	8	8	
RFT	**Mean**	8	3.7	3.3	7.7	**<0.001**[1,2]
	SD	1.1	1.9	1.3	1.3	
	Median	8	3.8	3.1	7	
	Minimum	6	1	1	6	
	Maximum	10	8	7	8	
CEB	**Mean**	7.6	3.6	4.3	7.5	**<0.001**[1,2]
	SD	0.8	1.2	1.5	0.9	
	Median	8	3	4	7	
	Minimum	7	2	1	6	
	Maximum	9	8	8	8	
CN+RFT	**Mean**	8	3.7	3.3	3.8	**<0.001**[1,2,3]
	SD	1.2	1.9	1.1	1.8	
	Median	7	4	3	4	
	Minimum	6	2	1	1	
	Maximum	10	9	6	8	
CN+CEB	**Mean**	8.3	3.2	3.6	7.2	**<0.001**[1,2]
	SD	1.1	1.7	1.2	1.1	
	Median	8	4	3	4	
	Minimum	6	2	2	1	
	Maximum	10	8	6	8	

[1]: There is a statistically significant difference between NRS 0 and NRS 1st month; [2]: There is a statistically significant difference between NRS 0 and NRS 6 months; [3]: There is a statistically significant difference between NRS 0 and NRS 12 months; SD: Standard deviation; NRS: Numeric rating scale; CEB: Continuous epidural block; CN: Chemical neurolysis; RFT: Radiofrequency thermocoagulation.

DISCUSSION

Peripheral artery disease is an important health problem that results in disability due to the increasing frequency of amputations. Early diagnosis of patients, especially in the early-mid stage, and treatment directed at the pathogenesis of the disease can be protective against amputation. For this purpose, applying chemical thermal denervation to the sympathetic chains as a minimally invasive method will increase extremity blood circulation with peripheral vasodilator activity. In this direction, there are many studies investigating the effectiveness of methods such as CN, RFT, and CEB applied to the sympathetic chain.[8-12]

RFT is a known method of effectiveness. However, the number and location of the lumbar sympathetic ganglia vary greatly. This may cause the degree of ablation to be insufficient for nerve ablation by being affected by temperature and location.[13]

Sympathetic nerve resection is achieved by damaging the lumbar sympathetic nerve through CN. Blood vessels dilate, peripheral vascular resistance decreases, collateral circulation increases, and skin and muscle blood perfusion in the lower extremities increases.[14] However, the duration of neurolysis effects is relatively short and symptoms usually recur within 3-6 months. CEB; it is a repeatable and effective analgesic method applied by continuously blocking the somatic and sympathetic nerve fibers located in the epidural. Its effectiveness depends on the duration of blockade and is evident in the short-term. In the long-term, its effectiveness decreases due to common reasons such as catheter migration and can be limited to a chronic persistent pain syndrome such as ischemic pain alone.

Although these methods are effective when applied alone, they are short-term. The effectiveness of combination treatments has not been sufficiently investigated. In our study, we examined 167 patients who underwent fluoroscopy-guided interventions due to peripheral artery disease in 5 groups to evaluate the results. We compared the effectiveness of combined interventional treatments and single applications. We found that pain scores were significantly lower in the combined CN+RFT group compared to the other groups at the 12th month follow-up. Ding et al.,[15] who conducted a study with 90 diabetic peripheral artery patients with a similar design to our study, found combined RFT and CN treatment under CT guidance to be effective and safe compared to single applications at the 1-year follow-up. They found the total remission period to be significantly higher in the combined treatment. This study also found combination interventional treatments to be more effective in the long-term follow-up with similar results to our study. In our study, we performed a more comprehensive examination by including CEB application in single and combined treatments. In addition, we provided less ionizing radiation exposure compared to CT by performing the interventions under fluoroscopy. We did not record any major complications during fluoroscopy-guided interventions.

In another study, Sun et al.[16] showed that CT-guided alcohol neurolysis followed by continuous lumbar sympathetic blockade in 60 patients with refractory diabetic neuropathy provided greater benefit than sympathetic alcohol neurolysis alone in the treatment of painful diabetic neuropathy at 6-month follow-up. This study was providing clinical evidence that pain in diabetic neuropathy may be and the analgesic effects of continuous blocks were long-lasting, In this study, it was concluded that diabetic neuropathic pain is a sympathetically mediated. It is emphasized that the analgesic effects of continuous sympathetic blocks combined with CN are long-lasting.

In a case of erythromelalgia in which combined therapy was offered, the positive results of the combination of lumbar sympathetic blockade and CEB were emphasized.[17]

The role of the sympathetic nervous system in the pain of primary erythermelalgia is unclear. Several theories have been proposed, including vasoconstriction. Epidural blockade is not always effective treatment. In patients who do not respond to epidural blockade may respond to sympathetic blockade. Lumbar sympathetic ganglion block is thought to reduce pain by increasing blood flow to the extremities and by blocking C and Aδ fibers in dorsal root and sympathetic ganglion neurons. Therefore, it has been assumed that the combination of CEB with lumbar sympathetic ganglion block is an effective treatment option for permenant erythromelalgia.

Although CN, RFT and CEB methods provide short-term pain control when applied alone in sympathetic or ischemic pain, we believe that combination treatments are effective in long-term pain relief. Current studies in interventional pain treatments highlight the importance of combining several effective methods to achieve long-term pain control. In this study, we combined both epidural and peripheral ganglion blocks to provide more effective and long-lasting sympathetic blockade. We also chose to combine both known destruction methods: Neurolysis and ablation. We believe that combining these interventional techniques will yield more effective results by targeting multiple pathophysiological mechanisms without creating safety vulnerabilities.

We believe that our study will contribute to the literature by emphasizing the effectiveness of combined methods. However, the limitation of our study is that it is a retrospective design. Prospective studies will shed light on our current findings. Homogeneity and inadequate within-group pain assessment analyses are another limitations of the study. The use of clinical scoring systems in evaluating results is among the recurring production limitations.

In conclusion, the combined application of methods such as RFT, CN and CEB, which are known to be effective in ischemic pain, is more effective in long-term pain relief. Combined interventional procedures are both effective and safe when performed under fluoroscopic guidance under optimum conditions with appropriate patient selection.

Ethics

Ethics Committee Approval: Approval of the Aydın Adnan Menderes University's Ethics Committee was obtained (approval no: 2024/118, date: 10.06.2024).

Informed Consent: Written informed consent forms were obtained from all patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.E.; Concept: E.E., D.E.; Design: E.E., D.E.; Data Collection or Processing: E.E., D.E.; Analysis or Interpretation: E.E., D.E.; Literature Search: D.E.; Writing: E.E.

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

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REFERENCES

1. Block JA, Sequeira W. Raynaud's phenomenon. Lancet. 2001;357:2042-8. doi: 10.1016/S0140-6736(00)05118-7.
2. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, et al.; ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO) the Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2018;39:763-816. doi: 10.1093/eurheartj/ehx095.
3. Sanni A, Hamid A, Dunning J. Is sympathectomy of benefit in critical leg ischaemia not amenable to revascularisation? Interact Cardiovasc Thorac Surg. 2005;4:478-83. doi: 10.1510/icvts.2005.115410.
4. Day M. Sympathetic blocks: the evidence. Pain Pract. 2008;8:98-109. doi: 10.1111/j.1533-2500.2008.00177.x. Erratum in: Pain Pract. 2008;18:335-6.
5. Kulkarni K, Kulkarni R. Chemical neurolysis and radiofrequency ablation of lumbar sympathetic ganglion in peripheral vascular diseases of the lower limbs. In: Novel Approaches in Regional Anesthesia & Pain Management. Open Access eBooks: Las Vegas, NV, USA; 2021.p.1-16.
6. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Validity of four pain intensity rating scales. Pain. 2011;152:2399-404. doi: 10.1016/j.pain.2011.07.005.
7. Fontaine R, Kim M, Kieny R. Die chirurgische behandlung der peripheren durchblutungsstörungen [Surgical treatment of peripheral circulation disorders]. Helv Chir Acta. 1954;21:499-533. German.
8. Dominkus M, Bauer R, Kepplinger B, Malikpur G. Die perkutane radiofrequenz-sympathikussausschaltung (PRFS) bei peripheren durchblutungsstörungen [Percutaneous radio-frequency sympathetic block in peripheral circulatory disorders]. Vasa Suppl. 1990;30:152-6. German.
9. Singh R, Kulkarni R, Kulkarni K, Chavannavar K, Evaluation of the radiofrequency ablation of lumbar sympathetic ganglia in lower limb ischemic ulcers in Indian population: radiofrequency ablation and lower limb ischemic ulcers. International Journal of Medical and Surgical Sciences. 2021;8. DOI: https://doi.org/10.32457/ijmss.v8i2.1358
10. Gleim M, Maier C, Melchert U. Lumbar neurolytic sympathetic blockades provide immediate and long-lasting improvement of painless walking distance and muscle metabolism in patients with severe peripheral vascular disease. J Pain Symptom Manage. 1995;10:98-104. doi: 10.1016/0885-3924(94)00070-2.
11. Abramov R. Lumbar sympathetic treatment in the management of lower limb pain. Curr Pain Headache Rep. 2014;18:403. doi: 10.1007/s11916-014-0403-x.
12. Verma YS, Thakur J, Sodhi SS. Evaluation of chemical lumbar sympathectomy for chronic arterial ischaemia of lower limb(s). Journal of Anaesthesiology Clinical Pharmacology. 2007;23:391-4.
13. Jain P, Raza K, Singh S, Kumari C, Kaler S, Rani N. Lumbar sympathetic chain: anatomical variation and clinical perspectives. Clin Ter. 2016;167:185-7. doi: 10.7417/CT.2016.1970.
14. Nickel J, Brinckmann W, Andresen R. Ambulante, CT-gestützte lumbale sympathikolyse bei patienten mit schwerer pAVK: einfluss auf die periphere perfusion sowie die klinischen beschwerden [Ambulatory, CT-assisted lumbar sympathicolysis in patients with severe peripheral artery disease: influence on peripheral blood flow and clinical outcome]. Zentralbl Chir. 2008;133:349-54. German. doi: 10.1055/s-2008-1076859.
15. Ding Y, Yao P, Li H, Zhao R, Zhao G. Evaluation of combined radiofrequency and chemical blockade of multi-segmental lumbar sympathetic ganglia in painful diabetic peripheral neuropathy. J Pain Res. 2018;11:1375-82. doi: 10.2147/JPR.S175514.
16. Sun H, He M, Pang J, Guo X, Huo Y, Ma J. Continuous lumbar sympathetic blockade enhances the effect of lumbar sympatholysis on refractory diabetic neuropathy: a randomized controlled trial. Diabetes Ther. 2020;11:2647-55. doi: 10.1007/s13300-020-00918-7.
17. Ogawa S, Ueno H, Maruyama A, Amaya F. Extensive lumbar sympathetic ganglion block combined with epidural block for primary erythromelalgia: a case report. A A Pract. 2020;14:e01325. doi: 10.1213/XAA.0000000000001325.

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CARDIOVASCULAR SURGERY AND INTERVENTIONS

Limitations of risk stratification in CABG: Calibration across elective and emergency cohorts at a regional center

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ABSTRACT

Objectives: This study aimed to compare the discrimination and calibration performances of the Society of Thoracic Surgeons (STS) PROM and European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) risk models in predicting early postoperative mortality and to evaluate the prognostic value of preoperative clinical factors in patients undergoing isolated coronary artery bypass grafting (CABG).

Methods: Sixty-four consecutive patients (mean age: 62.1±10.1 years; 71.9% male) who underwent isolated CABG were included in this retrospective, single-center study. The discriminative capacity of the models was evaluated using receiver operating characteristic (ROC) curve analysis and the DeLong test, while calibration was assessed using observed/expected (O/E) mortality ratios.

Results: The overall operative mortality was 21.9% (n=14), demonstrating a statistically significant increase with surgical urgency (2.8% in the elective group; p<0.001). Both models underestimated actual mortality, particularly in emergency and salvage cases (O/E ratios: EuroSCORE II 24.7, STS PROM 21.9). In comparative group analyses, preoperative leukocyte (white blood cell) levels were significantly higher in the mortality group (11.95±3.46 *vs.* 9.15±2.74, p=0.006). ROC analysis revealed similar discriminatory power for both models (area under the curve: STS PROM 0.749, EuroSCORE II 0.740; p=0.866). However, the sensitivity of the STS PROM model (71.4%) was higher than that of EuroSCORE II (57.1%).

Conclusion: In our small, single-center exploratory cohort undergoing isolated CABG, surgical urgency and elevated leukocyte levels were observed as potential clinical parameters associated with early mortality in comparative group analyses. Although the STS PROM and EuroSCORE II models demonstrated acceptable discriminatory capacity, they tend to underestimate operative mortality in cases of high surgical urgency. Nevertheless, for regional centers managing high-risk profiles, the STS PROM model may represent a more practical option when prioritizing sensitivity. These findings are strictly hypothesis-generating and warrant validation in larger, multicenter cohorts.

Keywords: Coronary artery bypass grafting, EuroSCORE, STS risk score, operative mortality, risk stratification.

Currently, various risk stratification models are utilized to predict operative mortality following open-heart surgery. Among these, the two most widely accepted and extensively validated models are the Society of Thoracic Surgeons (STS) score, which is based on North American databases, and the European System for Cardiac Operative Risk Evaluation II (EuroSCORE II), derived from European population data.[1,2] Both models employ complex, multivariable algorithms to calculate expected mortality rates, thereby providing surgeons with objective prognostic data.

However, the predictive performance of these risk scoring systems can vary significantly depending on the geographical region of application, population demographics, and the dynamics of the local healthcare system.[3] Studies have reported discrepancies in the "calibration" (the agreement between expected and observed mortality) and "discrimination" (the ability to distinguish between patients who survive and those who die) of these models. While some studies suggest that EuroSCORE II is a superior predictor of mortality, others emphasize the dominance of the STS score; conversely, several reports indicate that both scores may either overestimate or underestimate the actual operative risk.[4,5]

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In developing nations and among patient cohorts with distinct risk profiles, the local validation of these global metrics is of paramount importance for the accurate interpretation of surgical outcomes. Therefore, the primary objective of this study was to compare the predictive performance of the EuroSCORE II and STS PROM models in patients undergoing isolated coronary artery bypass grafting (CABG) at our center and to investigate the potential calibration defects these algorithms exhibit in clinical scenarios characterized by high surgical urgency.

METHODS

Study Design and Patient Selection

This retrospective, single-center, observational study was conducted at the Clinic of Cardiovascular Surgery, Batman Training and Research Hospital. The medical records of patients who underwent surgery at our clinic between January 2023 and January 2026 were retrospectively reviewed. Following the application of the exclusion criteria defined in the study protocol, 64 patients who underwent isolated CABG were included in the final study cohort. The study protocol was approved by the Clinical Research Local Ethics Committee of Batman Training and Research Hospital (decision no: 460, date: January 28, 2026), and the research was conducted in strict adherence to the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants included in the study prior to their surgical procedures, including consent for the use of their anonymized medical data for research purposes.

Patients aged 18 years or older who underwent isolated CABG under elective or emergency conditions were included in the study. Patients requiring concomitant cardiac procedures (e.g., valve repair/replacement, aortic surgery) and those undergoing re-operations were excluded. Furthermore, patients receiving preoperative mechanical circulatory support (IABP/ECMO) were excluded from the cohort. This methodological decision was implemented to prevent artificial deviations in the expected mortality calculations and to preserve the standardization of the statistical comparison between the STS PROM and EuroSCORE II models, owing to fundamental structural discrepancies in how these two models categorize and score mechanical support.

A total of 69 consecutive patients scheduled for CABG surgery at our clinic during the study period were initially evaluated. According to the predefined exclusion criteria in the study protocol, 5 patients (7.2%) who required concomitant cardiac procedures or received preoperative mechanical circulatory support systems were excluded. Following the application of these exclusion criteria, 64 patients who underwent isolated CABG were included in the final analysis.

Data Collection and Risk Scoring

The patients' demographic characteristics, preoperative clinical status, laboratory parameters, operative data, and postoperative outcomes were retrospectively extracted from the hospital data management system and patient medical records. Using preoperative data, the expected operative mortality risk percentages for each patient were calculated using the online calculators for EuroSCORE II (http://www.euroscore.org) and STS PROM (http://riskcalc.sts.org). The primary endpoint of the study was defined as operative mortality. Operative mortality was defined as in-hospital death or any-cause mortality occurring within the first 30 days post-discharge.

Surgical Strategy and Myocardial Protection

All procedures were performed via median sternotomy, utilizing standard cardiopulmonary bypass (CPB). As the revascularization strategy, the left internal mammary artery was routinely used to revascularize the left anterior descending artery, while saphenous vein grafts were preferred for other target vessels. Myocardial protection was achieved with isothermal blood cardioplegia across the entire cohort. In all cases involving saphenous vein grafts, proximal aortic anastomoses were routinely performed using a side-clamp technique.

Definition of Surgical Urgency Status and Calibration Analysis

he surgical urgency status of the included patients was classified into four categories in accordance with standard definitions from international cardiovascular surgery databases (STS and EuroSCORE): (1) Elective: Patients operated on a routine, scheduled basis without medical necessity for early intervention. (2) Urgent: Patients admitted via the emergency department or outpatient clinic who, for clinical reasons (e.g., unstable angina pectoris or critical coronary anatomy), underwent surgery during the same admission period without being discharged. (3) Emergency: Patients whose clinical status (e.g., hemodynamic instability or refractory ischemia) mandated surgical intervention before the beginning of the next routine working day. (4) Salvage: Patients in a life-threatening condition, such as cardiogenic shock, requiring emergency surgical intervention while intubated or under ongoing cardiopulmonary resuscitation.

The calibration performance of the risk scoring models was analyzed by calculating the observed-to-expected (O/E) mortality ratios across the entire cohort and within the aforementioned surgical urgency subgroups. An O/E ratio of 1.0 indicates perfect calibration, whereas values greater than 1.0 indicate that the model underestimates mortality.

Statistical Analysis

Statistical analyses of the study data were performed using R software (R Core Team, Vienna, Austria). The conformity of continuous variables to a normal distribution was evaluated using the Shapiro-Wilk test. The Mann-Whitney U test was used to compare continuous variables between two independent groups, while Fisher's exact test was preferred for analyzing the relationships between categorical variables. In the evaluation of operative times, because the limited number of cases in the subgroups would increase the risk of Type II error, no independent p-values were calculated for comparisons between these subgroups, and the data were presented solely as descriptive statistics. Analytical comparisons for these parameters were performed under non-parametric assumptions, using the Mann-Whitney U test to compare exclusively the "Elective" and "Emergency/Complicated" main groups.

The discriminative ability of the EuroSCORE II and STS PROM predictive models for forecasting mortality was evaluated using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) with its 95% confidence interval (CI) was calculated. The DeLong test was used to compare the AUCs of the two independent risk models. For model calibration, it was anticipated that the Hosmer-Lemeshow goodness-of-fit test would carry a high risk of violating asymptotic assumptions because of the limited sample size of the study cohort (n=64) and the low number of expected events (<5) in specific risk deciles. Therefore, this test was not applied. Instead, calibration performance was evaluated directly through O/E mortality ratios and

their corresponding 95% CIs. In all analyses, a two-tailed p-value of less than 0.05 was considered statistically significant.

RESULTS

Baseline Demographic and Clinical Characteristics

The mean age of the 64 patients included in the study was 62.1±10.1 years (range: 41-81), comprising 71.9% (n=46) males and 28.1% (n=18) females. Analysis of the preoperative comorbidity profile revealed the following comorbidities: Hypertension in 45.3% (n=29), diabetes mellitus (DM) in 26.6% (n=17), chronic obstructive pulmonary disease in 7.8% (n=5), previous cerebrovascular accident (CVA) in 6.2% (n=4), and chronic kidney disease (CKD) in 3.1% (n=2). The mean preoperative ejection fraction of the entire population was 53.5±8.7%, and the mean serum creatinine level was 0.94±0.24 mg/dL.

Analysis of Mortality and Associated Factors

Early postoperative mortality was observed in 21.9% (n=14) of the patients, while 78.1% (n=50) survived to discharge. When comparing the mortality (n=14) and survivor (n=50) groups, no statistically significant differences were detected with respect to age, gender, or the presence of DM, HT, CKD, or CVA (p>0.05). Quantitative analysis of preoperative hematological and biochemical parameters showed that although serum creatinine levels were relatively higher in the mortality group (1.03±0.29 mg/dL) compared to the survivor group (0.91±0.22 mg/dL), this difference did not reach statistical significance (p=0.154). Similarly, hematocrit levels (mortality: 43.13±4.74% *vs.* survivor: 42.74±4.95%, p=0.789) and platelet counts (mortality: 240.00±40.96×10³/µL *vs.* survivor: 244.76±79.38×10³/µL, p=0.763) demonstrated a homogeneous distribution between the two groups. In contrast, the preoperative white blood cell (WBC) count, a primary biomarker of the systemic inflammatory response, was significantly elevated in the mortality cohort (11.95±3.46×10³/µL) compared to the surviving cohort (9.15±2.74×10³/µL) (p=0.006) (Table 1).

Analysis of CPB and Cross-clamp Times Across Surgical Urgency Subgroups

Evaluation of operative durations across the entire study cohort (n=64) according to surgical urgency revealed that patients undergoing elective surgery (n=36) had a mean CPB time of 92.5 minutes and a mean aortic cross-clamp time of 50.8 minutes (Table 2). In patients operated on an urgent basis (n=19), the mean CPB time was 118.3 minutes (maximum: 208 min), and the mean cross-clamp time was 72.5 minutes (maximum: 133 min). In the emergency group (n=7), the mean CPB and cross-clamp times were 99.1 and 50.3 minutes, respectively. For cases in the salvage category (n=2), the mean CPB time was 139.0 minutes, and the mean cross-clamp time was 69.0 minutes.

When the cohort was dichotomized into two main categories: Elective (n=36) and emergency/complicated (urgent, emergency, and salvage; n=28) cases, the mean cross-clamp time in the emergency/complicated group (66.7 min) was significantly longer than in the elective cases (50.8 min) (p=0.037).

Calibration Performance of Risk Models Stratified by Surgical Urgency

Cross the overall population, the mean expected mortality rates were calculated as 0.88±0.58% for EuroSCORE II and 1.00±0.84% for STS PROM. The actual observed mortality was 21.9%, yielding overall cohort O/E ratios of 24.7 for EuroSCORE II and 21.9 for STS PROM. The calibration analysis findings, stratified by surgical urgency status, are as follows (Table 3).

- **Elective cases (n=36):** While the observed mortality was 2.8% (n=1), the expected mortality was calculated as 0.71% for EuroSCORE II and 0.74% for STS PROM; the O/E ratios were determined to be 3.9 for EuroSCORE II and 3.7 for STS PROM.

- **Urgent cases (n=19):** With an observed mortality of 31.6% (n=6), the expected mortality rates were calculated at 0.82% for EuroSCORE II and 0.96% for STS PROM, resulting in O/E ratios of 38.3 and 33.0, respectively.

Table 1. Distribution of demographic and clinical variables according to early mortality

Variables	Total (n=64)	Survivors (n=50)	Mortality (n=14)	p-value
Age (years)	62.12±10.05	61.30±9.32	65.07±12.24	0.300
Male sex, n (%)	46 (71.9%)	37 (74.0%)	9 (64.3%)	0.512
Diabetes mellitus, n (%)	17 (26.6%)	11 (22.0%)	6 (42.9%)	0.170
Hypertension, n (%)	29 (45.3%)	24 (48.0%)	5 (35.7%)	0.608
CKD, n (%)	2 (3.1%)	1 (2.0%)	1 (7.1%)	0.392
COPD, n (%)	5 (7.8%)	2 (4.0%)	3 (21.4%)	0.065
Previous CVA, n (%)	4 (6.2%)	3 (6.0%)	1 (7.1%)	1.000
EF (%)	53.52±8.67	53.90±8.22	52.14±10.32	0.565
WBC (10³/µL)	9.76±3.11	9.15±2.74	11.95±3.46	0.006*
HCT (%)	42.82±4.87	42.74±4.95	43.13±4.74	0.789
PLT (x10³/µL)	243.72±72.47	244.76±79.38	240.00±40.96	0.763
Creatinine (mg/dL)	0.94±0.24	0.91±0.22	1.03±0.29	0.154
STS score	1.00±0.84	0.81±0.46	1.66±1.42	0.005*
EuroSCORE II	0.88±0.58	0.75±0.28	1.36±1.01	0.006*

Continuous variables are presented as mean ± standard deviation; categorical variables are presented as absolute frequencies (n) and column percentages (%). EF: Ejection fraction; CKD: Chronic kidney disease; COPD: Chronic obstructive pulmonary disease; CVA: Cerebrovascular accident; WBC: White blood cell; HCT: Hematocrit; PLT: Platelet; STS: Society of Thoracic Surgeons; *: Indicates statistical significance (p<0.05).

Table 2. Statistical comparison of cardiopulmonary bypass and aortic cross-clamp times according to surgical urgency status

Surgical urgency	Patients (n)	CPB time (min)	p-value	Cross-clamp time (min)	p-value
Elective cases	36	92.5 (56-165)	0.061	50.8 (23-99)	0.037*
Emergency and complicated cases	28	115.0 (56-208)		66.7 (31-133)	
-Urgent	19	118.3 (56-208)	-	72.5 (31-133)	-
-Emergency	7	99.1 (67-144)	-	50.3 (33-75)	-
-Salvage	2	139.0 (80-198)	-	69.0 (51-87)	-

CPB: Cardiopulmonary bypass; min: Minutes. Data are presented as mean (minimum-maximum). Statistical analysis was performed exclusively between the two main categories ("Elective" and "Emergency and Complicated") using the Mann-Whitney U test; *: Indicates statistical significance (p<0.05).

Table 3. Calibration analysis of risk models according to surgical urgency status

Surgical urgency	Number of patients, n (%)	Observed mortality (%)	Expected EuroSCORE II (%)	Expected STS PROM (%)	EuroSCORE II O/E ratio (95% CI)*	STS PROM O/E ratio (95% CI)
Elective	36 (56.3%)	2.8% (n=1)	0.71%	0.74%	3.9 (0.1-21.8)	3.7 (0.1-20.9)
Urgent	19 (29.7%)	31.6% (n=6)	0.82%	0.96%	38.3 (14.1-83.8)	33.0 (12.1-71.6)
Emergency	7 (10.9%)	71.4% (n=5)	1.79%	1.57%	39.9 (13.0-93.1)	45.4 (14.8-106.2)
Salvage	2 (3.1%)	100.0% (n=2)	1.36%	3.97%	73.3 (8.9-265.6)	25.2 (3.1-91.0)
Overall cohort	64 (100%)	21.9% (n=14)	0.88%	1.00%	24.7 (13.6-41.7)	21.9 (12.0-36.7)

O/E: Observed/Expected; CI: Confidence interval, STS: Society of Thoracic Surgeons; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II.

- **Emergency cases (n=7):** The observed mortality was 71.4% (n=5), whereas the expected mortality was calculated as 1.79% for EuroSCORE II and 1.57% for STS PROM, yielding O/E ratios of 39.9 and 45.4, respectively.

- **Salvage cases (n=2):** Although a 100% observed mortality (n=2) was recorded, the expected risk scores were computed as 1.36% for EuroSCORE II and 3.97% for STS PROM; the resulting O/E ratios were 73.3 for EuroSCORE II and 25.2 for STS PROM.

Analysis of risk scores evaluating the preoperative risk stratification scores, the predicted risk scores of the patients who died were found to be significantly higher than those of the survivor group.

- **EuroSCORE II:** Calculated as a mean of 1.36±1.01 in the mortality group compared to 0.75±0.28 in the survivor group (p=0.006).

- **STS PROM:** Calculated as a mean of 1.66±1.42% in the mortality group versus 0.81±0.46% in the survivor group (p=0.005).

ROC analysis and predictive performance according to the ROC curve analysis conducted to evaluate the discriminative performances of the risk models in predicting mortality:

- The AUC for STS PROM was calculated as 0.749 (95% CI: 0.569-0.905),

- The AUC for EuroSCORE II was calculated as 0.740 (95% CI: 0.547-0.910) (Figure 1).

When the AUC values of the two risk models were compared using the DeLong test, no statistically significant difference was detected between them (p=0.866). The optimal cut-off points for both models were determined based on the maximum Youden index (J= Sensitivity + Specificity - 1) from the curve coordinates. Based on these calculations, the maximum Youden index (J=0.514) for the STS PROM model was identified at a threshold score >1.04. At this threshold, sensitivity and specificity were 71.4% and 80.0%, respectively (p<0.05). For the EuroSCORE II model, the maximum Youden index (J=0.511) was established at a score >1.17, yielding a sensitivity of 57.1% and a specificity of 94.0% (p<0.05).

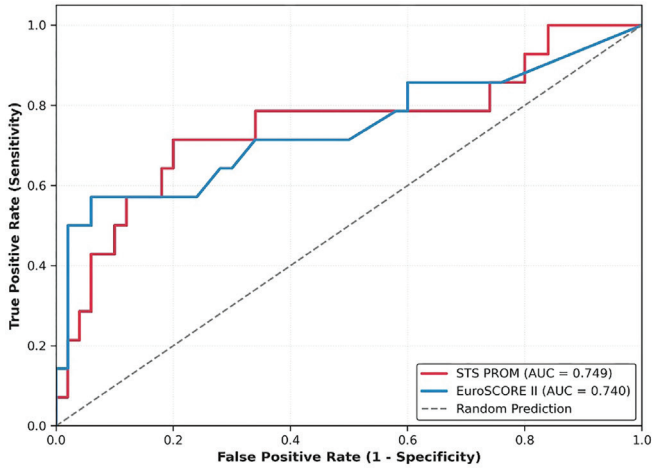

Figure 1. ROC curves demonstrating the discriminative performances of the STS PROM and EuroSCORE II risk models in predicting early postoperative mortality.

ROC: Receiver operating characteristic; STS: Society of Thoracic Surgeons; AUC: Area under the curve; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II.

DISCUSSION

In this study investigating the performance of the STS PROM and EuroSCORE II risk models in patients undergoing isolated CABG, surgical urgency had a marked effect on postoperative mortality. Our findings indicate that both models have a statistically acceptable discriminative ability for predicting mortality. However, no statistically significant differences were detected in the overall performance of the models. When evaluating model performance in our study cohort, the STS PROM model demonstrated greater sensitivity for identifying high-risk patients, whereas the EuroSCORE II model appeared more selective for identifying low-risk patients. This indicates that neither model provides absolute superiority over the other; rather, they offer different advantages in clinical application.

A review of the cardiovascular surgery literature reveals that mortality rates secondary to coronary artery bypass surgery range within a narrow band of 1-3% in stable elective cases,[6-8] whereas this rate can rise to 20-50% in patients operated on under emergency and salvage status due to cardiogenic shock or ongoing myocardial ischemia.[9] The overall operative mortality rate of 21.9% observed in our study is notably higher than that reported in standard elective series in the literature. This elevated operative mortality stems from the referral to our center of patients who could not be operated on at surrounding healthcare facilities because of high surgical risk or technical limitations. Consequently, this situation significantly increases the proportion of patients in our cohort who are taken directly to emergency surgery without the opportunity for preoperative stabilization. Therefore, the presented data do not reflect a standard, stable series of elective patients; rather, they represent the clinical outcomes of a specific high-risk patient population referred to our clinic because of regional circumstances.

The 2.8% mortality rate observed in elective cases in our study was consistent with global databases reported in the literature. In contrast, high mortality rates were recorded: 31.6% in the urgent group, 71.4% in the emergency group, and 100% in the salvage group. The elevated mortality observed in the emergency and salvage categories is associated with the patients' acute hemodynamic decompensation and limited physiological reserves during the perioperative period. This group comprises patients undergoing obligatory surgery against a background of cardiogenic shock or refractory ischemia, without the opportunity for preoperative medical optimization. The advanced comorbid burden and acute cardiovascular collapse diminish the capacity to compensate for additional systemic stress induced by surgical trauma and CPB, thereby increasing early mortality.

Although the mortality observed in the two cases operated on for salvage indications is not suitable for statistical generalization due to the limited sample size, it provides a clinical basis for explaining the prediction deviations of the models in high-risk groups. In patients undergoing surgery while in cardiogenic shock or receiving active resuscitation, the static parameters in standard risk-scoring systems may fail to fully reflect acute hemodynamic collapse. The high mortality trend observed in emergency and salvage operations may be related to dynamic pathophysiological processes, such as acute myocardial ischemia, profound systemic hypoperfusion, and cellular acidosis, which cannot be adequately incorporated into the mathematical scoring of the models in question.

In the performance evaluation of the risk scoring systems, the STS PROM and EuroSCORE II demonstrated statistically similar overall discriminative performance. The finding that the AUC values for both models were above the 0.70 threshold indicates that these scoring systems possess an acceptable level of discrimination in the examined cohort. Indeed, the analysis of the ROC curves using the DeLong test revealed no statistically significant difference between the two models. Model calibration was assessed descriptively using O/E ratios, and subgroup calibration estimates remain inherently unstable, with high variance due to very small sample sizes within these urgency strata.

When evaluating the clinical utility of risk models, sensitivity and specificity at pre-specified cut-off points are important alongside overall AUC values. Although the overall discriminatory capacities of both models were similar in our study, the sensitivity of the STS PROM model for predicting mortality (71.4%) was higher than that of EuroSCORE II (57.1%). This finding indicates that the STS PROM model may be more sensitive in detecting high-risk patients within the examined cohort, thereby reducing the probability of false negatives. On the other hand, the EuroSCORE II model, which exhibited a specificity of 94.0%, was more selective in distinguishing low-risk patients.

These performance differences between the two models may be related to the geographic origins and structural characteristics of the databases from which the algorithms were derived. Although both scoring systems were derived from large cardiac surgery populations, including valve and combined procedures, EuroSCORE II is based on a European-centric patient profile, whereas STS PROM originates from a North American database and incorporates much more detailed clinical variables in its calculation tool. Indeed, it has been reported in the literature that the EuroSCORE II model tends to underestimate mortality, particularly in the highest-risk patient quartile.[10] In our cohort, which predominantly comprises patients with severe clinical presentations referred to our clinic because of regional circumstances, the STS PROM model, which uses a more detailed set of variable parameters, was observed to predict mortality more accurately and to exhibit superior predictive performance in the high-risk group.

Another from our comparative group analyses is that preoperative leukocyte (WBC) levels were significantly higher in the group in which operative mortality was observed. The observed leukocytosis may indicate a systemic stress response secondary to acute myocardial injury or underlying subclinical inflammation. Indeed, there are studies in the literature reporting that preoperative systemic inflammatory burden may adversely affect postoperative clinical outcomes in patients undergoing CABG.[11] However, due to the retrospective nature of our study, the inability to evaluate more specific inflammatory.markers such as C-reactive protein, procalcitonin, or neutrophil-to-lymphocyte ratio across the entire cohort, and the inability to completely rule out potential concomitant infectious pathologies constitute important limitations. Considering that multivariate analysis could not be performed due to the limited number of events, the detected preoperative WBC elevation should be evaluated as an observed association and as a "hypothesis-generating" finding for future, more comprehensive studies rather than as a definitive independent risk factor.

In isolated CABG, surgical urgency status, which is a primary indicator of preoperative physiological status, emerges as one of the important clinical determinants of early postoperative mortality. Our research findings indicate that although the STS PROM and EuroSCORE II risk

models may possess a general discriminative ability in this patient group, they tend to underestimate the actual mortality rate, particularly in emergency and salvage cases. In this context, for hemodynamically unstable high-risk cases, it is clinically more appropriate to approach with caution the predictive deviations that standard scoring systems may present, and to center clinical decision-making on the patient's immediate physiological decompensation rather than on algorithmic scores. Furthermore, findings such as preoperative leukocyte elevation, which were found to be associated with mortality in comparative group analyses, may serve as hypothesis-generating features to be evaluated in future large-scale, multivariate studies.

Certain methodological limitations should be considered when evaluating the results of our study. First, the single-center, retrospective design of the study may limit the direct applicability of the findings to the general population. Although the consecutive inclusion of patients contributed to reducing the risk of selection bias, it cannot entirely eliminate this risk.

Second, the most fundamental limitation from a biostatistical perspective is the limited total number of operative mortality events. In the context of statistical validity, constructing a reliable multivariate logistic regression model requires a minimum of 10 events per independent variable, in accordance with the "events per variable" principle. Because the number of events in our sample did not fully meet this statistical assumption, we avoided multivariate analysis to prevent model overfitting. This methodological necessity restricted the ability to clearly evaluate whether factors such as surgical urgency, advanced age, or elevated leukocyte levels are independent prognostic predictors of postoperative mortality.

Third, due to the restricted sample size across different urgency strata, detailed and statistically powered subgroup analyses could not be performed. The highly limited number of patients undergoing salvage surgery necessitates that the high mortality observed in this group be interpreted as a clinical observational trend rather than definitive statistical evidence, which restricts the deep interpretability of subgroup-specific outcomes. Consequently, the data obtained are exploratory in nature; it is considered that multicenter and prospective studies with higher statistical power may be required to validate the independent prognostic value of these observed associations and the calibration performances of the models in high-risk groups.

Ethics

Ethics Committee Approval: The study protocol was approved by the Clinical Research Local Ethics Committee of Batman Training and Research Hospital (decision no: 460, date: January 28, 2026), and the research was conducted in strict adherence to the principles of the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all participants included in the study prior to their surgical procedures, including consent for the use of their anonymized medical data for research purposes.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.A., T.C., A.İ.B.; Concept: A.A.; Design: A.A., T.C.; Data Collection or Processing: A.A., A.İ.B.; Analysis or Interpretation: A.A.; Literature Search: A.A., T.C., A.İ.B.; Writing: A.A.

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REFERENCES

1. Jacobs JP, Shahian DM, Badhwar V, Thibault DP, Thourani VH, Rankin JS, et al. The Society of Thoracic Surgeons 2021 adult cardiac surgery risk models for multiple valve operations. Ann Thorac Surg. 2022;113:511-8. doi: 10.1016/j.athoracsur.2021.03.089.
2. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. EuroSCORE II. Eur J Cardiothorac Surg. 2012;41:734-44; discussion 744-5. doi: 10.1093/ejcts/ezs043.
3. Wolf PJW, Amato VL. Assessment of EuroSCORE II and STS score performance and the impact of surgical urgency in isolated coronary artery bypass graft surgery at a referral center in São Paulo, Brazil. Braz J Cardiovasc Surg. 2024;39:e20230282. doi: 10.21470/1678-9741-2023-0282.
4. Kunt AG, Kurtcephe M, Hidiroglu M, Cetin L, Kucuker A, Bakuy V, et al. Comparison of original EuroSCORE, EuroSCORE II and STS risk models in a Turkish cardiac surgical cohort. Interact Cardiovasc Thorac Surg. 2013;16:625-9. doi: 10.1093/icvts/ivt022.
5. Shapira-Daniels A, Blumenfeld O, Korach A, Rudis E, Izhar U, Shapira OM. The American Society of Thoracic Surgery Score versus EuroSCORE I and EuroSCORE II in Israeli patients undergoing cardiac surgery. Isr Med Assoc J. 2019;21:671-5.
6. Chua TKT, Gao F, Chia SY, Sin KYK, Naik MJ, Tan TE, et al. Long-term mortality after isolated coronary artery bypass grafting and risk factors for mortality. J Cardiothorac Surg. 2024;19:429. doi: 10.1186/s13019-024-02943-0.
7. Ferguson TB. Mortality in coronary artery bypass grafting: what's next? Circulation. 2012;125:2409-11. doi: 10.1161/CIRCULATIONAHA.112.106856.
8. Shahian DM, O'Brien SM, Sheng S, Grover FL, Mayer JE, Jacobs JP, et al. Predictors of long-term survival after coronary artery bypass grafting surgery: results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database (the ASCERT study). Circulation. 2012;125:1491-500. doi: 10.1161/CIRCULATIONAHA.111.066902.
9. Santarpino G, Ruggieri VG, Mariscalco G, Bounader K, Beghi C, Fischlein T, et al. Outcome in patients having salvage coronary artery bypass grafting. Am J Cardiol. 2015;116:1193-8. doi: 10.1016/j.amjcard.2015.07.034.
10. Patrat-Delon S, Rouxel A, Gacouin A, Revest M, Flécher E, Fouquet O, et al. EuroSCORE II underestimates mortality after cardiac surgery for infective endocarditis. Eur J Cardiothorac Surg. 2016;49:944-51. doi: 10.1093/ejcts/ezv223.
11. Walker AE, Seibert SM, Donato AJ, Pierce GL, Seals DR. Vascular endothelial function is related to white blood cell count and myeloperoxidase among healthy middle-aged and older adults. Hypertension. 2010;55:363-9. doi: 10.1161/HYPERTENSIONAHA.109.145870.

ORIGINAL ARTICLE

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CARDIOVASCULAR SURGERY AND INTERVENTIONS

Sleep quality, daytime dysfunction, and health-related quality of life in normotensive versus hypertensive pregnant women: A cross-sectional analytical study

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ABSTRACT

Objectives: Sleep disturbances are common during pregnancy and are increasingly associated with adverse maternal outcomes, including hypertensive disorders. However, direct comparisons of sleep quality and quality of life between normotensive and hypertensive pregnant women remain limited. The aim of this study is to compare sleep quality, daytime dysfunction, quality of life (QOL), and clinical parameters between normotensive and hypertensive pregnant women.

Patients and methods: This cross-sectional analytical study included 100 pregnant women attending an obstetrics outpatient clinic. Participants were divided into two groups of 50 each: Normotensive and hypertensive. Socio-demographic and clinical data were recorded. Sleep quality was assessed using the Pittsburgh sleep quality index (PSQI), and QOL was evaluated using the QOL-gravidarum scale. Laboratory parameters, including hemoglobin, platelet count, urea, creatinine, and glomerular filtration rate (GFR), were analyzed. Statistical analyses were performed using the independent-samples t-test, the Mann-Whitney U test, and the chi-square test; $p<0.05$ was considered significant.

Results: Hypertensive pregnant women had significantly higher systolic and diastolic blood pressure ($p<0.001$). They exhibited longer sleep latency, shorter sleep duration, and lower sleep efficiency (all $p<0.001$). PSQI total scores were significantly higher in the hypertensive group ($p<0.001$), indicating poorer sleep quality. Sleep disturbances and daytime dysfunction were more frequent ($p<0.001$), and QOL scores were significantly worse ($p<0.001$). In hypertensive pregnancies, urea and creatinine levels were higher, while GFR was lower ($p<0.001$).

Conclusion: Hypertensive pregnant women demonstrate significantly poorer sleep quality, increased daytime dysfunction, and reduced QOL. These findings highlight the importance of incorporating sleep assessment into routine clinical evaluation of hypertensive pregnancies.

Keywords: Pregnancy, hypertension, sleep quality, quality of life, daytime dysfunction.

Sleep is a core biological requirement that sustains physiological stability and orchestrates neuroendocrine balance. Disruptions in sleep architecture have been strongly associated with a broad spectrum of pathological conditions, including cardiovascular disorders, metabolic abnormalities, diabetes, and mental health disturbances.[1,2] Contemporary research increasingly recognizes that altered sleep patterns may not merely reflect underlying disease states but can actively contribute to their initiation and progression.[3]

Gestation is characterized by profound systemic adaptations involving endocrine, anatomical, and psychological domains. Although progesterone is known to promote sedation, several pregnancy-specific factors—such as mechanical pressure from the enlarging uterus, reflux symptoms, fetal movements, and nocturnal urinary frequency—may interfere with normal sleep physiology, particularly in advanced gestational stages.[4,5] Epidemiological findings suggest that impaired sleep quality affects nearly half of pregnant women, with reported

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rates ranging from 40% to 60%.[6] Despite this, such disturbances are frequently regarded as physiological variations rather than clinically significant abnormalities.

Hypertension continues to be a leading determinant of adverse health outcomes both globally and in pregnancy.[7] Hypertensive disorders of pregnancy, most notably preeclampsia, involve complex mechanisms including endothelial injury and systemic inflammatory activation.[8] Evidence suggests that sleep disturbances may amplify sympathetic nervous system activity, thereby increasing blood pressure and facilitating the emergence of hypertensive conditions.[9] Furthermore, insufficient sleep duration and compromised sleep quality have been identified as independent contributors to elevated blood pressure.[10]

The Pittsburgh sleep quality index (PSQI) is a standardized and widely accepted instrument used to quantify sleep quality across multiple domains, including sleep initiation, duration, efficiency, disturbances, medication use, and daytime impairment.[11,12] Quality of life (QOL), encompassing physical, emotional, and social dimensions, was evaluated in the present study using the QOL-gravidarum (GRAV) scale.[13]

Although both sleep disturbances and hypertensive conditions in pregnancy have been extensively examined individually, direct comparative analyses between normotensive and hypertensive pregnant populations remain scarce. Therefore, this study was designed to explore differences in sleep parameters, QOL, and clinical characteristics between these two groups.

PATIENTS AND METHODS

This cross-sectional study enrolled 100 pregnant women who presented to an obstetrics outpatient clinic. Participants were stratified into two groups of 50 each: Normotensive and hypertensive. The hypertensive cohort included individuals diagnosed with chronic hypertension, gestational hypertension, or preeclampsia.

Ethical approval was granted by the Clinical Research Ethics Committee İzmir Bakırçay University (approval no: 2258, date: 14.05.2025), and written informed consent was obtained from all participants. The study protocol adhered to the principles outlined in the Declaration of Helsinki.

Demographic and clinical data were collected, including age, education level, employment status, smoking habits, family structure, and obstetric history. Blood pressure measurements were obtained, and laboratory analyses included hemoglobin, platelet count, leukocyte count, urea, creatinine, and glomerular filtration rate (GFR).

Sleep quality was assessed using the PSQI, which evaluates sleep characteristics over the preceding month, with higher scores reflecting poorer sleep quality.[11,12] QOL was measured using the QOL-GRAV scale.[13]

Statistical Analysis

Statistical analyses were performed using SPSS software. Data distribution was assessed with the Shapiro-Wilk test. Parametric data were analyzed using the independent samples t-test, while non-parametric data were analyzed using the Mann-Whitney U test. Categorical variables were compared using the chi-square test. Statistical significance was defined as $p<0.05$.

RESULTS

Anthropometric characteristics were comparable between the two groups, with no statistically significant differences in body weight, height or body mass index ($p>0.05$), indicating homogeneous baseline physical parameters.

Socio-demographic analysis revealed significant disparities. Lower educational attainment, higher unemployment rates, greater prevalence of extended-family living arrangements, and higher smoking rates were observed in the hypertensive group ($p<0.05$). Residence and marital status did not differ significantly (Table 1).

Obstetric variables, including gestational age, gravidity, and parity, were similar across groups ($p>0.05$) (Table 2).

Biochemical analysis demonstrated that hypertensive pregnant women had significantly elevated urea and creatinine levels and a reduced GFR ($p<0.001$). Platelet counts were also lower in this group ($p<0.001$), while hemoglobin and leukocyte counts did not differ significantly. Thyroid-stimulating hormone levels were lower in the hypertensive group ($p=0.033$).

Sleep assessment revealed that hypertensive pregnant women had significantly prolonged sleep latency, reduced sleep duration, and decreased sleep efficiency ($p<0.001$). Total PSQI scores were significantly higher, indicating poorer sleep quality.

Subcomponent analysis confirmed increased sleep disturbances and daytime dysfunction in the hypertensive group ($p<0.001$). Subjective sleep quality was also significantly impaired.

QOL scores were significantly lower in hypertensive pregnant women ($p<0.001$) (Table 3).

DISCUSSION

The present findings indicate that hypertensive disorders during pregnancy are associated with substantial deterioration in both sleep quality and overall QOL. These results support the concept that hypertension in pregnancy represents a multifaceted condition involving not only vascular dysregulation but also neuroendocrine imbalance, metabolic alterations, and psychosocial stressors.

The significantly higher PSQI scores observed in hypertensive pregnant women confirm the presence of pronounced sleep impairment. This aligns with previous literature demonstrating a bidirectional relationship between sleep disturbances and hypertension.[9,14] Sleep plays a critical role in cardiovascular homeostasis, and its disruption may contribute to sustained elevations in blood pressure through autonomic imbalance.

Prolonged sleep latency may reflect heightened sympathetic nervous system activation. Under normal physiological conditions, sleep onset is facilitated by parasympathetic dominance; however, this regulatory mechanism appears to be impaired in hypertensive individuals.[15] This shift toward sympathetic predominance may also contribute to increased cardiovascular reactivity.

Reduced sleep duration observed in hypertensive pregnant women may further exacerbate neuroendocrine dysregulation. Sleep restriction has been associated with elevated cortisol levels and increased catecholamine secretion, both of which contribute to hypertension.[3,10]

Table 1. Socio-demographic characteristics

Parameter	Normal	Hypertensive	p-value
Age (year)	30.92±4.07	32.02±2.96	0.207
Weight (kg)	80.20±8.10	79.10±8.45	0.58
Height (m)	1.64±0.05	1.63±0.05	0.44
BMI (kg/m²)	29.80±3.10	29.50±3.25	0.67
Educational level			0.002
Primary school	6 (12%)	18 (36%)	
Secondary school	10 (20%)	14 (28%)	
High school	20 (40%)	12 (24%)	
University	14 (28%)	6 (12%)	
Place of residence			0.544
Rural	18 (36%)	20 (40%)	
Urban	32 (64%)	30 (60%)	
Employment status			0.006
Unemployed	30 (60%)	42 (84%)	
Employed	20 (40%)	8 (16%)	
Family structure			0.003
Nuclear family	38 (76%)	26 (52%)	
Extended family	12 (24%)	24 (48%)	
Smoking status			0.013
No	42 (84%)	30 (60%)	
Yes	8 (16%)	20 (40%)	
Marital status			>0.05
Single	10 (20%)	8 (16%)	
Married	40 (80%)	42 (84%)	

BMI: Body mass index.

Table 2. Obstetric and clinical characteristics

Parameter	Normal	Hypertensive	p-value
Number of pregnancies	2.20±1.28	2.42±1.51	0.724
Number of children	0.92±0.67	1.14±1.21	0.733
Gestational week			0.661
20-35 week	34 (68%)	32 (64%)	
36-38 week	16 (32%)	18 (36%)	
Blood pressure status			**<0.001**
Normal	40 (80%)	0 (0%)	
Chronic hypertension	0 (0%)	30 (60%)	
Gestational hypertension	8 (16%)	0 (0%)	
Preeclampsia	2 (4%)	20 (40%)	
Antihypertensive medication use			**<0.001**
No	46 (92%)	10 (20%)	
Yes	4 (8%)	40 (80%)	

Additionally, insufficient sleep has been linked to insulin resistance, oxidative stress, and systemic inflammation, suggesting a broader metabolic impact.

Decreased sleep efficiency indicates fragmented sleep architecture and frequent nocturnal awakenings. Such disruptions may impair restorative sleep processes, thereby contributing to both physical and psychological dysfunction. Prior studies have demonstrated that poor sleep quality is associated with hypertensive disorders of pregnancy, particularly preeclampsia,[16,17] suggesting a potential role in disease progression.

Table 3. Laboratory parameters, quality of life, and sleep characteristics

Parameter	Normal	Hypertensive	p-value
Hb (g/dL)	10.64±1.16	10.50±1.21	0.113
PLT (10^3/μL)	215.52±35.70	172.28±49.19	**<0.001**
WBC (10^3/μL)	9.79±1.10	9.16±0.88	0.324
Urea (mg/dL)	15.40±2.10	19.39±2.28	**<0.001**
Creatinine (mg/dL)	0.34±0.36	0.94±0.16	**<0.001**
GFR (mL/min)	111.02±4.44	102.74±6.01	**<0.001**
TSH (μIU/mL)	2.12±0.29	1.98±0.24	**0.033**
QOL-GRAV score	16.86±5.57	32.34±8.08	**<0.001**
QOL-GRAV category			**<0.001**
Excellent	12 (24%)	2 (4%)	
Very good	20 (40%)	8 (16%)	
Good	14 (28%)	18 (36%)	
Poor	4 (8%)	22 (44%)	
Sleep latency (min)	17.40±8.76	27.10±10.98	**<0.001**
Sleep duration (hours)	8.84±1.04	6.94±0.96	**<0.001**
Sleep efficiency (%)	85.10±5.30	72.60±7.77	**<0.001**
Subjective sleep quality			**<0.001**
Very good	16 (32%)	2 (4%)	
Good	22 (44%)	10 (20%)	
Poor	10 (20%)	22 (44%)	
Very poor	2 (4%)	16 (32%)	
Sleep disturbances			**<0.001**
None	20 (40%)	4 (8%)	
<1/week	18 (36%)	10 (20%)	
1-2/week	10 (20%)	18 (36%)	
≥3/week	2 (4%)	18 (36%)	
Daytime dysfunction			**<0.001**
None	24 (48%)	6 (12%)	
<1/week	16 (32%)	12 (24%)	
1-2/week	8 (16%)	18 (36%)	
≥3/week	2 (4%)	14 (28%)	
Pittsburgh score	1.98±1.55	6.36±2.21	**<0.001**

Hb: Hemoglobin; PLT: Platelet count; WBC: White blood cell count; GFR: Glomerular filtration rate; TSH: Thyroid-stimulating hormone; QOL-GRAV: Quality of life in pregnancy scale; PSQI: Pittsburgh sleep quality index.

The increased prevalence of daytime dysfunction highlights the functional consequences of impaired sleep. Cognitive domains such as attention, executive function, and decision-making are particularly vulnerable to sleep deprivation.[18] In pregnant women, these impairments may have additional implications for maternal well-being and daily functioning.

The observed reduction in QOL among hypertensive pregnant women underscores the multidimensional burden of the condition. Chronic disease, psychological stress, and the risk of adverse maternal and fetal outcomes likely contribute to this decline.[19,20] These findings emphasize the importance of addressing both physical and psychosocial aspects of care.

Renal function parameters further illustrate the systemic impact of hypertension. Elevated urea and creatinine levels, along with reduced GFR, suggest impaired renal perfusion and altered hemodynamics.[8] These changes may also reflect broader vascular dysfunction affecting multiple organ systems.

Inflammation appears to be a central mechanism linking sleep disturbances and hypertension. Sleep disruption has been shown to increase proinflammatory cytokine production, which may contribute to endothelial dysfunction and vascular injury.[15,21] This inflammatory cascade provides a plausible explanation for the observed associations between sleep impairment, hypertension, and adverse clinical outcomes.

Taken together, these findings support the hypothesis that sleep disturbances are not merely secondary symptoms but may play an active role in the pathophysiology of hypertensive disorders in pregnancy. Addressing sleep quality may, therefore, represent a therapeutic target.

This study has several limitations. First, due to its cross-sectional design, causal relationships between hypertensive disorders of pregnancy and sleep disturbances could not be established. In addition, the single-center setting and relatively limited sample size may reduce the generalizability of the findings. Sleep quality was assessed using self-reported questionnaires rather than objective methods, which may have introduced subjective bias into the assessment. Furthermore, psychological factors such as anxiety and stress were not comprehensively evaluated and may have acted as confounding variables. Despite these limitations, our study provides valuable evidence regarding the relationship between hypertensive disorders of pregnancy, impaired sleep quality, and reduced QOL.

Hypertensive pregnant women exhibit marked impairments in sleep quality, increased daytime dysfunction, and reduced QOL compared to normotensive individuals. These findings suggest that sleep disturbances are closely intertwined with the underlying mechanisms of hypertensive disorders in pregnancy rather than representing incidental observations. Integrating sleep assessment into routine clinical practice may enhance patient management and improve maternal outcomes. Future longitudinal and interventional studies are required to further elucidate causal pathways and evaluate the effectiveness of sleep-targeted interventions.

Ethics

Ethics Committee Approval: Ethical approval was granted by the Clinical Research Ethics Committee İzmir Bakırçay University (approval no: 2258, date: 14.05.2025).

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

Footnotes

Authorship Contributions

Concept: Z.Y.E.; Design: A.R.K.; Data Collection or Processing: Z.Y.E.; Analysis or Interpretation: A.R.K.; Literature Search: Z.Y.E.; Writing: A.R.K.

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

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REFERENCES

1. Buysse DJ. Sleep health: can we define it? Does it matter? Sleep. 2014;37:9-17. doi: 10.5665/sleep.3298.
2. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J. 2011;32:1484-92. doi: 10.1093/eurheartj/ehr007.
3. Grandner MA. Sleep, health, and society. Sleep Med Clin. 2017;12:1-22. doi: 10.1016/j.jsmc.2016.10.012.
4. Mindell JA, Jacobson BJ. Sleep disturbances during pregnancy. J Obstet Gynecol Neonatal Nurs. 2000;29:590-7. doi: 10.1111/j.1552-6909.2000.tb02072.x.
5. Facco FL, Kramer J, Ho KH, Zee PC, Grobman WA. Sleep disturbances in pregnancy. Obstet Gynecol. 2010;115:77-83. doi: 10.1097/AOG.0b013e3181c4f8ec.
6. Sedov ID, Cameron EE, Madigan S, Tomfohr-Madsen LM. Sleep quality during pregnancy: a meta-analysis. Sleep Med Rev. 2018;38:168-76. doi: 10.1016/j.smrv.2017.06.005.
7. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020;16:223-37. doi: 10.1038/s41581-019-0244-2.
8. Roberts JM, Hubel CA. The two stage model of preeclampsia: variations on the theme. Placenta. 2009;30(Suppl A):S32-7. doi: 10.1016/j.placenta.2008.11.009
9. Javaheri S, Redline S. Insomnia and risk of cardiovascular disease. Chest. 2017;152:435-44. doi: 10.1016/j.chest.2017.01.026.
10. Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, et al. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. Hypertension. 2006;47:833-9. doi: 10.1161/01.HYP.0000217362.34748.e0.
11. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28:193-213. doi: 10.1016/0165-1781(89)90047-4.
12. Mavi CÜ, Akdağ B, Kök B, Öztürk EÖ, Aydemir Ö. Validity and reliability of the Turkish version of the brief Pittsburgh sleep quality index. Noro Psikiyatr Ars. 2026;63:387-92. doi: 10.29399/npa.29240.
13. Ayan G, Apay SE. Turkish adaptation, validity, and reliability study of the quality of life gravidarum (QOL-GRAV) scale. BMC Pregnancy Childbirth. 2025;25:115. doi: 10.1186/s12884-025-07159-1.
14. Li L, Gan Y, Zhou X, Jiang H, Zhao Y, Tian Q, et al. Insomnia and the risk of hypertension: a meta-analysis of prospective cohort studies. Sleep Med Rev. 2021;56:101403. doi: 10.1016/j.smrv.2020.101403.
15. Irwin MR. Sleep and inflammation: partners in sickness and in health. Nat Rev Immunol. 2019;19:702-15. doi: 10.1038/s41577-019-0190-z.
16. Zhu J, Zheng T, Jin H, Wei M, Yu J, Ni J, et al.; Early Life Plan Project. Sleep disturbances in early gestation and the risks of hypertensive disorders of pregnancy: a prospective cohort study. Am J Epidemiol. 2024;193:479-88. doi: 10.1093/aje/kwad223.
17. Abbasi M, Rasoal D, Kharaghani R, Khanjari Z, Barati Z, Hosseinkhani A, et al. Association between sleep disorders and preeclampsia: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2024;37:2419383. doi: 10.1080/14767058.2024.2419383.
18. McSorley VE, Bin YS, Lauderdale DS. Associations of sleep characteristics with cognitive function and decline among older adults. Am J Epidemiol. 2019;188:1066-75. doi: 10.1093/aje/kwz037.
19. Trevisol DJ, Moreira LB, Kerkhoff A, Fuchs SC, Fuchs FD. Health-related quality of life and hypertension: a systematic review and meta-analysis of observational studies. J Hypertens. 2011;29:179-88. doi: 10.1097/HJH.0b013e328340d76f.
20. Carvalho MV, Siqueira LB, Sousa AL, Jardim PC. The influence of hypertension on quality of life. Arq Bras Cardiol. 2013;100:164-74. English, Portuguese. doi: 10.5935/abc.20130030.
21. Redman CW, Sargent IL. Placental stress and pre-eclampsia: a revised view. Placenta. 2009;30(Suppl A):S38-42. doi: 10.1016/j.placenta.2008.11.021.

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CARDIOVASCULAR SURGERY AND INTERVENTIONS

Predictive value of heart rate recovery and QT dispersion in determining the presence and severity of coronary artery disease

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ABSTRACT

Objectives: The aim of this study was to investigate the value of non-invasive parameters, including heart rate recovery (HRR), QT dispersion (QTd) and the Duke treadmill score (DTS), in predicting the presence and severity of coronary artery disease (CAD) as quantified by the Gensini score.

Patients and methods: In this prospective observational study, 200 patients with stable angina pectoris and positive exercise stress tests were enrolled. All participants underwent coronary angiography (CAG). Patients were categorized into three groups based on CAG results: Normal coronary arteries (27%), non-critical CAD (47%), and critical CAD (26%). Electrocardiogram markers (QTd) and exercise parameters (HRR1, HRR2, DTS, and rate-pressure product) were analyzed in relation to the Gensini score.

Results: Significant differences were observed among the three groups in QTd, HRR1, HRR2, and DTS ($p<0.001$). The critical CAD group exhibited the highest QTd and the lowest HRR and DTS values. Correlation analyses revealed that the Gensini score was strongly associated with QTd ($r=0.742$) and negatively associated with HRR1 ($r=-0.672$) and DTS ($r=-0.632$) ($p<0.001$). Receiver operating characteristic analysis identified QTd >32 ms (area under the curve [AUC]: 0.842) and HRR1 <11 bpm (AUC: 0.815) as significant predictors of critical stenosis, outperforming traditional markers. Multivariate logistic regression analysis identified QTd (odds ratio [OR]: 1.09, 95% confidence interval [CI]: 1.04-1.14, $p=0.002$), HRR1 (OR: 0.82, 95% CI: 0.75-0.90, $p=0.001$), and Duke score (OR: 0.88, 95% CI: 0.81-0.96, $p=0.015$) as independent predictors of critical CAD.

Conclusion: QTd and HRR1 are robust, non-invasive indicators of the presence and anatomical severity of CAD. Integrating these parameters into routine clinical evaluation can improve risk stratification and the early identification of patients requiring invasive intervention.

Keywords: Coronary artery disease, heart rate, arrhythmias, cardiac, exercise test, and severity of illness index.

Coronary artery disease (CAD) often remains asymptomatic until sudden cardiac death occurs, necessitating effective early diagnostic tools. While the exercise stress test (EST) is a cost-effective method, its variable sensitivity and specificity require additional parameters to enhance clinical efficacy.[1]

Heart rate recovery (HRR) is a powerful, non-invasive physiological index that reflects the dynamic interplay between the parasympathetic and sympathetic branches of the autonomic nervous system following exercise. While the overall decline in heart rate (HR) post-exertion serves as a marker of autonomic health, HRR during the first and second minutes (HRR1 and HRR2) represent distinct physiological phases. HRR1 (1-minute) is primarily driven by rapid vagal (parasympathetic) reactivation. Within the first 60 seconds of cessation, the sudden withdrawal of central command and the activation of baroreceptors lead to a surge in acetylcholine release, causing a sharp deceleration in heart rate.[2] A blunted HRR1 is widely recognized as an independent predictor of all-cause mortality and sudden cardiac death, as it signifies vagal incompetence.[3] In contrast, HRR2 reflects the subsequent

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phase of autonomic stabilization, which is more closely associated with sympathetic withdrawal and the gradual clearance of circulating catecholamines from the bloodstream. Research indicates that a delayed HRR2 is specifically linked to sustained hemodynamic recovery and advanced coronary atherosclerotic burden.[4] Furthermore, blunted HRR often serves as an early marker of autonomic dysfunction in chronic conditions such as diabetes mellitus, hypertension, and heart failure, reflecting diminished vagal tone long before clinical symptoms manifest.[5-7]

The clinical integration of these autonomic markers is particularly valuable when correlated with the anatomical severity of CAD, which is objectively quantified using the Gensini score. The Gensini score serves as a comprehensive angiographic tool that integrates the degree of luminal narrowing with the functional importance of specific vascular segments. Unlike other scoring systems, it offers a more granular assessment of the total atherosclerotic burden by incorporating lesions with as little as 25% stenosis, which are often overlooked but contribute significantly to overall disease prevalence.[8] Clinical trials have demonstrated that higher Gensini scores are strongly associated with multi-vessel disease and increased major adverse cardiovascular events.[9] By evaluating HRR and the Gensini score in tandem, clinicians can better understand how autonomic dysregulation parallels the extent of coronary artery stenosis, thereby enhancing risk stratification in patients with stable angina.

Alongside autonomic indices, QT dispersion (QTd) has gained prominence in clinical research as a crucial marker of ventricular repolarization heterogeneity.[10] QTd is defined as the difference between the maximum and minimum QT intervals measured on a standard 12-lead electrocardiogram (ECG); it reflecting the regional variations in myocardial recovery time. The clinical significance of QTd is well-documented across various cardiovascular pathologies. Seminal studies have demonstrated that elevated QTd is a potent predictor of sudden cardiac death, particularly in the post-myocardial infarction period and in patients with heart failure.[11] For instance, research has shown that patients with CAD exhibit significantly higher QTd values compared to healthy individuals, and this increase directly parallels the extent of myocardial ischemia.[12] Furthermore, contemporary studies have highlighted that QTd is not merely a static measure, but is dynamically influenced by the autonomic nervous system; a blunted vagal tone—similar to that seen in impaired HRR— often exacerbates repolarization heterogeneity. By evaluating QTd in conjunction with the Gensini score, researchers can identify a "high-risk phenotype" characterized by both advanced anatomical stenosis and heightened electrical instability.[13]

Rate pressure product (RPP), calculated as systolic blood pressure (SBP) × heart rate, reflects myocardial oxygen demand; values exceeding 10,000 are associated with increased cardiovascular risk.[14]

This study evaluates the relationship between CAD severity and the HRR, QTd, and RPP parameters. This investigation appears to be the first to analyze the combined correlation of these parameters with the Gensini score.

PATIENTS AND METHODS

Study Population

This prospective observational study enrolled consecutive patients presenting with stable angina pectoris between May 1, 2021, and December 1, 2021. Inclusion criteria were age >18 years, no prior CAD history, and stable angina pectoris. Exclusion criteria included previous coronary interventions (percutaneous coronary intervention or coronary artery bypass grafting), arrhythmias, severe valvular disease, heart failure, exhibited conduction abnormalities (such as left bundle branch block, right bundle branch block, or pacemaker rhythms), baseline ECG changes interfering with QT measurement, presence of active infections, malignancies, hematological or immunological disorders, as well as end-stage renal or hepatic diseases. A total of 1154 patients were initially screened. After applying the exclusion criteria, 200 patients were eligible (Figure 1) and successfully completed the study protocol, which included EST and invasive coronary angiography (ICA).

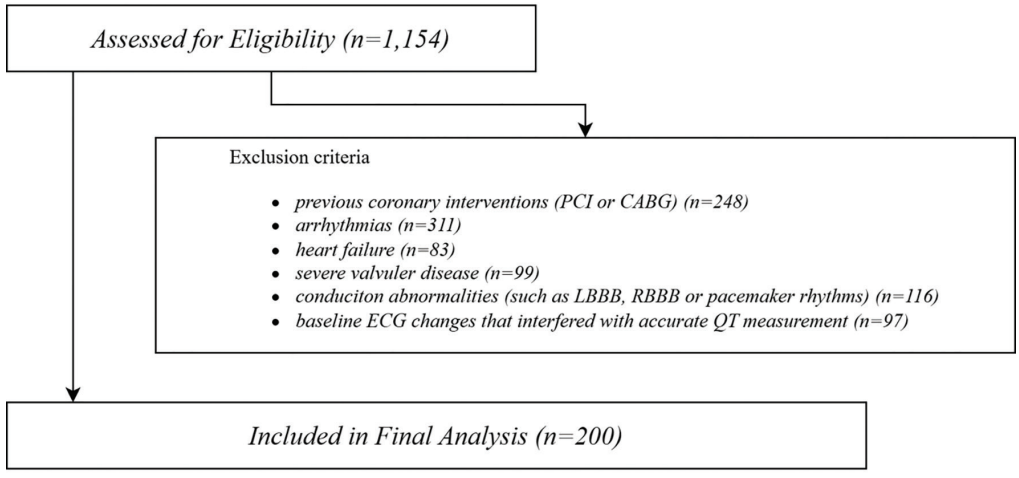

Figure 1. Flowchart of the study population recruitment and exclusion process.
CABG: Coronary artery bypass grafting; ECG: Electrocardiogram; LBBB: Left bundle branch block; PCI: Percutaneous coronary intervention; RBBB: Right bundle branch block.

Their EST parameters and coronary angiographic findings were analyzed to determine the relationship between autonomic/repolarization markers and the anatomical severity of CAD at the time of diagnosis.

Informed consent was obtained from all participants. Demographic, clinical, and laboratory data were recorded prior to coronary angiography (CAG).

QTd Measurement

QTd was calculated from a standard 12-lead resting ECG recorded at a paper speed of 25 mm/s and an amplitude of 10 mm/mV. The measurements were performed manually by two independent cardiologists who were blinded to the patients' clinical and angiographic data. To enhance precision, the ECG tracings were digitized and analyzed using high-resolution screen calipers with 3x magnification. The QT interval was measured from the onset of the QRS complex to the point where the descending limb of the T-wave met the isoelectric baseline. QTd was defined as the difference between the maximum and minimum QT intervals (QT_{max}-QT_{min}) across all measurable leads.

EST and HRR, DTS, RPP Calculation

All patients underwent a symptom-limited EST on a treadmill following the Bruce protocol. Upon reaching peak exercise, the test was not terminated abruptly; instead, an active recovery (cool-down) phase was performed, consisting of a 2-minute walk at 1.5 mph and 0% grade. HRR values were calculated as the absolute difference between the peak HR achieved during exercise and the HR recorded at specific recovery intervals:

HRR1: Calculated as (Peak HR- HR at 60 seconds of recovery).

HRR2: Calculated as (Peak HR- HR at 120 seconds of recovery).

In line with the active recovery protocol, an HRR1 value of ≤12 bpm was defined as abnormal, reflecting impaired vagal reactivation. For HRR2, values <22 bpm indicate an abnormal autonomic response.

The Duke treadmill score (DTS) was calculated using the standard formula: Exercise duration – (5×ST depression) – (4×Angina index).

Angina index:

Score 0: No angina occurs during exercise,

Score 1: Angina occurs during exercise but is not test-limiting (non-limiting angina),

Score 2: Angina is severe enough to cause termination of the test (exercise-limiting angina).

Myocardial oxygen demand was indirectly assessed by calculating the RPP. RPP was defined as the product of HR and systolic blood pressure, both measured at the peak of the EST (RPP = HR [bpm] × SBP [mmHg]).

CAG and Gensini Score

CAG was performed via the Judkins technique. Two blinded cardiologists assessed the results. CAD severity was quantified using the Gensini score, which weighs the degree of stenosis and vessel location. Critical coronary stenosis was defined as ≥50% narrowing in epicardial arteries. Patients were categorized into three groups: Normal coronary arteries, non-critical CAD (<50% stenosis or slow flow) and critical CAD.

Statistical Analysis

Analyses were performed using SPSS version 25.0. The sample size and statistical power were evaluated using G*Power software (version 3.1.9.7). A post-hoc power analysis based on the total study population of 200 participants revealed that the study had 92% statistical power to detect a medium effect size (d=0.5) with a two-tailed alpha level of 0.05. Normality was assessed using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean ± SD or medians, and categorical variables as frequencies. One-Way ANOVA with Tukey's post-hoc test was used for comparisons among three groups. Pearson correlation was used to evaluate relationships between the Gensini score and EST and ECG parameters. Receiver operating characteristic (ROC) curve analysis, with Youden's index, determined optimal cut-offs, and the area under the curves (AUCs) were compared using the DeLong test. Multivariate logistic regression identified independent predictors of critical CAD. Statistical significance was set at $p<0.05$.

Ethics Committee Approval

The study was conducted in accordance with the Declaration of Helsinki, and approval was obtained from the Local Ethics Committee (University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee, approval date: 19.04.2021, decision no: 2021-08-11).

RESULTS

Patient Characteristics

The study included 200 patients (57% male; mean age 56.21±9.35 years). Angiographic results identified normal coronary arteries in 27% of the population, non-critical CAD in 47%, and critical CAD in 26%. Demographic and laboratory findings were statistically similar across all groups ($p>0.05$) (Table 1).

Exercise and ECG Parameters

Significant variations were observed in exercise and ECG parameters across the study groups (Table 2). QTd values increased significantly with CAD severity and peaked in the critical CAD group ($p<0.001$). Conversely, HRR1, HRR2, DTSs, and RPP values significantly declined as disease severity progressed ($p<0.001$ for all measures except RPP, $p=0.003$). Post-hoc analyses confirmed that QTd and HRR parameters were statistically distinct for each group, indicating their discriminative potential.

Correlation and ROC Analysis

The mean Gensini score was 21.35±28.19 (range 0-166). Correlation analyses revealed that the Gensini score was strongly associated with QTd ($r=0.742$) and negatively associated with HRR1 ($r=-0.672$) and Duke scores ($r=-0.632$) ($p<0.001$ for all) (Figure 2a-c). ROC analysis identified QTd >32 ms (AUC: 0.842, 82% sensitivity, 76% specificity) and HRR1 <11 bpm (AUC: 0.815, 78% sensitivity, 80% specificity) as significant predictors of critical stenosis (Figure 3). According to the DeLong test, the AUCs for QTd and HRR1 were significantly higher than those of the Duke score and RPP ($p<0.05$), confirming their superior diagnostic performance.

Table 1. Baseline demographic, clinical, and laboratory characteristics of the study groups

Variables	Normal (n=54)	Non-critical CAD (n=94)	Critical CAD (n=52)	p-value
Age (years)	55.4±8.2	56.7±7.9	56.1±8.5	0.643[a]
Male gender, n (%)	30 (55.5%)	54 (57.4%)	30 (57.7%)	0.969[b]
Hypertension, n (%)	24 (44.4%)	43 (45.7%)	23 (44.2%)	0.983[b]
Diabetes mellitus, n (%)	15 (27.7%)	26 (27.6%)	14 (26.9%)	0.993[b]
Smoking, n (%)	19 (35.2%)	34 (36.2%)	18 (34.6%)	0.981[b]
Medications, n (%)				
ACE inhibitors/ARBs	24 (44.4%)	41 (43.6%)	23 (44.2%)	0.996[b]
Beta-blockers	11 (20.4%)	19 (20.2%)	10 (19.2%)	0.985[b]
Statins	17 (31.5%)	31 (33.0%)	17 (32.7%)	0.982[b]
Antiplatelet therapy	2 (3.7%)	4 (4.3%)	2 (3.8%)	0.986[b]
Laboratory parameters				
Glucose (mg/dL)	104.2±22.5	106.8±24.1	108.4±21.7	0.612[a]
Creatinine (mg/dL)	0.88 (0.80-0.96)	0.91 (0.82-1.02)	0.89 (0.81-0.98)	0.584[c]
Total cholesterol (mg/dL)	192.5±35.2	198.4±38.6	201.2±40.1	0.425[a]
LDL-cholesterol (mg/dL)	124.6±28.4	128.9±30.2	132.5±32.7	0.358[a]
HDL-cholesterol (mg/dL)	44 (38-51)	42 (36-49)	41 (39-42)	0.410[c]
Triglycerides (mg/dL)	154.3 (112.4-196.2)	162.7 (116.6-208.8)	165.4 (118.1-212.7)	0.635[c]
Hemoglobin (g/dL)	13.8±1.4	13.6±1.2	13.5±1.5	0.492[a]
WBC count (10^3/µL)	7.8±1.9	8.1±2.2	8.3±2.1	0.448[a]

Data are presented as mean ± SD, median (interquartile range), or n (%).
ACE: Angiotensin-converting enzyme; ARB: Angiotensin receptor blocker; CAD: Coronary artery disease; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; WBC: White blood cell; SD: Standard deviation; [a]: One-Way ANOVA; [b]: Chi-square or Fisher's exact test; [c]: Kruskal-Wallis test.

Table 2. Comparison of exercise stress test and ECG parameters among groups

Variables	Normal (n=54)	Non-critical CAD (n=94)	Critical CAD (n=52)	p-value
QTd (ms)	13.63±12.78[a]	22.62±8.79[b]	41.21±11.96[c]	<0.001
HRR1 (bpm)	33.33±9.94[a]	26.32±11.30[b]	9.79±2.15[c]	<0.001
HRR2 (bpm)	49.87±11.51[a]	43.63±13.18[b]	22.52±3.84[c]	<0.001
Duke score	3.20±1.69[a]	-1.46±5.24[b]	-6.29±3.66[c]	<0.001
RPP (bpm×mmHg)	26,850±4200[a]	25,120±5100[b]	22,450±4850[b]	0.003

Data are presented as mean ± standard deviation. P<0.05 was considered statistically significant.
CAD: Coronary artery disease; HRR1: Heart rate recovery at 1 minute; HRR2: Heart rate recovery at 2 minutes; QTd: QT dispersion; RPP: Rate-pressure product; [a]: Statistical significance was determined by One-Way ANOVA; [b]: Tukey's post-hoc test was used for multiple comparisons. Different superscript letters ([a, b, c]) in the same row indicate significant differences between groups (p<0.05).

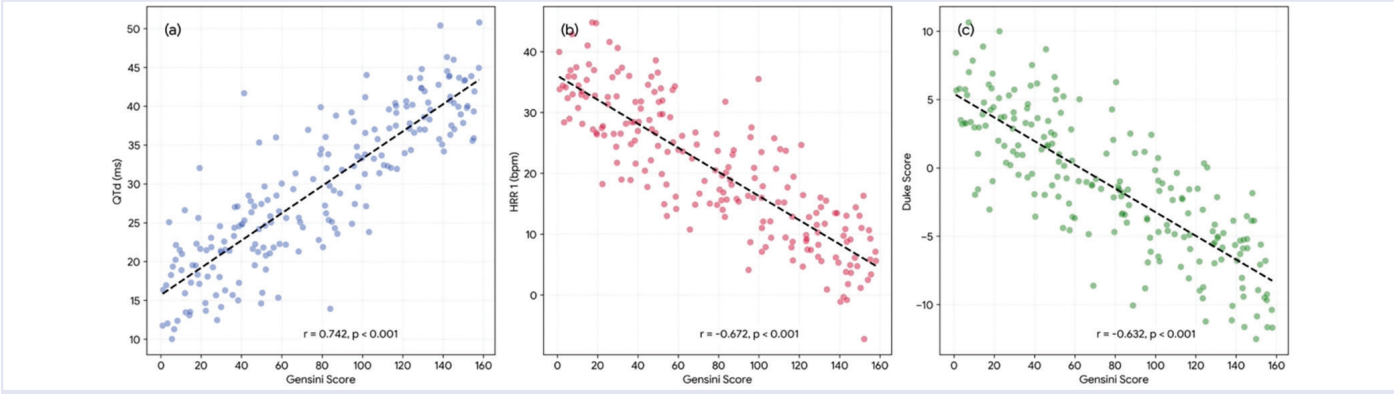

Figure 2. Scatter plots showing the Pearson's correlation coefficients between the Gensini score and study parameters: (a) strong positive correlation with QTd (r=0.742, p<0.001); (b) significant negative correlation with HRR1 (r=-0.672, p<0.001); (c) significant negative correlation with Duke treadmill score (r=-0.632, p<0.001).
QTd: QT dispersion; HRR1: Heart rate recovery at 1 minute.

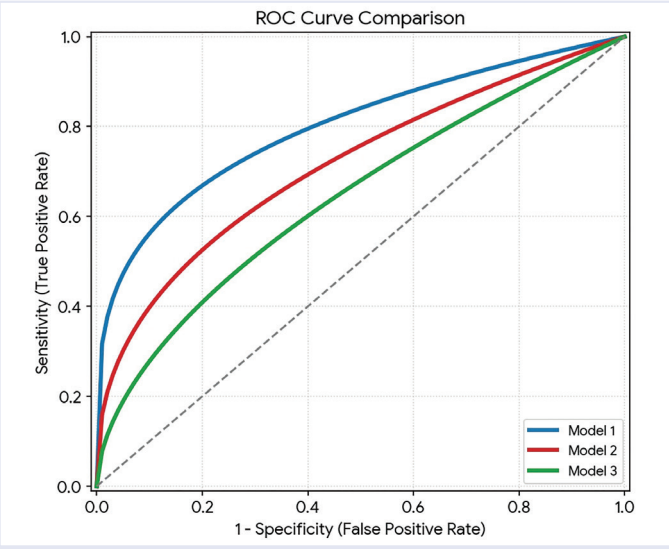

Figure 3. Comparison of receiver operating characteristic (ROC) curves of QTd, HRR1, and Duke score for the prediction of critical coronary artery disease. The AUCs were 0.842 for QTd, 0.815 for HRR1, and 0.760 for the Duke score.

QTd: QT dispersion; HRR1: Heart rate recovery at 1 minute; AUC: Area under the curve.

Logistic Regression Analysis

Univariate analysis showed that QTd, HRR1, HRR2, Duke score, and RPP were significantly associated with critical CAD. After adjusting for multicollinearity (excluding HRR2 due to VIF >10), multivariate logistic regression identified QTd (odds ratio [OR]: 1.09, 95% confidence interval [CI]: 1.04-1.14, p=0.002), HRR1 (OR: 0.82, 95% CI: 0.75-0.90, p=0.001), and Duke score (OR: 0.88, 95% CI: 0.81-0.96, p=0.015) as independent predictors of critical CAD [Table 3].

DISCUSSION

Our study demonstrates a strong negative correlation between HRR1 and the Gensini score, a finding that aligns with the results of Grad and Zdrenghea,[15] who established blunted HRR as a hallmark of autonomic dysfunction in patients with myocardial ischemia. Similar to our findings, Lachman et al.[16] reported that HRR values significantly decrease as the number of stenotic vessels increases.

However, some differences were observed when comparing our data to earlier studies. For instance, while some researchers reported a lower mean HRR1 value in CAD groups (e.g., <12 bpm), our value was 11 bpm.[16] This slight discrepancy may be attributed to our use of an active recovery protocol, which is known to produce higher HRR values than the passive supine recovery used in other cohorts. A notable difference in our study was the significant correlation of HRR2 with multi-vessel disease, which was more pronounced than in some previous reports.[17] We hypothesize that this reflects either more severe sympathetic overactivity or delayed catecholamine clearance in our specific patient population, highlighting the added value of measuring late-phase recovery in chronic coronary syndromes.

Regarding ventricular repolarization, we found a strong positive correlation between QTd and the Gensini score (r=0.742). This aligns with Bergfeldt et al.[18] and Dahrab et al.,[19] who proposed that QTd provides a non-invasive measure of repolarization heterogeneity related to the extent of coronary narrowing. With an AUC of 0.842, our findings confirm that a resting QTd >32 ms is a robust predictor of critical stenosis.

A noteworthy aspect of our study design is the use of the EST as a gateway to ICA. We acknowledge that the 2019 and 2024 European Society of Cardiology (ESC) Guidelines for chronic coronary syndromes have shifted the diagnostic paradigm away from EST toward non-invasive anatomical or functional imaging, such as coronary computed tomography angiography or stress echocardiography.[20] However, we hypothesized that the diagnostic sensitivity and specificity of EST for detecting CAD could be significantly enhanced by integrating it with HRR and QTd. By identifying patients with a high "anatomical burden" (as shown by higher Gensini scores) using these autonomic and electrical markers, our study provides evidence that EST can offer vital insights into coronary plaque load and myocardial vulnerability, particularly in settings where advanced imaging is not immediately available.

Recent large-scale meta-analyses have reaffirmed the prognostic power of HR dynamics in cardiovascular health. For instance, Qiu et al.[21] demonstrated that each 10-bpm decrease in HRR was associated with a 13% increase in the risk of cardiovascular events, emphasizing HRR as a fundamental marker of autonomic stability. Furthermore, contemporary research by Giga et al.[22] has highlighted that impaired HRR is not only a marker of mortality but also a significant predictor of the complexity and anatomical extent of coronary lesions. In alignment with these findings, our study shows that lower HRR1 and

Table 3. Univariate and multivariate logistic regression analysis of independent predictors for critical coronary artery disease

Variables	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Age	1.02 (0.98-1.06)	0.342	-	NS
Hypertension	1.15 (0.85-1.55)	0.412	-	NS
Diabetes mellitus	1.20 (0.88-1.64)	0.285	-	NS
QTd	1.12 (1.08-1.16)	<0.001	1.09 (1.04-1.14)	0.002
HRR1	0.78 (0.72-0.85)	<0.001	0.82 (0.75-0.90)	0.001
Duke score	0.82 (0.76-0.88)	<0.001	0.88 (0.81-0.96)	0.015
HRR2	0.85 (0.80-0.91)	<0.001	-	NS†
RPP	0.98 (0.96-1.01)	0.078	-	NS

CI: Confidence interval; HRR1: Heart rate recovery at 1 minute; HRR2: Heart rate recovery at 2 minutes; NS: Non-significant; OR: Odds ratio; QTd: QT dispersion; RPP: Rate-pressure product; p<0.05 was considered statistically significant; †: HRR2 was excluded from the multivariate model due to high multicollinearity with HRR1 (variance inflation factor >10).

HRR2 values directly correlate with higher Gensini scores, suggesting that autonomic dysfunction parallels the atherosclerotic burden. Similarly, recent studies on repolarization indices have underscored the value of QTd in identifying high-risk subsets among stable patients.[23] By integrating these modern insights with our findings, we suggest that the synergistic use of HRR and QTd enhances the diagnostic yield of EST beyond traditional ST-segment analysis, consistent with the evolving recommendations of the 2024 ESC Guidelines, which prioritize comprehensive risk stratification.

In our multivariate analysis, RPP did not emerge as an independent predictor of critical CAD. While the confounding influence of beta-blocker therapy on HR and blood pressure dynamics partially explains this finding, the physiological limitations of RPP itself must be considered. Although RPP is commonly used as a surrogate for myocardial oxygen consumption (MVO_2), it primarily reflects the heart's external work. As demonstrated in the seminal study by Kal et al.,[24] RPP may not fully account for all determinants of MVO_2, such as ventricular wall tension and contractility, particularly in the presence of obstructive CAD. Our findings suggest that markers of autonomic reactivation and repolarization heterogeneity provide more granular insights into the anatomical severity of CAD than traditional hemodynamic indices like RPP.

The present study demonstrates that impaired HRR1 and HRR2, increased QTd, and lower DTSs are significantly associated with the anatomical severity of CAD. Multivariate analysis identified QTd, HRR1, and DTS as independent predictors of critical CAD, suggesting that these non-invasive markers provide valuable diagnostic insights regarding the atherosclerotic burden prior to angiography.

To our knowledge, this is the first study to specifically investigate the correlation between HRR1 and the Gensini score. Although QTd and DTS require detailed calculations, HRR1 stands out as a more practical and easily measurable parameter in daily clinical practice. Our results demonstrate that this simple index not only reflects autonomic dysfunction but also serves as a robust indicator of the presence and severity of coronary atherosclerosis.

Our study has several limitations. First, it was a single-center study with a relatively small sample size, which may limit the generalizability of our findings. Second, the use of medications such as beta-blockers and calcium channel blockers, although similar across groups, might have influenced the HR and blood pressure responses during exercise. Finally, CAG is a 2D lumen-based assessment; hence, more advanced imaging such as intravascular ultrasound could provide a more detailed analysis of the atherosclerotic plaque burden.

In conclusion, QTd and HRR1 are powerful, non-invasive, and easily obtainable parameters that correlate strongly with the anatomical severity of CAD as measured by the Gensini score. A resting QTd >32 ms and an HRR1 <11 bpm are independent predictors of critical coronary stenosis. Incorporating these markers into routine EST evaluations can significantly enhance risk stratification and assist clinicians in the early identification of patients requiring invasive intervention.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki, and approval was obtained from the Local Ethics Committee (University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee, approval date: 19.04.2021, decision no: 2021-08-11).

Informed Consent: Informed consent was obtained from all participants.

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

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ö.K., R.A., F.N.T.Ç.; Concept: Ö.K., R.A., F.N.T.Ç.; Design: Ö.K., R.A., F.N.T.Ç.; Data Collection or Processing: Ö.K., R.A., F.N.T.Ç.; Analysis or Interpretation: Ö.K., R.A., F.N.T.Ç.; Literature Search: Ö.K., R.A., F.N.T.Ç.; Writing: Ö.K., R.A., F.N.T.Ç.

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REFERENCES

1. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al.; ESC Scientific Document Group. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020;41:407-77. doi: 10.1093/eurheartj/ehz425.
2. Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. N Engl J Med. 1999;341:1351-7. doi: 10.1056/NEJM199910283411804.
3. Jou J, Zhou X, Lindow T, Brudin L, Hedman K, Ekström M, et al. Heart rate response and recovery in cycle exercise testing: normal values and association with mortality. Eur J Prev Cardiol. 2025;32:32-42. doi: 10.1093/eurjpc/zwae308.
4. Dewar A, Kass L, Stephens RCM, Tetlow N, Desai T. Heart rate recovery assessed by cardiopulmonary exercise testing in patients with cardiovascular disease: relationship with prognosis. Int J Environ Res Public Health. 2023;20:4678. doi: 10.3390/ijerph20064678.
5. Qiu SH, Xue C, Sun ZL, Steinacker JM, Zügel M, Schumann U. Attenuated heart rate recovery predicts risk of incident diabetes: insights from a meta-analysis. Diabet Med. 2017;34:1676-83. doi: 10.1111/dme.13517.
6. Bélanger N, Zeid S, Velmeden D, Andreas S, Thomas K, Felix R, et al. Cardiac vagal activity is associated with insulin metabolism in heart failure: results from the myovasc study. Cardiovasc Diabetol. 2026;25:26. doi: 10.1186/s12933-025-03040-9.
7. Van de Vegte YJ, Van der Harst P, Verweij N. Heart rate recovery 10 seconds after cessation of exercise predicts death. J Am Heart Assoc. 2018;7:e008341. doi: 10.1161/JAHA.117.008341.

8. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol. 1983;51:606. doi: 10.1016/s0002-9149(83)80105-2.

9. Naser A. The Gensini score system is a useful tool in assessing the burden and severity of coronary artery atherosclerotic lesions. Int J Gen Med. 2024;17:4227-8. doi: 10.2147/IJGM.S495194.

10. Prenner SB, Shah SJ, Goldberger JJ, Sauer AJ. Repolarization heterogeneity: beyond the QT interval. J Am Heart Assoc. 2016;5:e003607. doi: 10.1161/JAHA.116.00360.

11. Bazoukis G, Yeung C, Wui Hang Ho R, Varrias D, Papadatos S, Lee S, et al. Association of QT dispersion with mortality and arrhythmic events-a meta-analysis of observational studies. J Arrhythm. 2019;36:105-15. doi: 10.1002/joa3.12253.

12. Helmy H, Abdel-Galeel A, Taha Kishk Y, Mohammed Sleem K. Correlation of corrected QT dispersion with the severity of coronary artery disease detected by SYNTAX score in non-diabetic patients with STEMI. Egypt Heart J. 2017;69:111-7. doi: 10.1016/j.ehj.2016.12.001.

13. Almyahi M, Alkinani TA, Majdl K, Azzawi FS, Basheer A. Relationship between QT interval dispersion and degree of coronary artery disease. Indian J Forensic Med Toxicol. 2020;14:1321-8. doi: 10.37506/ijfmt.v14i2.3092.

14. Zhou J, Li YJ, Zhou XD, Wang LJ. Rate-pressure product is a novel predictor for short-and long-term mortality in patients with acute coronary syndrome undergoing primary PCI/immediate invasive strategy. Clin Interv Aging. 2024;19:571-9. doi: 10.2147/CIA.S449905.

15. Grad C, Zdrenghea D. Heart rate recovery in patients with ischemic heart disease -risk factors. Clujul Med 2014;87:220-5. doi: 10.15386/cjmed-385.

16. Lachman S, Terbraak MS, Limpens J, Jorstad H, Lucas C, Scholte Op Reimer W, et al. The prognostic value of heart rate recovery in patients with coronary artery disease: a systematic review and meta-analysis. Am Heart J. 2018;199:163-9. doi: 10.1016/j.ahj.2018.02.008.

17. Lipinski MJ, Vetrovec GW, Froelicher VF. Importance of the first two minutes of heart rate recovery after exercise treadmill testing in predicting mortality and the presence of coronary artery disease in men. Am J Cardiol. 2004;93:445-9. doi: 10.1016/j.amjcard.2003.10.039.

18. Bergfeldt L, Gransberg L, Lundahl G. Ischemia induced repolarization dispersion changes and ventricular arrhythmia: validation of Frank vectorcardiography parameters: a review. Heart Rhythm O2. 2025;6:709-19. doi: 10.1016/j.hroo.2025.02.005.

19. Dahrab M, Gaddipati SP, Patel KB, Patel T, Gaddam AR, Jain M, et al. The effect of percutaneous coronary intervention on QT dispersion and the association between them: a systematic review. Cureus. 2023;15:e36226. doi: 10.7759/cureus.36226.

20. Vrints C, Doehner W, Koskinas KC, Rossello X, Adamo M, Ainslie J, et al. 2024 ESC guidelines for the management of chronic coronary syndromes. Eur Heart J. 2024;45:3429-551. doi: 10.1093/eurheartj/ehae177.

21. Qiu S, Cai X, Sun Z, Li L, Zuegel M, Steinacker JM, et al. Heart rate recovery and risk of cardiovascular events and all-cause mortality: a meta-analysis of prospective cohort studies. J Am Heart Assoc. 2017;6:e005505. doi: 10.1161/JAHA.117.005505.

22. Giga V, Boskovic N, Djordjevic-Dikic A, Beleslin B, Nedeljkovic I, Stankovic G, et al. Heart rate recovery as a predictor of long-term adverse events after negative exercise testing in patients with chest pain and pre-test probability of coronary artery disease from 15% to 65%. Diagnostics. 2023;13:2229. doi: 10.3390/diagnostics13132229.

23. Goulart MA, Moreira DAR, Cesena FY, Souza JB, Laurinavicius AG, Consolim-Colombo FM, et al. Analysis of ventricular repolarization in hypertensive patients: influence of nocturnal blood pressure dipping. Arq Bras Cardiol. 2025;122:e20240725. doi:10.36660/abc.20240725.

24. Kal JE, Van Wezel HB, Vergroesen I. A critical appraisal of the rate pressure product as index of myocardial oxygen consumption for the study of metabolic coronary flow regulation. Int J Cardiol. 1999;71:141-8. doi: 10.1016/s0167-5273(99)00141-2.

ORIGINAL ARTICLE

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CARDIOVASCULAR SURGERY AND INTERVENTIONS

Prognostic value of inflammatory indices and end-organ damage in predicting perioperative mortality following emergent repair of type A aortic dissection

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ABSTRACT

Objectives: This study aimed to evaluate whether preoperative biochemical markers and inflammatory indices, in conjunction with established clinical risk factors, can serve as reliable predictors of early postoperative mortality in patients undergoing surgery for type A aortic dissection (TAAD).

Patients and methods: In this retrospective cohort analysis conducted at a single institution, a total of 156 consecutive adult patients who underwent urgent surgical intervention for TAAD were included. The cohort was stratified into the mortality group (n=42) and the survivor group (n=114). Demographic, clinical, intraoperative, and laboratory variables were analyzed and compared between groups. Independent predictors of mortality were determined using multivariable logistic regression analysis.

Results: The overall perioperative mortality rate was 26.9%. Univariate analysis demonstrated that the mortality group had significantly higher rates of preoperative malperfusion (23.8% *vs.* 1.7%, p<0.001) and aortic rupture (21.4% *vs.* 3.5%, p<0.001). Non-survivors demonstrated significantly higher levels of preoperative inflammatory markers, including C-reactive protein (p<0.001), neutrophil-to-lymphocyte ratio (p=0.039), and red cell distribution width (p=0.001), and higher serum creatinine concentrations (p<0.001). However, multivariable analysis identified malperfusion (odds ratio [OR]: 20.707, p=0.007), aortic rupture (OR: 9.525, p=0.002) and elevated creatinine levels (OR: 1.785, p=0.022) as the only independent predictors of mortality. Inflammatory markers were no longer statistically significant (p>0.05).

Conclusion: In acute TAAD, perioperative mortality is primarily driven by end-organ malperfusion, aortic rupture, and renal dysfunction. Although inflammatory markers reflect disease severity, they do not independently predict early mortality in the presence of organ failure.

Keywords: Creatinine, predictor, mortality, type A aortic dissection.

Type A aortic dissection (TAAD), initially classified by Stanford in 1970, is a catastrophic and life-threatening cardiovascular emergency that necessitates rapid multidisciplinary intervention.[1] Left untreated, TAAD is associated with an exceptionally high mortality rate; historical and contemporary registries indicate that approximately 40% of patients succumb to the condition prior to hospital admission, with early mortality increasing by 1% to 2% per hour following symptom onset.[2] Accordingly, urgent surgical intervention remains the definitive standard of care. However, despite significant advancements in surgical techniques, cardiopulmonary bypass (CPB) technologies, and intensive care management over the past decades, the perioperative mortality rate for patients undergoing emergency TAAD surgery remains alarmingly

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high, ranging between 15% and 30% in major international registries.[3] This persistently high mortality burden underscores the critical need for novel, easily accessible prognostic biomarkers to preoperatively risk-stratify patients and identify high-risk individuals who might require tailored therapeutic and hemodynamic strategies.

The pathogenesis and early progression of TAAD are intrinsically linked to a profound systemic inflammatory response syndrome (SIRS), triggered by the exposure of circulating blood to the deeper layers of the dissected aortic media and subsequent visceral or peripheral tissue ischemia.[4] Identifying factors that predict perioperative morbidity in patients undergoing TAAD surgery is important because it allows for the development of preventive and therapeutic strategies. In addition to known determinants of mortality such as advanced age, malperfusion, and unstable preoperative condition, the prognostic roles of numerous hematological, biochemical, and inflammatory parameters in patients undergoing TAAD surgery have recently been investigated. Therefore, these parameters are guiding factors for identifying potential interventions and prospective treatment targets for high-risk patients.[5-7]

Nevertheless, the existing literature presents inconsistent findings. Therefore, this study sought to assess the predictive significance of various hematological, biochemical, and inflammatory markers for perioperative mortality in patients undergoing surgery for TAAD, while also examining additional clinical variables that may contribute to risk stratification.

PATIENTS AND METHODS

Ethical Considerations

The study protocol received approval from the Institutional Clinical Research Ethics Committee of University of Health Sciences Türkiye, Bursa City Hospital (approval no: 2023-19/12; date: November 22, 2023). All procedures were carried out in accordance with the ethical standards set forth in the Declaration of Helsinki. Prior to enrollment, comprehensive information regarding the purpose of the study and surgical interventions was provided to all patients or their legal surrogates; both verbal and written informed consent were obtained.

Study Population and Design

This study was conducted as a retrospective, single-center observational cohort analysis. A total of 156 adult patients who underwent urgent surgical repair for TAAD at our institution from July 2019 to October 2023 were retrospectively evaluated. The cohort was stratified into two groups based on perioperative outcomes: The mortality group (n=42) and the survivor group (n=114).

Baseline demographic data—including age, sex, height, weight, and body mass index (BMI)—and relevant comorbid conditions such as diabetes mellitus, chronic obstructive pulmonary disease (COPD), hypertension, and chronic renal insufficiency were systematically retrieved from the institution's electronic medical record system. Preoperative hematological parameters, biochemical markers (the inflammatory prognostic index [IPI] was calculated using the formula: (C-reactive protein [CRP] × neutrophil-to-lymphocyte ratio [NLR])/albumin) and echocardiographic findings recorded upon hospital admission were also analyzed. Malperfusion was defined by preoperative clinical findings, computed tomography angiography findings, and, when present, evidence of end-organ ischemia or dysfunction. Aortic rupture was defined according to preoperative imaging or intraoperative findings indicating free rupture, pericardial tamponade, mediastinal hematoma, or hemothorax. In addition, perioperative variables—including CPB duration, aortic cross-clamp (ACC) time, lengths of stay in the intensive care unit (ICU) and overall hospitalization, incidence of postoperative cerebrovascular events (CVE), and requirement for re-exploration for bleeding—were systematically recorded. Perioperative mortality was defined as all-cause in-hospital mortality during the index hospitalization. Patients with a history of median sternotomy (redo surgery), documented malignancies, active infectious diseases or sepsis, and underlying autoimmune, hematological, or chronic inflammatory disorders were excluded to prevent confounding of inflammatory biomarkers.

Surgical Approach

All surgical interventions were carried out under general anesthesia through a conventional median sternotomy. Before cannulation, systemic anticoagulation was administered using unfractionated heparin (350 IU/kg) to ensure an activated clotting time (ACT) exceeding 400 seconds. The right subclavian artery was the primary vessel for arterial cannulation to facilitate antegrade cerebral perfusion; femoral artery cannulation was reserved for cases in which the subclavian approach was unsuitable. Venous return was established via a two-stage right atrial cannula to complete the CPB circuit.

Throughout CPB, a non-pulsatile flow of 2.0-2.5 L/min/m² was maintained, with a target mean arterial pressure of 50-70 mmHg and a hematocrit of 20-25%. After placement of the ACC, diastolic cardiac arrest was achieved via antegrade cardioplegia, enabling comprehensive assessment of the aortic root, valve, ascending aorta, and aortic arch.

The subsequent surgical strategy was tailored to the extent of the dissection and valvular pathology. For intimal tears confined to the ascending aorta with preserved aortic valve morphology and intact coaptation, a supracoronary ascending aortic replacement was executed using an appropriately sized Dacron graft. In cases where the dissection involved the aortic arch or its branch vessels, the repair was extended distally. Concomitant aortic valve repair or replacement was undertaken when intrinsic valvular structural abnormalities were detected. Distal anastomoses were routinely performed using the open technique during a brief period of circulatory arrest, with selective antegrade cerebral perfusion applied for neuroprotection under moderate hypothermia (24-28 °C). Upon completion of the anastomoses, patients were systematically rewarmed, weaned from CPB, and decannulated. Heparin was reversed using protamine sulfate (1-1.3 mg per 1 mg of administered heparin) to normalize the ACT. All surgical procedures were performed by a consistent, dedicated cardiovascular surgical team. Following surgery, patients were promptly admitted to the cardiovascular ICU for continuous hemodynamic surveillance.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were expressed as mean ± standard deviation and compared using the independent samples t-test. Non-normally distributed continuous variables were reported as medians (minimum-maximum) and compared using the Mann-Whitney U test. Categorical variables were presented as frequencies and percentages,

with inter-group comparisons conducted via the chi-square test. Variables that were statistically significant in univariate analysis were included in a multivariable logistic regression model to identify independent predictors of mortality. Categorical variables were entered into the model using "absence" as the reference category; perioperative mortality was coded as the event (1) and survival as (0). Although CPB duration is an intraoperative variable reflecting surgical complexity, it was included in the multivariable model to provide a more comprehensive assessment of factors associated with perioperative mortality in emergent surgery. Receiver operating characteristic (ROC) curve analysis was employed to establish optimal cut-off values for these predictors. For all statistical tests, a two-sided p-value of <0.05 was considered indicative of significance.

RESULTS

A total of 156 patients were included in the study: 42 in the mortality group and 114 in the survivor group. Patients in the mortality group were significantly older compared to the survivor group (65.6±12.8 years *vs.* 58.8±11.1 years, p=0.002) (Table 1). No significant differences were observed between the groups with respect to sex, height, weight, BMI, or the prevalence of preoperative comorbidities, including hypertension, diabetes mellitus, COPD, and chronic renal failure (all p>0.05) (Table 1).

With respect to preoperative clinical severity, the incidences of malperfusion and aortic rupture were markedly higher in the mortality group. Preoperative malperfusion was present in 23.8% of non-survivors compared with 1.7% of survivors (p<0.001). The incidence of aortic rupture was 21.4% in the non-survivor group, compared with 3.5% in the survivor group (p<0.001) (Table 1).

Intraoperatively, while ACC durations were comparable between the cohorts, the CPB duration was significantly prolonged in the mortality group (227.8±116.2 min *vs.* 166.2±83.8 min, p=0.003) (Table 1). Postoperatively, durations of both ICU stay and total hospital stay were significantly shorter in the mortality group, primarily because of early postoperative mortality (p=0.001 and p<0.001, respectively). The frequency of re-exploration for bleeding and the occurrence of postoperative CVE were comparable between the two groups, with no statistically significant differences observed (p>0.05) (Table 1).

Preoperative laboratory analyses revealed heightened systemic inflammation and tissue stress in the mortality group (Table 2). The red cell distribution width (RDW) (p=0.001), CRP levels (p<0.001), and the NLR (p=0.039) were significantly elevated in patients who did not survive. Furthermore, markers of renal impairment, specifically urea (p=0.040) and creatinine (p<0.001), were significantly higher in the mortality cohort (Table 2). There were no significant differences between the groups in hemoglobin levels, white blood cell counts, platelet parameters, liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT]), or composite inflammatory markers, including the platelet-to-lymphocyte ratio (PLR) and systemic immune-inflammation index (all p>0.05) (Table 2). Extremely elevated

Table 1. Perioperative patient characteristics

Variable	Mortality group (n=42)	Survivor group (n=114)	p-value
Age (year)	65.6±12.8	58.8±11.1	0.002*
Gender (female)	15 (35.7%)	38 (33.3%)	0.781
Height (cm)	168.7±9.7	168.3±8.8	0.794
Weight (kg)	80.2±13.8	81.7±13.9	0.534
BMI (kg/m^2)	28.5±5.8	28.7±4.6	0.846
Hypertension	34 (80.9%)	84 (73.6%)	0.300
Diabetes mellitus	5 (11.9%)	18 (15.7%)	0.405
COPD	3 (7.1%)	8 (7.0%)	0.662
CRF	3 (7.1%)	5 (4.3%)	0.332
Malperfusion	10 (23.8%)	2 (1.7%)	<0.001*
Rupture	9 (21.4%)	4 (3.5%)	<0.001*
ACC duration (min)	101 (41-384)	90.5 (25-244)	0.135
CPB duration (min)	227.8±116.2	166.2±83.8	0.003*
ICU stay duration (day)	2 (0-14)	3 (2-19)	0.001*
Hospital stay duration (day)	2 (0-14)	7 (5-43)	<0.001*
Re-exploration for bleeding	7 (16.6%)	9 (7.8%)	0.098
Postoperative CVE	5 (11.9%)	8 (7.0%)	0.381

ACC: Aortic cross-clamp; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; CPB: Cardiopulmonary bypass; CRF: Chronic renal failure; CVE: Cerebrovascular event; ICU: Intensive care unit.

Table 2. Laboratory data

Variable	Mortality group (n=42)	Survivor group (n=114)	p-value
Hemoglobin (g/dL)	11.5±2.7	11.8±2.6	0.786
RDW (fL)	44.3 (38.1-68.7)	42.0 (34.6-60.3)	0.001*
WBC (10^3/µL)	13.2±4.6	12.2±4.7	0.284
Neutrophil (10^3/µL)	10.4±4.4	9.4±4.5	0.214
Lymphocyte (10^3/µL)	1.09 (0.27-5.53)	1.48 (0.24-36.1)	0.094
Monocyte (10^3/µL)	0.76 (0.18-1.80)	0.75 (0.18-6.8)	0.829
Eosinophil (10^3/µL)	0.03 (0-0.79)	0.04 (0-1.00)	0.394
Platelet (10^3/µL)	166.8±108.2	192.5±83.1	0.118
PDW (fL)	13.5±3.2	12.9±3.2	0.242
MPV (fL)	11.0±1.1	10.5±0.8	0.265
Plateletcrit (%)	0.18±0.10	0.19±0.08	0.438
CRP (mg/L)	12.0 (1.2-178.5)	4.5 (0.5-279.4)	<0.001*
Urea (mg/dL)	41.4 (15-178.5)	37.0 (16.3-171.4)	0.040*
Creatinine (mg/dL)	1.37 (0.45-9.9)	0.95 (0.48-8.0)	<0.001*
AST (IU/L)	30 (15-10075)	28 (9-1237)	0.123
ALT (IU/L)	20.5 (7-5483)	20 (5-485)	0.376
Albumin (g/L)	30.7±8.8	33.3±7.6	0.097
NLR	8.5 (1.0-53.6)	7.0 (0.13-26.9)	0.039*
PLR	101.2 (17.6-915.2)	126.7 (5.5-929.4)	0.541
SII	1184 (93-22578)	1090 (27-8513)	0.689

ALT: Alanine transaminase; AST: Aspartate aminotransferase; CRP: C-reactive protein; MPV: Mean platelet volume; NLR: Neutrophil-to-lymphocyte ratio; PDW: Platelet distribution width; PLR: Platelet-to-lymphocyte ratio; RDW: Red cell distribution width, SII: Systemic immune-inflammation index; WBC: White blood cell.

Table 3. Multivariable logistic regression analysis

Variable	Beta	Standard error	Wald	Expected beta	p-value
Age	0.033	0.022	2.255	1.034	0.133
CPB duration	0.004	0.002	3.158	1.004	0.076
Malperfusion	3.030	1.126	7.238	20.707	0.007*
Rupture	2.254	0.739	9.315	9.525	0.002*
NLR	0.029	0.036	0.656	1.029	0.418
RDW	0.083	0.054	2.339	1.087	0.126
CRP	0.003	0.005	0.328	1.003	0.567
Urea	-0.009	0.010	0.813	0.991	0.367
Creatinine	0.579	0.253	5.249	1.785	0.022*

CPB: Cardiopulmonary bypass; CRP: C-reactive protein; NLR: Neutrophil-to-lymphocyte ratio; RDW: Red cell distribution width.

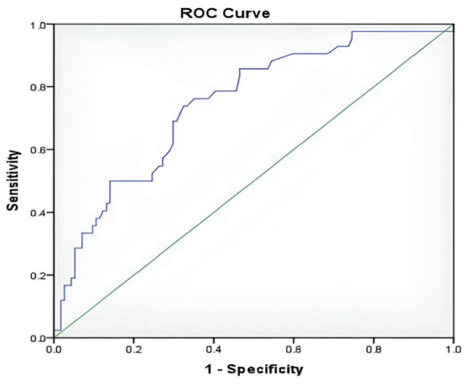
AST and ALT values observed in several patients were rechecked in the institutional database and considered to reflect severe hypoperfusion-related hepatic injury in these critically ill patients.

A multivariable logistic regression analysis was conducted to identify independent predictors of perioperative mortality by including variables that were significant in the univariate analysis (age, CPB duration, malperfusion, rupture, NLR, RDW, CRP, urea, and creatinine) (Table 3). Odds ratios (ORs) are presented according to the predefined reference categories used in the logistic regression model. As summarized in Table 3, the model identified the following parameters as independent predictors of mortality:

- Malperfusion (OR: 20.707, p=0.007)
- Rupture (OR: 9.525, p=0.002)
- Elevated creatinine (OR: 1.785, p=0.022).

Conversely, age, CPB duration, inflammatory markers (NLR, RDW, CRP) and urea lost their statistical significance in the multivariable model (p>0.05) (Table 3).

The predictive utility of preoperative serum creatinine for mortality was assessed through ROC curve analysis.



Area under the curve (AUC)	Optimum cut-off value	Sensitivity	Specificity	P value
0.746 (0.660-0.831)	1.14	69.0%	69.3%	<0.001

Figure 1. Receiver operating characteristic (ROC) curve for creatinine.

In the ROC analysis, creatinine had an optimal threshold of 1.14 with 69% sensitivity and 69.3% specificity (AUC=0.746 (0.660-0.831), p<0.001; Figure 1).

DISCUSSION

Despite significant advancements in surgical and anesthetic techniques, acute TAAD remains a catastrophic cardiovascular emergency with substantial perioperative mortality.[8,9] The main finding of this study was that, although preoperative inflammatory markers—including the NLR, RDW, and CRP—were associated with mortality in univariate analysis, they did not retain independent predictive significance in the multivariable model. Instead, the true independent predictors of early surgical mortality were preoperative malperfusion syndrome, aortic rupture, and elevated serum creatinine. These results clearly indicate that the prognosis in TAAD surgery is fundamentally dictated by the severity of gross end-organ damage rather than the isolated magnitude of systemic inflammation.

Extensive data from the literature robustly support our findings. Comprehensive analyses from the German Registry for Acute Aortic Dissection Type A have demonstrated that the presence of preoperative malperfusion exponentially increases surgical mortality and the rate of postoperative complications.[8] The exceptionally high mortality risk observed in patients with malperfusion in our cohort can be attributed to the dissection flap obstructing the arterial supply to vital organs, leading to irreversible ischemic shock.[10] Similarly, aortic rupture is directly associated with massive hemorrhage, cardiac tamponade, and profound cardiogenic shock, establishing it as one of the most formidable independent causes of death across major international centers.[8]

Another potent, independent predictor of perioperative mortality identified in our study was an elevated preoperative creatinine level. In the setting of aortic dissection, acute kidney injury is frequently triggered by either direct involvement of the renal arteries by the dissection flap or global hypoperfusion secondary to shock.[11] Furthermore, indispensable surgical modalities such as prolonged CPB and hypothermic circulatory arrest completely exhaust the already compromised baseline renal reserve. It has been unequivocally established in the literature that renal dysfunction—whether pre-existing or exacerbated by the deleterious effects of extracorporeal circulation—directly amplifies mortality following major aortic arch surgery.[11,12] Because of the retrospective design and the emergency setting, the present study could not determine whether elevated creatinine reflected chronic kidney disease, acute renal malperfusion, or shock-related hypoperfusion. The rationale for investigating the IPI and its components (NLR, CRP, RDW) lies in their ability to reflect the SIRS, which is initiated when subendothelial tissues are exposed to circulating blood following an intimal tear.[13,14]

Consequently, our univariate analysis revealed significantly elevated levels of these markers in the mortality group. However, their loss of independent predictive value when organ damage parameters (malperfusion and creatinine) were introduced into the multivariable model highlights a critical pathophysiological reality: Once tissue necrosis, shock, and major organ ischemia are established, the cellular-level inflammatory response becomes a secondary reaction.[15] Moreover, the profound systemic inflammation induced by CPB itself often overrides the preoperative baseline inflammatory status.[16] During the acute crisis of TAAD, the ultimate determinant of patient survival is whether vital organs are adequately perfused, rather than the mere presence of inflammation. Therefore, while inflammatory parameters serve as excellent prognostic tools in chronic cardiovascular or oncological diseases, they lag behind end-organ perfusion defects in catastrophic emergencies such as TAAD, where every second counts.[17-20] Recent studies have also shown that inflammatory markers may be associated with adverse postoperative outcomes, including atrial fibrillation, among patients undergoing cardiovascular surgery. However, similar to our findings, these markers do not always remain independent predictors after adjustment for major clinical variables.[7] Conversely, other reports evaluating perioperative inflammatory indices in cardiac surgery populations have demonstrated that certain inflammatory parameters may independently predict mortality and morbidity under specific clinical conditions.[21] These findings suggest that the prognostic significance of inflammatory markers may vary according to the patient population, timing of biomarker assessment, and the severity of end-organ injury.

This study has several limitations. First, the retrospective single-center design and the relatively modest sample size (n=156) may restrict the generalizability of our findings and limit the statistical power of multivariable analyses. The relatively low number of outcome events compared with the number of variables included in the multivariable model may pose a risk of overfitting and should be considered when interpreting the results. Second, inflammatory markers were evaluated from a single preoperative blood sample collected at admission. Because the systemic inflammatory response in TAAD is a highly dynamic process, this single "snapshot" precludes the assessment of longitudinal biomarker kinetics and their postoperative variations. Biomarkers in acute aortic syndromes exhibit significant temporal variations.[22] In addition, specific malperfusion territories (cerebral, coronary, mesenteric, renal, or extremity) and individual rupture subtypes were not analyzed separately, which may have influenced the prognostic impact of these variables. The inclusion of intraoperative variables such as CPB duration in the multivariable model may limit strict preoperative risk stratification, although it provides additional

insight into overall perioperative risk. Third, detailed operative variables such as extent of aortic repair, circulatory arrest time, cerebral perfusion strategy, nadir temperature, and cannulation site were not included in the analysis; this omission may have influenced perioperative outcomes. Finally, due to the emergent nature of the disease and the retrospective study design, the exact time intervals from symptom onset to hospital admission and to surgical intervention could not be reliably standardized or analyzed. This factor may have influenced the degree of end-organ dysfunction and inflammatory marker elevation observed at presentation. The prognostic impact of different malperfusion territories and rupture subtypes may not be uniform, and this issue warrants further investigation in larger prospective studies. Future multicenter, prospective studies evaluating longitudinal changes in these markers during the postoperative period are warranted to draw more definitive conclusions.

Malperfusion syndrome, aortic rupture, and elevated preoperative creatinine levels are the most robust independent risk factors for early surgical mortality in patients undergoing emergent repair for TAAD. Although inflammatory markers such as the IPI, NLR, and CRP reflect the severity of the dissection, they lose their independent prognostic utility in clinical scenarios dominated by major ischemic insult and organ failure, particularly renal dysfunction. When stratifying preoperative risk in TAAD patients, clinicians must prioritize assessment of gross organ malperfusion and baseline renal reserve.

Ethics

Ethics Committee Approval: The study protocol received approval from the Institutional Clinical Research Ethics Committee of University of Health Sciences Türkiye, Bursa City Hospital (approval no: 2023-19/12; date: November 22, 2023).

Informed Consent: Both verbal and written informed consent were obtained.

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

Footnotes

Authorship Contributions

Surgical and Medical Practices: D.Ç., H.G., A.Y., Y.V., S.H., A.Mü.; Concept: D.Ç., A.Y., G.K., T.T., A.M., A.Mü.; Design: D.Ç., A.Y., G.K., T.T., A.M.; Data Collection or Processing: A.Y., Y.V., S.H.; Analysis or Interpretation: H.G., A.Y., S.H.; Literature Search: H.G., G.K., A.Mü.; Writing: D.Ç., H.G., A.Y., G.K., A.Mü.

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

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REFERENCES

1. Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al.; ESC Committee for Practice Guidelines. 2014 ESC guidelines on the diagnosis and treatment of aortic diseases: document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. Eur Heart J. 2014;35:2873-926. Erratum in: Eur Heart J. 2015;36:2779. doi: 10.1093/eurheartj/ehv178.
2. Nienaber CA, Clough RE. Management of acute aortic dissection. Lancet. 2015;385:800-11. doi: 10.1016/S0140-6736(14)61005-9.
3. Evangelista A, Isselbacher EM, Bossone E, Gleason TG, Eusanio MD, Sechtem U, et al.; IRAD Investigators. Insights from the international registry of acute aortic dissection: a 20-year experience of collaborative clinical research. Circulation. 2018;137:1846-60. doi: 10.1161/CIRCULATIONAHA.117.031264.
4. Luo F, Zhou XL, Li JJ, Hui RT. Inflammatory response is associated with aortic dissection. Ageing Res Rev. 2009;8:31-5. doi: 10.1016/j.arr.2008.08.001.
5. Fest J, Ruiter R, Ikram MA, Voortman T, van Eijck CHJ, Stricker BH. Reference values for white blood-cell-based inflammatory markers in the Rotterdam study: a population-based prospective cohort study. Sci Rep. 2018;8:10566. doi: 10.1038/s41598-018-28646-w.
6. Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivo M, Zuzut M, et al. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis. 2012;225:456-60. doi: 10.1016/j.atherosclerosis.2012.09.009.
7. Badem S, Pekcolaklar A. Inflammatory prognostic index predicts new-onset atrial fibrillation and mortality after on-pump coronary artery bypass grafting. Rev Assoc Med Bras (1992). 2023;69:e20230226. doi: 10.1590/1806-9282.20230226.
8. Czerny M, Schoenhoff F, Etz C, Englberger L, Khaladj N, Zierer A, et al. The impact of pre-operative malperfusion on outcome in acute type A aortic dissection: results from the GERAADA registry. J Am Coll Cardiol. 2015;65:2628-35. doi: 10.1016/j.jacc.2015.04.030.
9. Chiappini B, Schepens M, Tan E, Dell' Amore A, Morshuis W, Dossche K, et al. Early and late outcomes of acute type A aortic dissection: analysis of risk factors in 487 consecutive patients. Eur Heart J. 2005;26:180-6. doi: 10.1093/eurheartj/ehi024.
10. Geirsson A, Szeto WY, Pochettino A, McGarvey ML, Keane MG, Woo YJ, et al. Significance of malperfusion syndromes prior to contemporary surgical repair for acute type A dissection: outcomes and need for additional revascularizations. Eur J Cardiothorac Surg. 2007;32:255-62. doi: 10.1016/j.ejcts.2007.04.012.
11. Ko T, Higashitani M, Sato A, Uemura Y, Norimatsu T, Mahara K, et al. Impact of acute kidney injury on early to long-term outcomes in patients who underwent surgery for type A acute aortic dissection. Am J Cardiol. 2015;116:463-8. doi: 10.1016/j.amjcard.2015.04.043.
12. Roh GU, Lee JW, Nam SB, Lee J, Choi JR, Shim YH. Incidence and risk factors of acute kidney injury after thoracic aortic surgery for acute dissection. Ann Thorac Surg. 2012;94:766-71. doi: 10.1016/j.athoracsur.2012.04.057.
13. Badem S, Atasoy MS. Inflammatory prognostic index is a new predictive marker for perioperative mortality in patients undergoing type A aortic dissection surgery. Turk J Vasc Surg. 2025;34:25-32. doi: 10.9739/tjvs.2024.12.060.
14. Yuksel A, Velioglu Y, Korkmaz UTK, Deser SB, Topal D, Badem S, et al. Systemic immune-inflammation index for predicting poor outcome after carotid endarterectomy: a novel hematological marker. Vascular. 2024;32:565-72. doi: 10.1177/17085381221141476.
15. Zindovic I, Gudbjartsson T, Ahlsson A, Fuglsang S, Gunn J, Hansson EC, et al. Malperfusion in acute type A aortic dissection: an update from the nordic consortium for acute type A aortic dissection. J Thorac Cardiovasc Surg. 2019;157:1324-33.e6. doi: 10.1016/j.jtcvs.2018.10.134.
16. Paparella D, Yau TM, Young E. Cardiopulmonary bypass induced inflammation: pathophysiology and treatment. An update. Eur J

Cardiothorac Surg. 2002;21:232-44. doi: 10.1016/s1010-7940(01)01099-5.

17. Gawinecka J, Schönrath F, von Eckardstein A. Acute aortic dissection: pathogenesis, risk factors and diagnosis. Swiss Med Wkly. 2017;147:w14489. doi: 10.4414/smw.2017.14489.
18. Suzuki T, Distante A, Zizza A, Trimarchi S, Villani M, Salerno Uriarte JA, et al.; IRAD-Bio Investigators. Diagnosis of acute aortic dissection by D-dimer: the international registry of acute aortic dissection substudy on biomarkers (IRAD-Bio) experience. Circulation. 2009;119:2702-7. doi: 10.1161/CIRCULATIONAHA.108.833004.
19. Muduroglu A, Atasoy MS, Badem S, Yuksel A, Velioglu Y. Routine one-third arch replacement in type 1 acute aortic dissection surgery. J Thorac Cardiovasc Surg. 2025;170:e95-6. doi: 10.1016/j.jtcvs.2024.11.011.
20. Yuksel A, Velioglu Y. Different approaches to the surgical management of acute type A aortic dissection. Ann Thorac Surg. 2026:S0003-4975(26)00133-5. doi: 10.1016/j.athoracsur.2026.01.048. Epub ahead of print.
21. Güner A, Ceran MT, Taban VB, Yıldırım S, Günerhan Y, Dereli Y. Retrospective cohort study: association of monocyte/HDL cholesterol ratio with early mortality in patients undergoing sutureless aortic valve replacement for aortic stenosis. J Cardiothorac Surg. 2026. doi: 10.1186/s13019-026-04244-0. Epub ahead of print.
22. Badem S, Atasoy MS, Yüksel A, Müdüroğlu A, Güven H, Kılıç AÖ, et al. Multi-inflamatuar index is a new predictive parameter for early-term mortality in patients undergoing endovascular aortic repair for ruptured abdominal aortic aneurysm. Eurasian J Med. 2025;57:1-6. doi: 10.5152/eurasianjmed.2025.25736.

ORIGINAL ARTICLE

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CARDIOVASCULAR SURGERY AND INTERVENTIONS

Gamma-glutamyl transferase levels and coronary artery disease severity assessed by SYNTAX score: Impact of premature atherosclerosis

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ABSTRACT

Objectives: Gamma-glutamyl transferase (GGT) has emerged as a biomarker reflecting oxidative stress and low-grade inflammation, both of which play key roles in the development and progression of coronary artery disease (CAD). However, its association with angiographic CAD severity, particularly in patients with premature atherosclerosis, remains incompletely defined.

Patients and methods: A total of 454 consecutive patients with angiographically confirmed CAD managed with an invasive strategy were included. The study aimed to investigate the relationship between serum GGT levels and CAD severity assessed by the SYNTAX score, with a particular focus on premature CAD. Patients were categorized into four age groups: ≤49 years, 50-59 years, 60-69 years, and ≥70 years. Demographic characteristics, cardiovascular risk factors, and laboratory parameters including GGT levels were recorded. Coronary lesion complexity was quantified using the SYNTAX score. Correlation analysis was performed to evaluate the association between GGT levels and SYNTAX score.

Results: GGT levels showed a significant decreasing trend with advancing age ($p<0.001$). Serum GGT demonstrated a weak but statistically significant positive correlation with SYNTAX score ($r=0.136$, $p=0.05$). Notably, patients with premature CAD (≤49 years) exhibited the highest GGT levels compared to older age groups.

Conclusion: Serum GGT levels are positively associated with CAD severity as assessed by the SYNTAX score, particularly in patients with premature atherosclerosis. GGT may serve as a simple, widely available biomarker reflecting coronary atherosclerotic burden, with potential utility in risk stratification, especially in younger patients.

Keywords: Gamma-glutamyl transferase, coronary artery disease, premature atherosclerosis, SYNTAX score.

Gamma-glutamyl transferase (GGT) has emerged as a biomarker reflecting oxidative stress and low-grade inflammation, both of which contribute to the development and progression of coronary artery disease (CAD).[1-3] Coronary artery disease remains the leading cause of morbidity and mortality worldwide despite advances in preventive and therapeutic strategies.[4-6]

Beyond its traditional role as a marker of hepatobiliary dysfunction and alcohol consumption, increasing evidence suggests that GGT is associated with endothelial dysfunction, oxidative stress, and atherosclerotic processes.[1-3] Elevated serum GGT levels have also been linked to adverse cardiovascular outcomes and cardiovascular mortality in patients with established CAD.[4,5]

The severity and complexity of coronary atherosclerosis can be objectively evaluated using angiographic scoring systems. In this context, the SYNTAX score is widely used to assess coronary lesion complexity and overall atherosclerotic burden.[7] However, the relationship between serum GGT levels and angiographic CAD severity, particularly in patients with premature atherosclerosis, remains incompletely understood.

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Premature CAD represents a distinct clinical phenotype characterized by accelerated atherosclerosis and increased oxidative stress burden. Whether circulating GGT levels reflect angiographic CAD severity differently across age groups remains unclear. Therefore, the present study aimed to investigate the association between serum GGT levels and CAD severity assessed by the SYNTAX score, with particular emphasis on premature CAD.

PATIENTS AND METHODS

Study Population

This single-center observational study included 454 consecutive patients with angiographically confirmed CAD who underwent invasive coronary angiography and were managed with an invasive strategy. Consecutive enrollment was used to minimize selection bias. Patients were categorized into four age groups: Group 1: ≤49 years, group 2: 50-59 years, group 3: 60-69 years, group 4: ≥70 years. Premature CAD was defined as age ≤49 years, consistent with prior literature.[7]

Clinical and Laboratory Data

Baseline demographic characteristics, cardiovascular risk factors, and laboratory parameters were obtained.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation and categorical variables as percentages. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. For variables showing normal distribution, One-Way ANOVA was used for group comparisons, whereas for non-normally distributed variables, the Kruskal-Wallis test was applied. Pearson correlation analysis was performed to assess the relationship between serum GGT levels and SYNTAX score. A p-value <0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of serum GGT levels for CAD severity. The area under the curve (AUC) with 95% confidence intervals (CI) was calculated. The optimal cut-off value was determined using the Youden index. Sensitivity and specificity values corresponding to the optimal cut-off point were reported. Variables with p<0.10 in univariate analysis were included in the multivariate logistic regression model. This study was approved by the Ethics Committee of İzmir Bakırçay University Faculty of Medicine (approval no: 2234, date: 07 May 2025). Due to the retrospective design of the study, the requirement for informed consent was waived by the ethics committee.

RESULTS

The study population consisted of 454 patients, of whom 165 (36.3%) were female. Hypertension was present in 60.4%, diabetes mellitus in 40.7%, hyperlipidemia in 39.4%, and 31.5% were active smokers. Percutaneous coronary intervention was performed in 63.2% of patients, while 36.8% underwent coronary artery bypass grafting. Premature CAD patients constituted 8.8% of the cohort. The distribution of patients across age groups was as follows: ≤49 years (n=40), 50-59 years (n=121), 60-69 years (n=159), and ≥70 years (n=134). Serum GGT levels showed a weak but statistically borderline significant positive correlation with SYNTAX score (r=0.136, p=0.05) (Figure 1). SYNTAX score did not differ significantly across age groups (p=0.189). Although a statistically significant correlation was observed between age and SYNTAX score, the strength of this association was very weak (r=0.093, p=0.049) and is unlikely to be clinically meaningful (Figure 2). HDL cholesterol increased with age, while triglyceride and GGT levels decreased significantly across age groups. Detailed clinical, laboratory, and angiographic characteristics according to age groups are presented in Table 1. ROC curve analysis was performed to evaluate the ability of serum GGT levels to predict premature atherosclerosis (Figure 3). The AUC was 0.610 (95% CI: 0.519-0.701, p=0.021), indicating a modest discriminatory performance. At the optimal cut-off value of 30.5 U/L, GGT demonstrated a sensitivity of 70% and a specificity of 53.4% for predicting premature atherosclerosis. While the sensitivity was relatively acceptable, the limited specificity suggests a restricted ability to accurately distinguish between patients with and without premature disease. Overall, these findings indicate that GGT has a statistically significant but clinically modest predictive value for premature atherosclerosis.

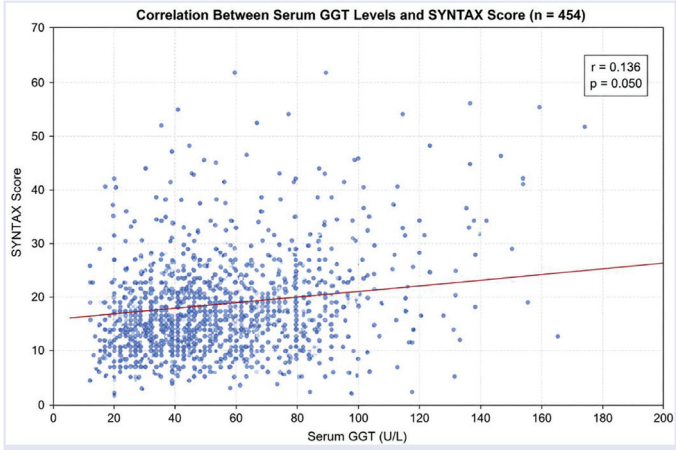

Figure 1. Scatter plot illustrating the relationship between serum gamma-glutamyl transferase (GGT) levels and SYNTAX score.

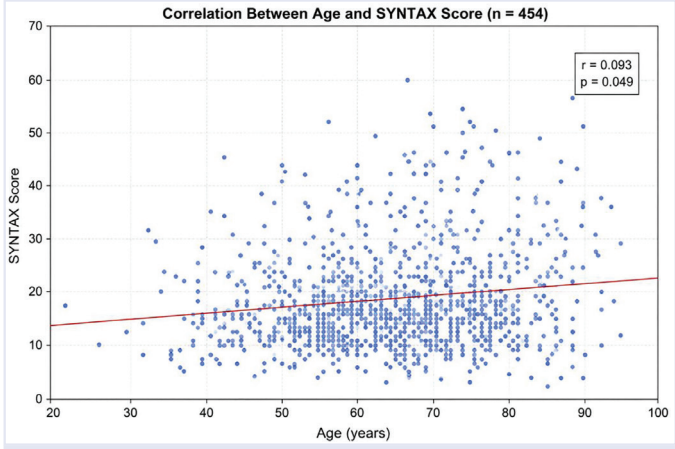

Figure 2. Scatter plot demonstrating the relationship between age and SYNTAX score.

Table 1. Clinical, laboratory, and angiographic characteristics according to age groups

Parameter	Group 1	Group 2	Group 3	Group 4	p-value
Age (years)	43.9±4.5	55.1±2.6	64.9±2.9	75.2±4.2	<0.001
SYNTAX score	16.2±10.5	19.2±10.2	20.1±12.7	21.6±13.9	0.083
Total cholesterol (mg/dL)	201.8±51.1	203.2±51.7	196.8±45.4	191.1±43.3	0.161
LDL-C (mg/dL)	126.1±40.4	121.0±40.2	122.1±38.1	115.2±38.1	0.109
HDL-C (mg/dL)	35.7±6.3	41.4±11.4	42.1±11.8	42.5±12.1	0.003
Triglycerides (mg/dL)	217.3±160.3	193.4±137.9	158.2±79.5	156.5±92.5	0.031
Fasting glucose (mg/dL)	113.3±37.4	130.3±58.8	125.1±46.6	124.3±46.4	0.249
Uric acid (mg/dL)	5.9±1.2	5.9±1.4	6.2±1.5	5.8±1.5	0.212
GGT (U/L)	50.3±45.2	41.0±31.3	40.3±40.5	36.7±47.4	<0.001
TSH (µIU/mL)	1.37±0.86	1.56±1.57	1.43±0.91	1.73±1.63	0.661
HbA1c (%)	6.3±1.4	6.5±1.4	6.5±1.3	6.6±1.5	0.839
BMI (kg/m²)	28.4±4.3	29.3±5.2	28.2±4.2	29.0±4.4	0.282

LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; GGT: Gamma-glutamyl transferase; TSH: Thyroid-stimulating hormone; HbA1c: Glycated hemoglobin; BMI: Body mass index.

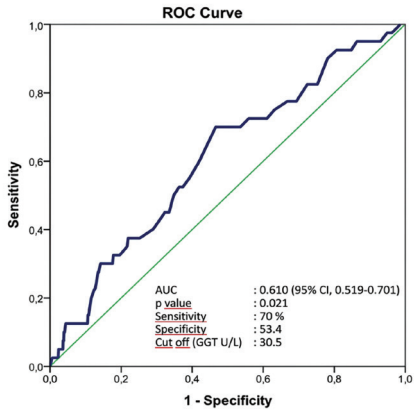

Figure 3. Receiver operating characteristic (ROC) curve analysis demonstrating the predictive performance of serum gamma-glutamyl transferase (GGT) levels for premature coronary artery disease. The area under the curve (AUC) was 0.610 (95% confidence interval [CI]: 0.519-0.701, p=0.021), indicating modest discriminatory ability.

DISCUSSION

In this angiographic study, serum GGT levels demonstrated a statistically borderline but positive association with CAD severity assessed by the SYNTAX score. Although the observed correlation coefficient was modest, this finding may still be biologically meaningful considering the multifactorial nature of coronary atherosclerosis and the complex determinants of angiographic disease burden.[2,3,6] Therefore, the present findings should be interpreted cautiously and considered hypothesis-generating rather than definitive evidence of a direct causal relationship between GGT and CAD complexity.

GGT is traditionally recognized as a hepatobiliary enzyme; however, accumulating evidence suggests that it may also reflect systemic oxidative stress, low-grade inflammation, and cardiometabolic risk burden.[1,2,8-10] Experimental and histopathological studies have demonstrated enzymatically active GGT within human atherosclerotic plaques, particularly in macrophage-rich and lipid-laden regions.[11-15] In this setting, GGT may contribute to oxidative modification of LDL cholesterol and promote plaque progression and instability through reactive oxygen species generation.[12,13] These mechanisms provide a biologically plausible explanation for the observed association between elevated GGT levels and more complex CAD.

Several previous studies have reported associations between GGT and cardiovascular outcomes, including myocardial infarction, heart failure, and cardiovascular mortality.[3-6,8] In addition, studies evaluating angiographic disease burden have demonstrated a relationship between elevated GGT levels and the extent of coronary atherosclerosis in patients with acute coronary syndromes and stable CAD.[16] Our findings are generally consistent with these reports, although the strength of the observed association was relatively weak. This is not unexpected, since SYNTAX score is influenced by numerous clinical and anatomical factors, including age, diabetes mellitus, hypertension, dyslipidemia, smoking, inflammatory activity, and genetic predisposition.[6,7] Accordingly, GGT should not be interpreted as an independent marker of CAD severity based solely on the present study, but rather as a potential adjunctive biomarker reflecting oxidative and metabolic risk.

One of the notable observations of this study was the higher GGT levels observed in patients with premature CAD. Premature coronary atherosclerosis has been associated with increased oxidative stress, metabolic dysregulation, insulin resistance, obesity, smoking, and hypertriglyceridemia, all of which are conditions closely linked to elevated GGT levels.[17,18] In addition, previous studies focusing on premature CAD populations have demonstrated distinct risk profiles and unfavorable cardiovascular characteristics in younger patients with coronary disease.[19,20] These findings suggest that GGT may be more informative in younger or middle-aged patients, in whom oxidative and metabolic mechanisms may contribute more prominently to accelerated atherosclerosis. However, because SYNTAX scores did not significantly differ across age groups, this observation should be interpreted carefully. Higher GGT levels in younger patients may reflect a distinct metabolic and inflammatory phenotype rather than directly indicating greater angiographic disease severity.

In our cohort, triglyceride levels also tended to decrease with advancing age, paralleling the decline in GGT levels. This observation further

supports the close relationship between GGT and metabolic risk profile described in previous studies.[16,17,18] Additionally, the inverse trend observed between bilirubin levels and CAD severity may support the proposed antioxidant role of bilirubin in atherosclerosis progression, although this relationship was not specifically designed as a primary endpoint of the study.

From a clinical perspective, GGT is an inexpensive, widely available, and routinely measured laboratory parameter. If confirmed in larger prospective studies, elevated GGT levels may help identify patients with increased oxidative stress burden and unfavorable cardiometabolic profiles, particularly among individuals with premature CAD. Nevertheless, GGT should not replace established cardiovascular risk markers or imaging-based assessments. Rather, it may serve as a complementary biomarker within a broader cardiovascular risk stratification approach.

Future studies should evaluate the relationship between GGT and CAD severity using clinically meaningful SYNTAX score categories, such as low, intermediate, and high SYNTAX groups.[7] Separate analyses in premature and non-premature CAD populations may further clarify whether GGT has differential relevance according to age-related atherosclerotic phenotype. In addition, prospective studies incorporating serial GGT measurements, plaque imaging, multivariable adjustment, and long-term cardiovascular outcomes are needed to determine whether GGT provides incremental prognostic value beyond established cardiovascular risk markers.

The present study has several limitations that should be considered while interpreting the findings. Due to its observational and cross-sectional design, a causal relationship between GGT levels and CAD severity cannot be established. Serum GGT levels were measured at a single time point, and serial measurements reflecting temporal changes in oxidative stress burden were not available. In addition, important confounding factors such as alcohol consumption, non-alcoholic fatty liver disease, hepatic dysfunction, and medications potentially affecting GGT levels were not systematically evaluated and the single-center design may limit the generalizability and external validity of the findings. The possible influence of cardiovascular therapies, including statins, antiplatelet agents, beta-blockers, and reninangiotensin system inhibitors, also could not be fully assessed.

Furthermore, previous coronary artery disease history, including prior percutaneous coronary intervention or coronary artery bypass grafting, was not analyzed separately, although these factors may affect both angiographic complexity and biochemical parameters. Concomitant atherosclerotic involvement in other vascular territories, such as carotid or peripheral artery disease, was not evaluated. Patients presenting with acute coronary syndromes and elective cases were analyzed together, and separate subgroup analyses according to clinical presentation were not performed, although acute ischemic conditions may influence inflammatory and oxidative biomarkers. Additionally, no multivariable regression analysis was performed to adjust for potential confounding variables, and additional inflammatory or oxidative stress biomarkers were not available. These limitations may have influenced the strength and interpretation of the observed associations.

Serum GGT levels were modestly and positively associated with SYNTAX score in patients with angiographically documented CAD. Higher GGT levels in patients with premature CAD may reflect an oxidative stress– and metabolism-related atherosclerotic phenotype. However, given the borderline statistical significance, modest correlation strength, and absence of multivariable adjustment, these findings should be interpreted cautiously and require confirmation in larger prospective studies incorporating multivariable adjustment and clinically relevant cardiovascular outcomes.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of İzmir Bakırçay University Faculty of Medicine (approval no: 2234, date: 07 May 2025).

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

Acknowledgments

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

Footnotes

Authorship Contributions

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

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

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REFERENCES

1. Turgut O, Tandogan I. Gamma-glutamyltransferase to determine cardiovascular risk: shifting the paradigm forward. J Atheroscler Thromb. 2011;18:177-81. doi: 10.5551/jat.6189.
2. Ndrepepa G, Kastrati A. Gamma-glutamyl transferase and cardiovascular disease. Ann Transl Med. 2016;4:481. doi: 10.21037/atm.2016.12.27.
3. Ndrepepa G, Colleran R, Kastrati A. Gamma-glutamyl transferase and the risk of atherosclerosis and coronary heart disease. Clin Chim Acta. 2018;476:130-8. doi: 10.1016/j.cca.2017.11.026.
4. Yang P, Wu P, Liu X, Feng J, Zheng S, Wang Y, et al. Association between γ-glutamyltransferase level and cardiovascular or all-cause mortality in patients with coronary artery disease: a systematic review and meta-analysis. Angiology. 2019;70:844-52. doi: 10.1177/0003319719850058.
5. Wang J, Zhang D, Huang R, Li X, Huang W. Gamma-glutamyltransferase and risk of cardiovascular mortality: a dose-response meta-analysis of prospective cohort studies. PLoS One. 2017;12:e0172631. doi: 10.1371/journal.pone.0172631.
6. Ruttmann E, Brant LJ, Concin H, Diem G, Rapp K, Ulmer H; Vorarlberg Health Monitoring and Promotion Program Study Group. Gamma-glutamyltransferase as a risk factor for cardiovascular disease mortality: an epidemiological investigation in a cohort of 163,944 Austrian adults. Circulation. 2005;112:2130-7. doi: 10.1161/CIRCULATIONAHA.105.552547.

7. Serruys PW, Onuma Y, Garg S, Sarno G, van den Brand M, Kappetein AP, et al. Assessment of the SYNTAX score in the Syntax study. EuroIntervention. 2009;5:50-6. doi: 10.4244/eijv5i1a9. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention. 2005;1:219-27.

8. Kunutsor SK, Laukkanen JA, Bluemke DA, Butler J, Khan H. Baseline and long-term gamma-glutamyltransferase, heart failure and cardiac arrhythmias in middle-aged Finnish men: prospective study and pooled analysis of published evidence. Eur J Prev Cardiol. 2016;23:1354-62. doi: 10.1177/2047487316644086.

9. Koenig G, Seneff S. Gamma-glutamyltransferase: a predictive biomarker of cellular antioxidant inadequacy and disease risk. Dis Markers. 2015;2015:818570. doi: 10.1155/2015/818570.

10. Bulusu S, Sharma M. What does serum γ-glutamyltransferase tell us as a cardiometabolic risk marker? Ann Clin Biochem. 2016;53:312-32. doi: 10.1177/0004563215597010.

11. Paolicchi A, Emdin M, Ghliozeni E, Ciancia E, Passino C, Popoff G, et al. Images in cardiovascular medicine. Human atherosclerotic plaques contain gamma-glutamyl transpeptidase enzyme activity. Circulation. 2004;109:1440. doi: 10.1161/01.CIR.0000120558.41356.E6.

12. Emdin M, Pompella A, Paolicchi A. Gamma-glutamyltransferase, atherosclerosis, and cardiovascular disease: triggering oxidative stress within the plaque. Circulation. 2005;112:2078-80. doi: 10.1161/CIRCULATIONAHA.105.571919.

13. Pompella A, Emdin M, Passino C, Paolicchi A. The significance of serum gamma-glutamyltransferase in cardiovascular diseases. Clin Chem Lab Med. 2004;42:1085-91. doi: 10.1515/CCLM.2004.224.

14. Paolicchi A, Emdin M, Passino C, Lorenzini E, Titta F, Marchi S, et al. Beta-lipoprotein- and LDL-associated serum gamma-glutamyltransferase in patients with coronary atherosclerosis. Atherosclerosis. 2006;186:80-5. doi: 10.1016/j.atherosclerosis.2005.07.012.

15. Franzini M, Corti A, Martinelli B, Del Corso A, Emdin M, Parenti GF, et al. Gamma-glutamyltransferase activity in human atherosclerotic plaques--biochemical similarities with the circulating enzyme. Atherosclerosis. 2009;202:119-27. doi: 10.1016/j.atherosclerosis.2008.03.023.

16. Duran M, Uysal OK, Yılmaz Y, Günebakmaz O, Arınç H, Topsakal R, et al. Serum gamma-glutamyltransferase and the burden of atherosclerosis in patients with acute coronary syndrome. Turk Kardiyol Dern Ars. 2013;41:275-81. doi:10.5543/tkda.2013.99896.

17. Matsha TE, Macharia M, Yako YY, Erasmus RT, Hassan MS, Kengne AP. Gammaglutamyltransferase, insulin resistance and cardiometabolic risk profile in a middle-aged African population. Eur J Prev Cardiol. 2014;21:1541-8. doi: 10.1177/2047487313501967.

18. Kang YH, Min HK, Son SM, Kim IJ, Kim YK. The association of serum gamma glutamyltransferase with components of the metabolic syndrome in the Korean adults. Diabetes Res Clin Pract. 2007;77:306-13. doi: 10.1016/j.diabres.2006.11.009.

19. Cojocaru PA, Țieranu ML, Piorescu MTL, Buciu IC, Belu AM, Cureraru SI, et al. Myocardical infarction in young adults: revisiting risk factors and atherothrombotic pathways. Medicina (Kaunas). 2025;61:1615. doi: 10.3390/medicina61091615.

20. Rakam K, Dayanand P, Chepuri S. Early-onset coronary artery disease in young adults: a systematic review. Cardiovasc Med. 2025;15:301-9. DOI : 10.61336/ejcm/25-09-48.

ORIGINAL ARTICLE

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CARDIOVASCULAR SURGERY AND INTERVENTIONS

Predictors of first-attempt puncture success in distal radial access for coronary procedures

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ABSTRACT

Objectives: This study aimed to identify patient-based clinical and demographic factors affecting the success of the first puncture attempt in patients undergoing distal radial access (dTRA) for coronary angiography and interventional procedures.

Patients and methods: The study was designed as a retrospective, single-center observational study. Two hundred eighty-six consecutive patients who underwent dTRA procedures between January 2023 and March 2026 were included in the analysis. All puncture procedures were performed by a single experienced operator, with palpation guidance from the anatomical snuffbox region. Univariate and multivariate logistic regression analysis and receiver operating characteristic (ROC) curve analysis were used to identify independent variables predicting first-attempt success.

Results: Successful puncture was achieved on the first attempt in 70.6% (n=202) of the study population. Multivariate analysis showed that advanced age (odds ratio [OR]: 0.93, p<0.001) and female sex (OR: 0.50, p=0.015) were associated with a lower likelihood of first-attempt success, whereas higher body mass index (BMI) (OR: 1.17, p=0.001) was associated with a higher likelihood of success. The group with failure on the first attempt had significantly longer puncture time and a higher rate of access site complications (hematoma, spasm, *etc.*) (14.3% *vs.* 6.9%; p=0.049). The discriminatory power of the model was calculated as area under the curve: 0.721 (95% confidence interval: 0.658-0.785) in the ROC analysis.

Conclusion: The first-attempt success rate of dTRA was associated with patient age, sex, and BMI. Ultrasound-guided puncture strategies are recommended to increase procedural success and reduce vascular complications, especially in high-risk patient groups such as the elderly, women, and those with low BMI.

Keywords: Distal radial access, first-attempt success, coronary angiography, body mass index, sex differences.

Since its initial description by Kiemeneij,[1] distal radial access (dTRA) has gradually gained a place in coronary diagnostic and interventional practice. It is performed at the level of the anatomical snuffbox. It is an alternative to classic transradial access. Compared with conventional radial access, dTRA may offer practical advantages, including easier hemostasis, earlier mobilization, and a lower risk of radial artery occlusion.[1] However, the artery diameter is smaller, and anatomical variations may be observed. Therefore, it is technically more challenging and requires a significant learning curve.[2]

Recent studies have shown that dTRA is safe and feasible for both diagnostic and interventional procedures. However, the success of distal radial puncture depends not only on operator experience but also on patient-related factors. First-attempt puncture success in dTRA is critically important in terms of reducing puncture time, increasing patient comfort, and reducing the risk of vascular complications.[3] In contrast, multiple puncture attempts may lead to vascular spasm, hematoma formation, and prolonged puncture time.

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Several factors that can affect the success of distal radial puncture have been identified in the literature. Variables such as advanced age, female sex, small vessel diameter, and body mass index (BMI) have been reported to affect puncture success.[3,4] It has been shown that female patients have a smaller distal radial artery diameter, which can negatively affect puncture succes.[4] In addition, female sex has been reported to be associated with a lower success rate and higher access site complications in dTRA.[4,5] According to Korean Prospective Registry for Evaluating the Safety and Efficacy of Distal Radial Approach (KODRA) data, female sex is an independent risk factor. This is particularly evident in terms of minor bleeding.[5]

The effect of BMI on dTRA is more complex. Some studies have shown that obesity has no significant effect on overall cannulation success or complication rates.[5] However, increased subcutaneous fat tissue can prolong puncture time by making palpation of arterial pulsation more difficult.[5] On the other hand, low BMI and small artery diameter can be important determinants in terms of technical difficulties due to increased vascular mobility.[3]

However, comprehensive studies evaluating the combined effect of age, sex, and BMI on first-attempt puncture success in dTRA are limited in the current literature. This study aims to evaluate patient-related factors affecting first-attempt puncture success in dTRA and to contribute to the determination of appropriate patient selection and procedure strategy in clinical practice.

PATIENTS AND METHODS

Patient Selection and Research Design

This research was structured as a retrospective observational study at a specialized tertiary heart center. The study population comprised individuals scheduled for coronary procedures where the dTRA approach was utilized as the primary access site.

Patients underwent coronary angiography or percutaneous coronary intervention (PCI) via dTRA. All procedures were performed at the Cardiology Clinic of Mardin Training and Research Hospital. The study period was between January 2023 and March 2026.

All consecutive patients who underwent dTRA procedures within the specified time period were screened. Only patients with complete clinical and procedural records were included in the analysis. Individuals aged 18 years and older were included in the study.

Inclusion and Exclusion Criteria

Adult individuals who underwent coronary angiography or PCI via dTRA were eligible for inclusion. The exclusion criteria were defined as follows:

1. Lack of clinical or procedural data,

2. Use of a vascular access route other than dTRA,

3. Inability to confirm the accuracy of the records.

Procedure Description

Distal radial puncture was performed under palpation guidance from the anatomical snuffbox area. Standard interventional cardiology protocols were applied throughout the procedure. Necessary anticoagulation therapy was provided during the procedure in accordance with standard practices. All procedures were performed by a single interventional cardiologist with experience in over 200 cases of dTRA.

Study Endpoints and Operational Definitions

Success on the first attempt was defined as achieving cannulation after a single-needle puncture. Failure was considered to be the need for multiple needle punctures. The outcome variables evaluated in the study included total number of punctures, puncture time, and site-related complications. Puncture time was defined as the time from skin puncture to successful cannulation.[3] Since the standard approach in our clinic is left radial access, left dTRA was most frequently used according to operator preference. Access site complications were evaluated based on hospital records and defined as a composite endpoint including complications such as hematoma, radial artery occlusion, radial artery spasm, ecchymosis, and local numbness. For analytical comparisons, patients were stratified into two distinct groups:

- Successful puncture on the first attempt,

- Failed puncture on the first attempt.

Data Collection

Patient demographic and clinical characteristics were extracted from the institutional electronic medical record system. Procedural data were obtained from catheterization laboratory records. The number of punctures and the success rate on the first attempt were recorded by the operator as part of routine post-procedure records. Data were reviewed retrospectively. Recorded variables included age, sex, BMI, diabetes mellitus, hypertension, hyperlipidemia, smoking, and a known history of coronary artery disease. Procedure-related data included procedure type (diagnostic angiography or PCI), number of punctures, puncture time, first-attempt success and site complications.

Sample Size

A minimum of 197 patients was calculated as required based on G*Power 3.1 analysis. During the study period, 286 patients who fulfilled the inclusion criteria were enrolled in the analysis.

Statistical Analysis

Data processing and statistical assessments were executed via IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was verified before analysis; based on the distribution, these data were reported as mean ± standard deviation or median (interquartile range). Inter-group comparisons were conducted using either parametric or non-parametric methods, depending on the data's distributional characteristics. For categorical data, frequencies and percentages were utilized, with differences evaluated through Fisher's exact test or the chi-square test where applicable.

To determine the predictors of successful first-attempt puncture, a logistic regression framework was employed. Factors exhibiting a p-value <0.10 in the univariable screen, alongside clinically significant variables, were incorporated into the multivariable regression model. To maintain model parsimony and prevent overfitting, the total number of predictors was strictly limited. The diagnostic accuracy of the resulting model was quantified using the area under the curve (AUC) derived from receiver operating characteristic (ROC) analysis, including

95% confidence intervals. The Youden index was utilized to identify the optimal cut-off point. Furthermore, model calibration was validated using the Hosmer-Lemeshow test. Statistical significance was defined as a two-tailed p-value <0.05.

Ethical Approval

Ethical clearance for this investigation was granted by the Mardin Training and Research Hospital Medical Ethics Committee (approval number: 2026/04-10, dated: 24.04.2026). The research protocols complied with the standards set forth in the Declaration of Helsinki. Due to the study's retrospective design, individual consent was not required; however, all datasets were completely de-identified prior to analysis to maintain confidentiality.

RESULTS

Demographic and clinical characteristics of the groups according to the success of the first puncture attempt are presented in Table 1. The first puncture attempt was successful in 202 patients (70.6%) and unsuccessful in 84 patients (29.4%). Patients with failed first-attempt puncture were older (p<0.001). Female sex was more frequent in the unsuccessful group (47.6% *vs.* 31.3%, p=0.009). BMI was higher in the successful group (p=0.002). The groups were similar in terms of hypertension, diabetes, smoking, and hyperlipidemia (all p>0.05). There was no difference in history of coronary artery disease and ipsilateral radial intervention history (p>0.05). Systolic blood pressure and creatinine levels were similar (p>0.05). The rate of presentation with acute coronary syndrome was not different between the two groups (p=0.354).

Table 2 summarizes the data related to the procedures. Patients in the unsuccessful first-attempt category required a substantially greater number of punctures compared to the successful group (p<0.001). Similarly, the duration of the puncture process was notably extended in the failed group (p<0.001). No significant disparity was observed in PCI rates between the cohorts (p=0.658). Regarding safety, the incidence of access site complications was significantly higher among those with failed first attempts (14.3% *vs.* 6.9%, p=0.049). However, the groups showed no statistical difference in the preference for left dTRA (p=0.362) or the utilization of 6F sheaths (p=0.209).

Regression and ROC Analysis Results

Factors affecting first-attempt success are shown in Table 3. In univariable analysis, age, female sex, and BMI were found to be associated with first attempt success. As age increased, the probability of success decreased (odds ratio [OR]: 0.92, 95% confidence interval [CI]: 0.89-0.95, p<0.001). Female sex was associated with lower success (OR: 0.50, 95% CI: 0.29-0.84, p=0.010). As BMI increased, the probability of success increased (OR: 1.15, 95% CI: 1.05-1.27, p=0.003). In multivariate analysis, age (OR: 0.93, 95% CI: 0.90-0.96, p<0.001), female sex (OR: 0.50, 95% CI: 0.29-0.87, p=0.015), and BMI (OR: 1.17, 95% CI: 1.06-1.30, p=0.001) remained significant. No significant association was found with previous radial intervention, diabetes, and creatinine levels (all p>0.05).

Table 1. Baseline characteristics according to first-attempt puncture success

Variable	Overall (n=286)	Successful first-attempt (n=202)	Failed first-attempt (n=84)	p-value
Age, years	64.15±8.57	62.61±7.77	67.84±9.29	<0.001
Female sex, n (%)	103 (36.1)	63 (31.3)	40 (47.6)	0.009
BMI, kg/m²	25.76±2.69	26.08±2.57	25.01±2.82	0.002
Hypertension, n (%)	152 (53.1)	102 (50.5)	50 (59.5)	0.163
Diabetes mellitus, n (%)	85 (29.7)	58 (28.7)	27 (32.1)	0.563
Current smoking, n (%)	84 (29.4)	61 (30.2)	23 (27.4)	0.634
Hyperlipidemia, n (%)	59 (20.6)	38 (18.8)	21 (25.0)	0.239
Previous CAD, n (%)	51 (17.8)	32 (15.8)	19 (22.6)	0.173
Previous ipsilateral radial access, n (%)	37 (12.9)	23 (11.4)	14 (16.7)	0.226
Systolic blood pressure, mmHg	130.38±8.23	129.94±8.08	131.45±8.52	0.158
Creatinine, mg/dL	1.04 (0.82-1.24)	1.10 (0.81-1.24)	0.92 (0.84-1.22)	0.253
ACS indication, n (%)	30 (10.5)	19 (9.4)	11 (13.1)	0.354

Data are presented as mean ± standard deviation, median (interquartile range), or n (%), as appropriate. BMI: Body mass index; CAD: Coronary artery disease; ACS: Acute coronary syndrome.

Table 2. Procedural characteristics according to first-attempt puncture outcome

Variable	Overall (n=286)	Successful first-attempt (n=202)	Failed first-attempt (n=84)	p-value
Puncture attempts, n	1 (1-2)	1 (1-1)	2 (2-3)	<0.001
Puncture time, s	65 (40-90)	55 (35-80)	93 (65-130)	<0.001
Procedure type, PCI, n (%)	142 (49.7)	102 (50.5)	40 (47.6)	0.658
Access-site complications, n (%)	26 (9.1)	14 (6.9)	12 (14.3)	0.049
Puncture side, left, n (%)	265 (92.7)	189 (93.6)	76 (90.5)	0.362
Sheath size, 6F, n (%)	199 (69.6)	145 (71.8)	54 (64.3)	0.209

Values are presented as median (interquartile range) or n (%), as appropriate. PCI: Percutaneous coronary intervention; F: French.

Model Performance and Diagnostics

The multivariable model demonstrated a moderate-to-good predictive capacity, with an AUC of 0.721 (95% CI: 0.658-0.785, p<0.001) according to the ROC analysis. Assessment of the model's calibration via the Hosmer-Lemeshow test indicated an adequate fit (χ^2=10.085, df=8, p=0.259). Based on the Youden index, the optimal probability threshold was identified as 0.683. At this cut-off point, the model yielded a sensitivity of 67.2% and a specificity of 65.5%, as illustrated in Figure 1.

DISCUSSION

The first-attempt success rate in dTRA was 70.6%. Advanced age, female sex, and low BMI were independent predictors of failed first-attempt puncture. Failed first-attempt puncture was also associated with longer puncture time and higher access-site complication rates.

dTRA has emerged as an alternative to the classic transradial approach in recent years. Data from different centers show that dTRA is a safe and feasible method.[6,7] Its significant advantages include lower radial artery occlusion and shorter hemostasis time.[1,7] Overall procedural success rates for dTRA have been reported in the literature to be between 88% and 95.5%.[6,7] However, these studies have mostly focused on overall cannulation success. Data on success on the first attempt are limited.

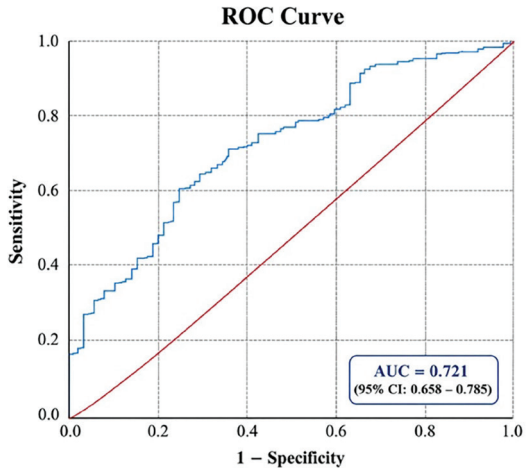

Figure 1. ROC curve of the multivariable prediction model. The AUC was 0.721 (95% CI: 0.658-0.785). The optimal cut-off value was 0.683 (sensitivity: 67.2%, specificity: 65.5%).

AUC: Area under the curve; ROC: Receiver operating characteristic; CI: Confidence interval.

Achieving success on the first attempt shortens the puncture time. It reduces complications such as spasm and hematoma. It contributes positively to patient comfort.[3]

A negative correlation was found between female sex and puncture success. This is a key finding of the study. A possible explanation is the smaller diameter of the distal radial artery in women.[3,8] The more delicate vascular structure may also make the procedure more difficult.[3] KODRA data show that female sex is an independent risk factor for access site complications. This increase has been reported to be largely due to minor bleeding events.[4] Therefore, a more careful and controlled puncture approach should be preferred in female patients.

Our study showed that low BMI reduced puncture success. This finding is consistent with studies reporting that low body weight and small vessel diameter pose technical challenges.[3,5,8] In patients with low BMI, the arterial diameter is generally smaller, and the subcutaneous supporting tissue is also more limited. This can lead to increased arterial mobility, making vessel stabilization during puncture more difficult.[9] Consequently, cannulation becomes more challenging, and the probability of failure on the first attempt increases. Conversely, an increase in subcutaneous tissue with increasing BMI may have facilitate palpation of the artery.

The relationship between BMI and puncture success is not clear. Results in the literature are heterogeneous. A large-scale analysis based on KODRA data showed that obesity did not affect the success rate. However, it was reported that the puncture time was prolonged.[4] These findings suggest that BMI may have different effects. In our study, the success rate increased as BMI increased. This may be related to the small vessel diameter seen in low BMI. Increased vessel mobility may also pose technical challenges. Therefore, low BMI can be considered a factor that increases the likelihood of failure on the first attempt.

A negative correlation was found between advanced age and puncture success. Advanced age may negatively affect puncture success because of vascular calcification, tortuosity, and reduced arterial elasticity.[10,11] Therefore, dTRA should be planned more carefully in the elderly age group.

When procedure-related variables were evaluated, the sheath size did not have an effect on success in the first attempt. This observation suggests that success is primarily determined in the initial stage of puncture. That is, the critical step is the first entry into the artery. It is known that dTRA has a significant learning curve. Success rates have been shown to stabilize after approximately 200 cases.[2] This highlights the importance of operator experience. In our study, all procedures

Table 3. Univariable and multivariable logistic regression analysis of predictors of first-attempt puncture success

Variable	Univariable OR (95% CI)	p-value	Multivariable OR (95% CI)	p-value
Age	0.92 (0.89-0.95)	<0.001	0.93 (0.90-0.96)	<0.001
Female sex	0.50 (0.29-0.84)	0.010	0.50 (0.29-0.87)	0.015
BMI	1.15 (1.05-1.27)	0.003	1.17 (1.06-1.30)	0.001
Previous ipsilateral radial access	0.64 (0.31-1.31)	0.228	-	-
Diabetes mellitus	0.85 (0.49-1.47)	0.563	-	-
Creatinine	1.34 (0.81-2.24)	0.248	-	-

Variables with p<0.10 in univariable analysis and clinically relevant factors were included in the multivariable logistic regression model. A p-value <0.05 was considered statistically significant. OR: Odds ratio; CI: Confidence interval; BMI: Body mass index.

were performed by an experienced operator. Therefore, it can be assumed that the results obtained reflect more patient-related factors.

Ultrasound-guided puncture has been reported to increase the success rate. This effect is particularly pronounced in patients with low BMI and women.[3,12] It has also been shown to reduce complication rates.[3,12] In our series, all interventions were performed with palpation. This may have increased technical difficulties in some patient groups. The use of ultrasound may be beneficial, especially in high-risk patients. Adding this approach to routine practice may increase success rates.

Our study has a single-center and retrospective design. All procedures were performed by a single operator with experience in more than 200 dTRA cases. While this increases technical standardization, it may limit the generalizability of the results. Furthermore, recording bias cannot be completely ruled out due to the operator recording the number of punctures. The lack of ultrasound-guided puncture may also have affected the results.

In conclusion, the success of puncture on the first attempt in dTRA is closely related to the patient's age, sex, and BMI. Technical challenges should be anticipated, especially in elderly, female, and low BMI patients, and auxiliary methods such as ultrasound guidance should be planned when necessary.

Ethics

Ethics Committee Approval: Ethical clearance for this investigation was granted by the Mardin Training and Research Hospital Medical Ethics Committee (approval number: 2026/04-10, dated: 24.04.2026). The research protocols complied with the standards set forth in the Declaration of Helsinki.

Informed Consent: Due to the study's retrospective design, individual consent was not required; however, all datasets were completely de-identified prior to analysis to maintain confidentiality.

Acknowledgments

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

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.A.; Concept: A.A., R.K., T.G., M.Z.K.; Design: A.A., R.K., T.G., B.A., A.E., A.Ar., M.S.C., M.R.T., M.Z.K.; Data Collection or Processing: A.A., R.K., T.G., B.A., A.E., A.Ar., M.S.C., M.R.T., M.Z.K.; Analysis or Interpretation: A.A., R.K., T.G., B.A.; Literature Search: A.A., R.K., T.G., B.A., M.S.C., M.Z.K; Writing: A.A., R.K., T.G.

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REFERENCES

1. Kiemeneij F. Left distal transradial access in the anatomical snuffbox for coronary angiography (ldTRA) and interventions (ldTRI). EuroIntervention. 2017;13:851-7. doi: 10.4244/EIJ-D-17-00079.
2. Roh JW, Kim Y, Lee OH, Im E, Cho DK, Choi D, et al. The learning curve of the distal radial access for coronary intervention. Sci Rep. 2021;11:13217. doi: 10.1038/s41598-021-92742-7.
3. Ikuta A, Kubo S, Osakada K, Takamatsu M, Takahashi K, Ohya M, et al. Predictors of success and puncture site complications in the distal radial approach. Heart Vessels. 2023;38:147-56. doi: 10.1007/s00380-022-02152-6.
4. Roh JW, Heo SJ, Lee OH, Im E, Cho DK, Lee JW, et al. Distal radial access and women: implications for access site outcomes in coronary procedures. J Am Heart Assoc. 2025;14:e036285. doi: 10.1161/JAHA.124.036285.
5. Roh JW, Heo SJ, Lee OH, Im E, Cho DK, Lee JW, et al. Impact of obesity on palpation-guided distal radial access for coronary procedures: subgroup analysis of the multicenter, prospective KODRA registry. Cardiol J. 2025;32:598-606. doi: 10.5603/cj.106255.
6. Lee JW, Park SW, Son JW, Ahn SG, Lee SH. Real-world experience of the left distal transradial approach for coronary angiography and percutaneous coronary intervention: a prospective observational study (LeDRA). EuroIntervention. 2018;14:e995-1003. doi: 10.4244/EIJ-D-18-00635.
7. Mhanna M, Beran A, Nazir S, Al-Abdouh A, Barbarawi M, Sajdeya O, et al. Outcomes of distal versus conventional transradial access for coronary angiography and intervention: an updated systematic review and meta-analysis. Int J Cardiol. 2021;344:47-53. doi: 10.1016/j.ijcard.2021.10.003.
8. Norimatsu K, Kusumoto T, Yoshimoto K, Tsukamoto M, Kuwano T, Nishikawa H, et al. Importance of measurement of the diameter of the distal radial artery in a distal radial approach from the anatomical snuffbox before coronary catheterization. Heart Vessels. 2019;34:1615-20. doi: 10.1007/s00380-019-01404-2.
9. Sgueglia GA, Di Giorgio A, Gaspardone A, Babunashvili A. Anatomic basis and physiological rationale of distal radial artery access for percutaneous coronary and endovascular procedures. JACC Cardiovasc Interv. 2018;11:2113-9. doi: 10.1016/j.jcin.2018.04.045.
10. Wang SY, Qiu Q, Shen X, Shen QH. Development and validation of a nomogram for predicting difficult radial artery cannulation in adult surgical patients. Heliyon. 2024;10:e24524. doi: 10.1016/j.heliyon.2024.e24524.
11. Barry M, Barry F, Gun M, Padurean P, Ikoli JF, Havet E, et al. Influence of age and sex on the thickness of the radial artery wall. Curr Probl Cardiol. 2024;49:102523. doi: 10.1016/j.cpcardiol.2024.102523.
12. Seto AH, Roberts JS, Abu-Fadel MS, Czak SJ, Latif F, Jain SP, et al. Real-time ultrasound guidance facilitates transradial access: RAUST (radial artery access with ultrasound trial). JACC Cardiovasc Interv. 2015;8:283-91. doi: 10.1016/j.jcin.2014.05.036.

ORIGINAL ARTICLE

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CARDIOVASCULAR SURGERY AND INTERVENTIONS

Long COVID meets the pump: Identifying who declines after cardiopulmonary bypass

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ABSTRACT

Objectives: Long coronavirus (COVID) is increasingly encountered in patients undergoing major cardiac surgery. Cardiopulmonary bypass (CPB) induces systemic inflammation that may overlap with proposed mechanisms of Long COVID; however, its contribution to postoperative symptom progression remains unclear. This study evaluated the prevalence of long COVID and predictors of postoperative symptom worsening in patients undergoing coronary artery bypass surgery.

Patients and methods: This retrospective analysis used prospectively collected perioperative symptom surveillance data from 1,421 adults undergoing CPB-assisted coronary artery bypass grafting, with or without concomitant valve surgery (November 2020-September 2025). Only patients with a complete 3-month follow-up were included. Symptoms were assessed preoperatively and at 3 months using a structured questionnaire and scoring system.

Results: Long COVID symptoms were present in 5.6% of patients. Affected individuals were more often ≥65 years, female, and had poor glycemic control, severe obesity, repeated COVID-19 infections, sleep disturbances, and neuropsychiatric or immunologic disorders. The factor V Leiden mutation was more frequent. Symptom worsening was independently associated with HbA1c >9%, multivessel coronary artery disease, severe obesity, and neuropsychiatric or immunologic comorbidities. CPB exposure was not independently associated with symptom progression.

Conclusion: CPB was not associated with increased progression of postoperative symptoms. Findings suggest that symptom worsening is primarily related to underlying metabolic and neuropsychiatric vulnerability, supporting the importance of perioperative risk stratification.

Keywords: Long COVID, cardiopulmonary bypass, coronary artery bypass grafting, postoperative complications, risk factors.

Long coronavirus (COVID) syndrome, also referred to as post-acute coronavirus disease-2019 (COVID-19) condition, is increasingly recognized as a heterogeneous multisystem disorder characterized by persistent fatigue, dyspnea, neurocognitive impairment, dysautonomia, sleep disturbance, and affective symptoms following severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection.[1-3]

Persistent symptoms have been documented across a wide spectrum of clinical severity and may substantially affect functional recovery and quality of life.[4,5] Although initially described in ambulatory populations, subsequent studies have demonstrated that symptom persistence is also common after hospitalization, with measurable physical, cognitive, and psychological impairment extending beyond the acute phase of illness.[6,7] Reduced physical performance and impaired functional capacity at hospital discharge further suggest sustained physiologic vulnerability in affected patients.[8]

The pathophysiology of long COVID appears multifactorial and includes persistent immune activation, endothelial dysfunction, autonomic imbalance, and thromboinflammatory signaling.[9,10] Endothelial injury and microvascular inflammation may contribute to ongoing multisystem symptoms and prolonged recovery.[10] Cardiovascular involvement following SARS-CoV-2 infection has also been increasingly recognized, including myocardial inflammation and long-term cardiovascular sequelae.[11,12] These findings suggest that patients with long COVID may present with underlying physiologic vulnerability that could influence perioperative outcomes.

Cardiac surgery performed with cardiopulmonary bypass (CPB) represents a particularly relevant physiologic setting in which postoperative symptom evolution may differ from that observed in non-surgical populations. CPB induces a systemic inflammatory response characterized by endothelial activation, cytokine release, oxidative stress,

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and microvascular dysfunction.[13] In addition, perioperative alterations in cerebral perfusion, microembolic exposure, and neurohumoral stress may contribute to postoperative neurocognitive dysfunction.[14] These mechanisms overlap with domains commonly affected in long COVID, including cognitive impairment and autonomic dysregulation.

Beyond systemic inflammatory activation, CPB is associated with alterations in microcirculatory flow, endothelial permeability, and coagulation pathways, which may influence postoperative recovery. These effects may be particularly relevant in patients with pre-existing endothelial dysfunction or persistent immune activation, both of which have been implicated in long COVID.

In this context, patients undergoing coronary artery bypass grafting (CABG) with CPB represent a population that substantially overlaps with established long COVID risk groups. Advanced age, diabetes mellitus, obesity, and cardiometabolic disease have all been associated with increased persistence of post-COVID-19 symptom burden.[4,5,11] These comorbidities are highly prevalent in contemporary cardiac surgical cohorts.[15] Emerging evidence also suggests that autoimmune and inflammatory mechanisms may contribute to symptom persistence in susceptible individuals.[9]

Despite these considerations, data describing longitudinal symptom evolution in patients with long COVID undergoing cardiac surgery remain limited. Most available studies have focused on early postoperative morbidity rather than on the structured assessment of symptom trajectories beyond hospital discharge.[16] This represents an important knowledge gap, particularly as the number of patients with prior SARS-CoV-2 infection undergoing cardiac surgery continues to increase.

To address this knowledge gap, we performed a retrospective analysis of prospectively collected institutional perioperative symptom surveillance data from a large cohort of patients undergoing CABG with CPB, with or without concomitant valve surgery. The objectives were to determine the prevalence of long COVID, characterize longitudinal symptom trajectories, and identify predictors of clinically meaningful postoperative symptom worsening.

PATIENTS AND METHODS

Study Design and Reporting Standards

This study is a retrospective analysis of prospectively collected data from an institutional perioperative symptom surveillance program. The surveillance program was introduced in November 2020 to clinically monitor persistent post-infectious and vaccination-related symptoms in patients undergoing cardiac surgery requiring CPB. Subsequently, the scientific relevance of the accumulated dataset was recognized, and a structured research protocol was developed. Ethical approval was obtained from the Institutional Ethics Committee of Dr. İsmail Fehmi Cumalioğlu City Hospital (approval number: AN-261203-16, date: 12.03.2026). The present investigation therefore combines prospective data acquisition with a retrospective, hypothesis-driven analysis.

The study was designed to evaluate perioperative symptom trajectories in patients with prior SARS-CoV-2 infection and to determine predictors of postoperative symptom worsening. The study adhered to the strengthening the reporting of observational studies in epidemiology recommendations for observational cohort studies.[17] The study was conducted in accordance with the Declaration of Helsinki. The requirement for individual informed consent was waived by the ethics committee because the study was observational. No prespecified sample size calculation was performed because all consecutive eligible patients within the study period were included

Study Population

Between November 1, 2020, and September 30, 2025, consecutive adult patients undergoing CABG performed with CPB, with or without concomitant valve procedures, were included. Patients undergoing emergent surgery were excluded because acute perioperative instability may confound longitudinal symptom assessment. Off-pump procedures were excluded to isolate the physiologic effects attributable to CPB. Additional exclusion criteria included isolated valve procedures, isolated aortic surgery, preoperative mechanical circulatory support, stroke within 90 days before surgery, incomplete symptom assessment, and missing three-month follow-up data.

To ensure complete three-month postoperative follow-up data were available at the time of analysis, patients undergoing surgery after September 30, 2025, were excluded from the final dataset.

Exposure Variables and Operative Management

Standard CPB techniques with moderate systemic hypothermia and conventional perfusion strategies were used. CPB duration was modeled as a continuous exposure variable, and potential non-linearity was assessed using restricted cubic splines.

Recorded intraoperative variables included aortic cross-clamp time, nadir temperature, cardioplegia characteristics, intraoperative hematocrit, degree of hemodilution, transfusion requirements, peak lactate concentration, vasoactive and inotropic support, intraoperative arrhythmias, low cardiac output syndrome, and regional cerebral oxygen saturation measured by near-infrared spectroscopy.

SARS-CoV-2 Exposure Variables

Confirmed SARS-CoV-2 infection was defined as documented polymerase chain reaction or antigen positivity or hospitalization attributable to COVID-19. Infection burden was modeled as an ordinal variable based on the number of infection episodes. Additional variables included COVID-19–related hospitalization, intensive care unit (ICU) admission, mechanical ventilation, vaccination dose count, and the interval between infection and surgery.

Sensitivity analyses were prespecified according to the infection-to-surgery interval (<6 months *vs.* ≥6 months) and restricted to laboratory-confirmed infection.

Baseline Clinical Variables

Baseline demographic, clinical, and laboratory variables were collected prospectively, including cardiometabolic risk factors, neurologic and psychiatric comorbidities, inflammatory biomarkers, and established surgical risk scores.

Long COVID Definition

Long COVID was defined as the persistence of symptoms for at least 12 weeks after confirmed SARS-CoV-2 infection without an alternative explanation, consistent with the World Health

Organization post-COVID-19 condition criteria.[18] Symptom burden was assessed using a structured long COVID questionnaire (LCQ), which was administered preoperatively and again at three months postoperatively. A composite symptom score was calculated, and clinically meaningful worsening was predefined as an increase of at least five points.

Predefined Predictive Risk Phenotype

An a priori metabolic and neuropsychiatric vulnerability phenotype was constructed based on biological plausibility. The phenotype included HbA1c >9%, body mass index ≥36 kg/m², three-vessel coronary artery disease, neurologic, psychiatric, and immunologic disease, and an infection-to-surgery interval <6 months. The cumulative number of phenotype components was modeled as an ordinal variable.

Outcomes

The primary outcome was clinically meaningful worsening of long COVID symptoms at three months. Secondary outcomes included the change in the composite symptom score, domain-specific symptom trajectories, and the interaction between CPB exposure and the predefined vulnerability phenotype.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median (interquartile range), as appropriate. Group comparisons were performed using parametric or non-parametric tests, as appropriate. Longitudinal symptom evolution was analyzed using mixed-effects models for repeated measures. Multivariable logistic regression was used to identify predictors of symptom worsening. The interaction between CPB duration and the predefined vulnerability phenotype was tested. Multicollinearity was assessed using variance inflation factors. Model discrimination was evaluated using the area under the receiver operating characteristic curve, and calibration was evaluated using the Hosmer-Lemeshow test. Internal validation was performed using bootstrap resampling with 1,000 iterations. When missing data were below 5%, complete-case analysis was used. Statistical significance was defined as two-sided $p<0.05$. All analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY, USA).

RESULTS

Study Population and Long COVID Prevalence

Between November 2020 and September 2025, 1,421 consecutive adult patients who underwent CABG with CPB, with or without concomitant valve procedures, met the inclusion criteria. Prior confirmed SARS-CoV-2 infection was documented in 912 patients (64.2%). At baseline, long COVID symptoms were identified in 80 patients, corresponding to 5.6% of the overall cohort and 8.8% of previously infected individuals. At three months, symptom trajectories improved in 41 patients (51.3%), remained stable in 27 (33.7%), and worsened in 12 (15.0%). The study flow and symptom evolution are illustrated in Figure 1.

Demographic and Vascular Vulnerability Profile

Patients with long COVID differed substantially from those without persistent symptoms in demographic characteristics, cardiometabolic burden, and markers of systemic vascular vulnerability (Table 1).

Patients with long COVID were older, more often female, and had higher body mass index, increased waist-hip ratio, and lower ankle-brachial index values. Reinfection burden and recent infection within six months before surgery were more common, and rates of COVID-19-related hospitalization and ICU admission were higher. Frailty scores and operative risk estimates were also significantly higher in the long COVID group.

Baseline Clinical and Laboratory Characteristics

Baseline clinical characteristics demonstrated clustering of metabolic, neurologic, immunologic, and inflammatory comorbidities among patients with long COVID (Table 2).

Patients with long COVID had a higher prevalence of diabetes mellitus, poor glycemic control (particularly HbA1c >9%), obstructive sleep apnea, and neurologic, psychiatric, and immunologic disorders. Laboratory findings indicated a persistent inflammatory and prothrombotic profile, reflected by elevated CRP, ferritin, fibrinogen, and D-dimer levels, along with lower albumin and hemoglobin concentrations. Symptomatic ≥70% carotid artery stenosis was also more frequent in patients with long COVID.

Operative Characteristics and Early Postoperative Outcomes

Operative characteristics and CPB parameters were comparable between patients with and without postoperative worsening of symptoms (Table 3).

No significant differences were observed in CPB duration, aortic cross-clamp time, intraoperative hematocrit, cardioplegia volume, transfusion

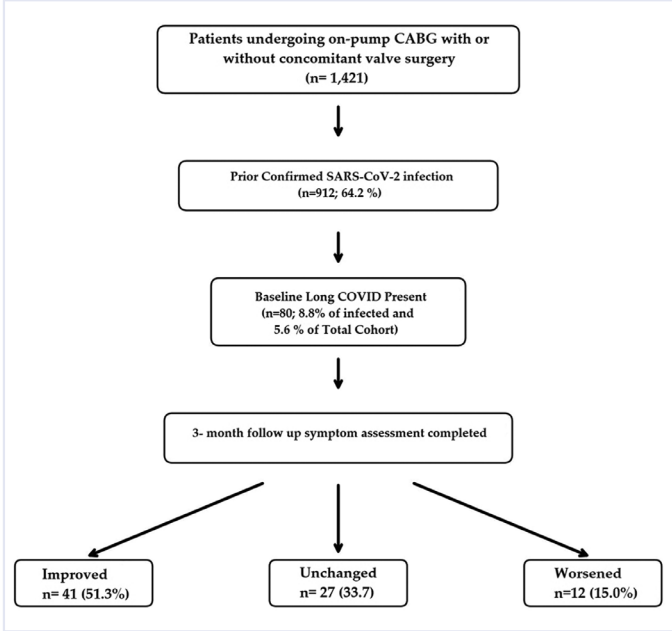

Figure 1. Study flow diagram and postoperative symptom trajectories. Flow of consecutive patients undergoing coronary artery bypass grafting (CABG) performed with cardiopulmonary bypass, with or without concomitant valve procedures. The diagram illustrates prior severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection status, baseline long coronavirus (COVID) prevalence, and the distribution of symptom trajectories at three-month follow-up (improved, unchanged, worsened).

Table 1. Demographic characteristics, cardiometabolic profile, and markers of systemic vascular vulnerability according to long COVID status

Variable	Long COVID (n=80)	No long COVID (n=1.341)	p-value
Age (years)	67.8±8.9	63.4±9.7	<0.001
Female sex	32 (40.0%)	302 (22.5%)	<0.001
BMI (kg/m²)	31.7±4.6	28.9±4.1	<0.001
BMI ≥36 kg/m²	14 (17.5%)	108 (8.1%)	0.004
Waist-hip ratio	0.96±0.08	0.92±0.07	0.002
Ankle-brachial index	0.86±0.11	0.93±0.09	<0.001
Current smoker	21 (26.3%)	412 (30.7%)	0.38
Former smoker	34 (42.5%)	487 (36.3%)	0.27
Educational level ≤8 years	46 (57.5%)	528 (39.4%)	0.002
Sedentary lifestyle	39 (48.7%)	471 (35.1%)	0.01
Confirmed prior SARS-CoV-2 infection	80 (100%)	832 (62.0%)	—
Reinfection count	1.88±0.91	1.36±0.71	<0.001
Last infection <6 months	26 (32.5%)	200 (14.9%)	<0.001
Hospitalized COVID	18 (22.5%)	129 (9.6%)	<0.001
COVID-19 ICU admission	7 (8.8%)	41 (3.1%)	0.008
Mechanical ventilation history	4 (5.0%)	17 (1.3%)	0.01
Vaccination doses	2.3±1.2	2.8±1.1	0.002
NYHA class III-IV	39 (48.7%)	399 (29.7%)	<0.001
LVEF (%)	48.9±9.4	51.8±8.6	0.01
Frailty score	4.6±1.1	3.6±1.2	<0.001
EuroSCORE II (%)	3.92±2.21	2.77±1.89	<0.001
STS mortality risk (%)	2.94±1.71	2.16±1.42	0.001

Continuous variables are presented as mean ± standard deviation and categorical variables as number (percentage). BMI: Body mass index; LVEF: Left ventricular ejection fraction; NYHA, New York Heart Association; STS: Society of thoracic surgeons risk score; COVID: Coronavirus; COVID-19: Coronavirus disease-2019; ICU: Intensive care unit; SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2.

requirements, or intraoperative metabolic stress markers. Among early postoperative outcomes, delirium and the need for postoperative rehabilitation were more frequent in the worsening group.

Longitudinal Symptom Burden

A longitudinal mixed-effects analysis demonstrated heterogeneous postoperative symptom trajectories within the long COVID cohort (Table 4).

Greater increases in composite LCQ score were observed in patients with a recent infection (<6 months), severe obesity, poor glycemic control, neurologic or psychiatric disorders, immunologic disorders, and higher frailty scores. Procedural complexity, including concomitant valve surgery, was not associated with symptom progression.

The distribution of changes in composite LCQ scores is illustrated in Figure 2A. The largest increases were observed in patients with recent infection, severe obesity, poor glycemic control, neurologic or psychiatric disease, immunologic disorders, and elevated frailty scores. Subgroup effect sizes are summarized in Figure 2B. The ranked contribution of each vulnerability factor to symptom worsening risk is illustrated in Figure 2C.

Pandemic Variant Era

The distribution of index SARS-CoV-2 infections across pandemic variant periods differed significantly between groups (Table 5).

Patients with long COVID were more frequently infected during earlier pandemic waves (2020-2021), whereas infections during later periods (2024-2025) were less common among these patients. Temporal distribution across variant periods is presented in Table 5.

SARS-CoV-2 Exposure Severity

Measures of cumulative SARS-CoV-2 exposure severity and recency differed significantly between patients with and without long COVID (Table 6).

Patients with persistent symptoms had higher reinfection counts, shorter infection-to-surgery intervals, and higher rates of COVID-19–related hospitalization, ICU admission, and prior mechanical ventilation. The number of vaccine doses was lower in the Long COVID group.

Multivariable Predictors of Postoperative Symptom Worsening

Multivariable logistic regression identified body mass index ≥36 kg/m², HbA1c >9%, three-vessel coronary artery disease, neurologic disease, psychiatric disease, immunologic disease, infection-to-surgery interval <6 months, and frailty score ≥5 as independent predictors of clinically meaningful postoperative symptom worsening (Table 7).

CPB duration showed borderline statistical significance, and no interaction was observed between female sex and HbA1c. A graphical representation of adjusted odds ratios is provided in Figure 2D.

Table 2. Baseline clinical comorbidities, laboratory findings, and SARS-CoV-2 exposure characteristics according to long COVID status

Variable	Long COVID-19 (n=80)	No long COVID-19 (n=1.341)	p-value
Hypertension	64 (80.0%)	964 (71.9%)	0.12
Diabetes mellitus	46 (57.5%)	490 (36.5%)	<0.001
HbA1c (%)	8.9±1.8	7.7±1.5	<0.001
HbA1c >9%	21 (26.3%)	141 (10.5%)	<0.001
COPD	17 (21.3%)	204 (15.2%)	0.14
Obstructive sleep apnea	19 (23.8%)	179 (13.3%)	0.009
Neurologic disease	21 (26.3%)	153 (11.4%)	<0.001
Psychiatric disease	27 (33.8%)	182 (13.6%)	<0.001
Immunologic disease	12 (15.0%)	84 (6.3%)	0.003
Factor V Leiden mutation	8 (10.0%)	50 (3.7%)	0.006
≥70% symptomatic carotid artery stenosis	11 (13.8%)	83 (6.2%)	0.01
Confirmed prior SARS-CoV-2 infection	80 (100%)	832 (62.0%)	—
Reinfection count (ordinal)	1.88±0.91	1.36±0.71	<0.001
Time from last infection to surgery (months)	8.1±4.7	11.4±6.2	<0.001
Last infection <6 months	26 (32.5%)	200 (14.9%)	<0.001
Hospitalized COVID-19 history	18 (22.5%)	129 (9.6%)	<0.001
COVID-19 ICU admission	7 (8.8%)	41 (3.1%)	0.008
Prior mechanical ventilation	4 (5.0%)	17 (1.3%)	0.01
Vaccination doses	2.3±1.2	2.8±1.1	0.002
Variant period 2020-2021	29 (36.3%)	275 (20.5%)	0.002
Variant period 2022-2023	39 (48.7%)	654 (48.8%)	0.98
Variant period 2024-2025	12 (15.0%)	412 (30.7%)	0.004
LVEF (%)	48.9±9.4	51.8±8.6	0.01
LVEF <40%	16 (20.0%)	197 (14.7%)	0.19
NYHA class III-IV	39 (48.7%)	399 (29.7%)	<0.001
Creatinine (mg/dL)	1.32±0.48	1.20±0.41	0.03
eGFR (mL/min/1.73 m²)	61.7±17.9	69.0±18.5	0.002
Hemoglobin (g/dL)	12.1±1.7	13.0±1.8	<0.001
Preoperative anemia	29 (36.3%)	289 (21.6%)	0.002
Albumin (g/dL)	3.6±0.5	3.9±0.4	<0.001
CRP (mg/L)	12.8±6.3	7.2±4.9	<0.001
Ferritin (ng/mL)	364±168	279±141	<0.001
Fibrinogen (mg/dL)	452±121	409±106	0.002
D-dimer (µg/mL)	1.06±0.54	0.76±0.38	<0.001
Frailty score	4.6±1.1	3.6±1.2	<0.001
EuroSCORE II (%)	3.92±2.21	2.77±1.89	<0.001
STS predicted mortality (%)	2.94±1.71	2.16±1.42	0.001

Values are expressed as mean ± standard deviation or number (percentage). CRP: C-reactive protein; eGFR: Estimated glomerular filtration rate; ICU: Intensive care unit; STS: Society of Thoracic Surgeons risk score; LVEF: Left ventricular ejection fraction; NYHA, New York Heart Association; COVID: Coronavirus; COVID-19: Coronavirus disease-2019; SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2; COPD: Chronic obstructive pulmonary disease.

DISCUSSION

In this retrospective analysis of prospectively collected data from a perioperative surveillance program, we observed heterogeneous postoperative trajectories of long COVID symptoms among patients undergoing CABG with CPB. Clinically meaningful worsening occurred primarily in patients with metabolic, neuropsychiatric, and frailty-related vulnerability features, whereas CPB duration showed only a modest association with postoperative symptom burden. These findings suggest that postoperative evolution of long COVID following cardiac surgery is largely determined by host susceptibility rather than by procedural exposure alone.

Long COVID is increasingly recognized as a multisystem condition characterized by persistent immune activation, endothelial dysfunction, autonomic imbalance, and neurocognitive vulnerability.[1-3,9,10] These mechanisms overlap with physiologic responses triggered by CPB, including systemic inflammation, endothelial activation, oxidative stress,

Table 3. Operative characteristics, CPB parameters, and early postoperative outcomes according to postoperative long COVID symptom worsening (any degree of worsening at any timepoint by subjective report, including transient worsening, n=28; clinically meaningful worsening defined as ΔLCQ ≥5 points confirmed by objective assessment at three months, n=12)

Variable	Symptom worsening (n=28)	No worsening (n=52)	p-value
Operative characteristics			
Number of distal anastomoses	3.4±0.9	3.2±1.0	0.31
Concomitant valve procedure	7 (25.0%)	11 (21.2%)	0.68
Total operative time (min)	274±61	261±55	0.29
Cardiopulmonary bypass parameters			
CPB duration (min)	108±34	101±29	0.22
Aortic cross-clamp time (min)	74±22	69±19	0.26
Lowest core temperature (°C)	32.1±1.4	32.4±1.3	0.18
Intraoperative hematocrit (%)	23.8±3.1	24.6±2.8	0.17
Crystalloid cardioplegia volume (mL)	1280±340	1210±310	0.33
Packed RBC transfusion (units)	1.8±1.2	1.5±1.0	0.21
Peak intraoperative lactate (mmol/L)	3.1±1.4	2.7±1.2	0.14
Vasopressor requirement	11/28 (39.3%)	17 (32.7%)	0.53
Inotropic support	9 (32.1%)	14 (26.9%)	0.61
NIRS desaturation episodes	6 (21.4%)	8 (15.4%)	0.48
Early postoperative outcomes			
Delirium	8/28 (28.6%)	6 (11.5%)	0.048
New neurologic deficit/stroke	2 (7.1%)	2 (3.8%)	0.59
New-onset atrial fibrillation	10 (35.7%)	16 (30.8%)	0.64
Prolonged ventilation (>24 h)	7/28 (25.0%)	6 (11.5%)	0.11
Re-intubation	2 (7.1%)	1 (1.9%)	0.26
Acute kidney injury (KDIGO ≥2)	5 (17.9%)	5 (9.6%)	0.28
Deep sternal wound infection	1 (3.6%)	1 (1.9%)	0.66
Reoperation for bleeding	2 (7.1%)	3 (5.8%)	0.81
ICU length of stay (days)	2.9±1.7	2.3±1.2	0.07
Hospital length of stay (days)	8.7±3.4	7.9±2.8	0.21
30-day mortality	1 (3.6%)	1 (1.9%)	0.66
90-day readmission	4 (14.3%)	5 (9.6%)	0.52
Postoperative rehabilitation needs	9 (32.1%)	8 (15.4%)	0.048

Continuous variables are reported as mean ± standard deviation. CPB: Cardiopulmonary bypass; NIRS: Near-infrared spectroscopy; RBC: Red blood cell; ICU: Intensive care unit; COVID: Coronavirus; LCQ: Long COVID questionnaire.

and microvascular perturbation.[13] In addition, neurologic vulnerability after cardiac surgery is influenced by cerebral hypoperfusion, microembolization, and perioperative neuroinflammation.[14] Based on these pathophysiologic parallels, it has been hypothesized that CPB might exacerbate pre-existing long COVID manifestations. However, the present findings do not demonstrate uniform deterioration associated with bypass exposure. Instead, symptom progression appeared to cluster within identifiable high-risk clinical phenotypes, suggesting that CPB may act as a permissive stressor rather than a primary driver of symptom persistence.

The demographic and clinical profile observed in the present cohort is consistent with previous reports describing risk factors for persistent post-COVID-19 symptoms. Older age, female sex, obesity, and diabetes mellitus have been repeatedly associated with prolonged symptom burden in observational studies.[3,4] Similarly, post-hospitalization cohorts have demonstrated persistent functional limitation and reduced exercise tolerance even after resolution of acute infection[6,8] Cardiovascular involvement following SARS-CoV-2 infection, including myocardial inflammation and endothelial dysfunction, may further impair perioperative adaptation in patients undergoing coronary surgery.[11,12] The enrichment of these characteristics among patients with long COVID in the present study supports the concept that persistent symptoms reflect an underlying systemic vulnerability rather than an isolated residual infection.

Metabolic dysregulation emerged as a central determinant of postoperative symptom evolution. Severe obesity and poor glycemic control were independently associated with clinically meaningful worsening. This observation is biologically plausible, as hyperglycemia amplifies endothelial injury, oxidative stress, and inflammatory signaling pathways implicated in long COVID pathophysiology.[3,9,10]

Table 4. Change in composite long COVID symptom score (ΔLCQ) and subgroup analysis of predefined clinical vulnerability features

Subgroup	n	Preoperative LCQ score	Postoperative LCQ score	ΔLCQ score (postop-preop)	Clinically meaningful worsening (%)	Time × subgroup interaction p-value
Entire long COVID-19 cohort	80	15.8±4.2	17.6±4.8	+1.8±2.9	28 (35.0%)	—
Confirmed PCR/antigen-positive infection only	64	15.9±4.3	17.8±4.9	+1.9±3.0	23 (35.9%)	0.82
Time since last infection <6 months	26	15.2±4.1	18.3±5.2	+3.1±3.4	14 (53.8%)	0.004
Time since last infection ≥6 months	54	16.1±4.3	17.3±4.5	+1.2±2.5	14 (25.9%)	Reference
Isolated CABG	62	15.7±4.1	17.3±4.6	+1.6±2.7	20 (32.3%)	0.41
CABG + valve procedure	18	16.1±4.5	18.5±5.1	+2.4±3.2	8 (44.4%)	Reference
Diabetes mellitus	46	15.5±4.0	18.1±4.9	+2.6±3.1	20 (43.5%)	0.01
No diabetes	34	16.2±4.4	17.1±4.3	+0.9±2.2	8 (23.5%)	Reference
Female sex	32	15.3±4.1	18.0±5.0	+2.7±3.3	15 (46.9%)	0.02
Male sex	48	16.1±4.3	17.2±4.5	+1.1±2.4	13 (27.1%)	Reference
Age ≥65 years	52	15.6±4.2	17.9±4.8	+2.3±3.0	21 (40.4%)	0.03
Age <65 years	28	16.2±4.1	17.1±4.2	+0.9±2.1	7 (25.0%)	Reference
BMI ≥36 kg/m²	14	15.0±4.0	18.4±5.3	+3.4±3.6	9 (64.3%)	<0.001
BMI <36 kg/m²	66	16.0±4.3	17.4±4.5	+1.4±2.5	19 (28.8%)	Reference
HbA1c >9%	21	15.1±4.2	18.7±5.4	+3.6±3.5	12 (57.1%)	0.002
HbA1c ≤9%	59	16.0±4.2	17.2±4.4	+1.2±2.3	16 (27.1%)	Reference
Neurologic disease present	21	15.2±4.1	18.3±5.0	+3.1±3.2	12 (57.1%)	0.003
Neurologic disease absent	59	16.0±4.2	17.2±4.5	+1.2±2.4	16 (27.1%)	Reference
Psychiatric disease present	27	15.0±4.0	18.3±5.2	+3.3±3.4	15 (55.6%)	0.002
Psychiatric disease absent	53	16.2±4.2	17.2±4.3	+1.0±2.2	13 (24.5%)	Reference
Immunologic disease present	12	15.1±4.3	18.6±5.6	+3.5±3.7	7 (58.3%)	0.008
Immunologic disease absent	68	15.9±4.2	17.4±4.5	+1.5±2.6	21 (30.9%)	Reference
Frailty score ≥5	34	15.2±4.1	18.2±5.1	+3.0±3.3	18 (52.9%)	0.001
Frailty score <5	46	16.2±4.2	17.2±4.2	+1.0±2.1	10 (21.7%)	Reference

ΔLCQ represents the postoperative score minus the preoperative score. Clinically meaningful worsening was defined as ΔLCQ ≥5. Interaction p-values were derived from mixed-effects repeated-measures models. COVID: Coronavirus; LCQ: Long COVID questionnaire; COVID-19: Coronavirus disease-2019; PCR: Polymerase chain reaction; BMI: Body mass index.

In addition, metabolic disease is a well-established determinant of postoperative recovery after CABG.[15] These findings therefore suggest that metabolic vulnerability may represent a shared mechanistic substrate linking long COVID and adverse postoperative recovery and highlight the importance of perioperative metabolic optimization in this population.

Neuropsychiatric and immunologic comorbidities also showed strong associations with postoperative symptom worsening. Long COVID has been linked to persistent neuroinflammatory activation and dysregulation of central autonomic networks.[3,9] Cardiac surgery introduces additional neurologic stress via fluctuations in cerebral perfusion and activation of inflammatory pathways.[14] The interaction between these factors may explain why symptom deterioration in the present cohort was concentrated among patients with pre-existing neurologic or psychiatric disease. These findings support a vulnerability model in which postoperative symptom progression reflects amplification of pre-existing neuroimmune susceptibility rather than *de novo* injury.

Another important observation was an association between a shorter infection-to-surgery interval and worsening of postoperative symptoms. Patients undergoing surgery within six months of SARS-CoV-2 infection experienced less favorable trajectories, suggesting persistence of physiologic instability beyond the acute phase. Previous perioperative studies have focused primarily on early postoperative complications; however, emerging data in cardiac surgery populations with prior SARS-CoV-2 infection suggest increased vasoactive requirements, thromboembolic risk, and altered postoperative recovery patterns, although longitudinal symptom trajectories remain poorly characterized.[19-21] The present data extend this concept by demonstrating a time-dependent relationship between the recency of infection and postoperative symptom burden in patients undergoing cardiac surgery.

Although CPB duration retained a modest association with symptom worsening, the absence of consistent relationships between other intraoperative variables and postoperative trajectories suggests that procedural exposure alone is insufficient to explain symptom evolution. Instead, CPB appears to interact with host vulnerability factors. From a clinical perspective, this distinction is important. It indicates that the presence of long COVID should not be interpreted as a contraindication to on-pump coronary surgery. Perioperative risk appears to be stratifiable by metabolic control, frailty, neuropsychiatric burden, and recency of infection.

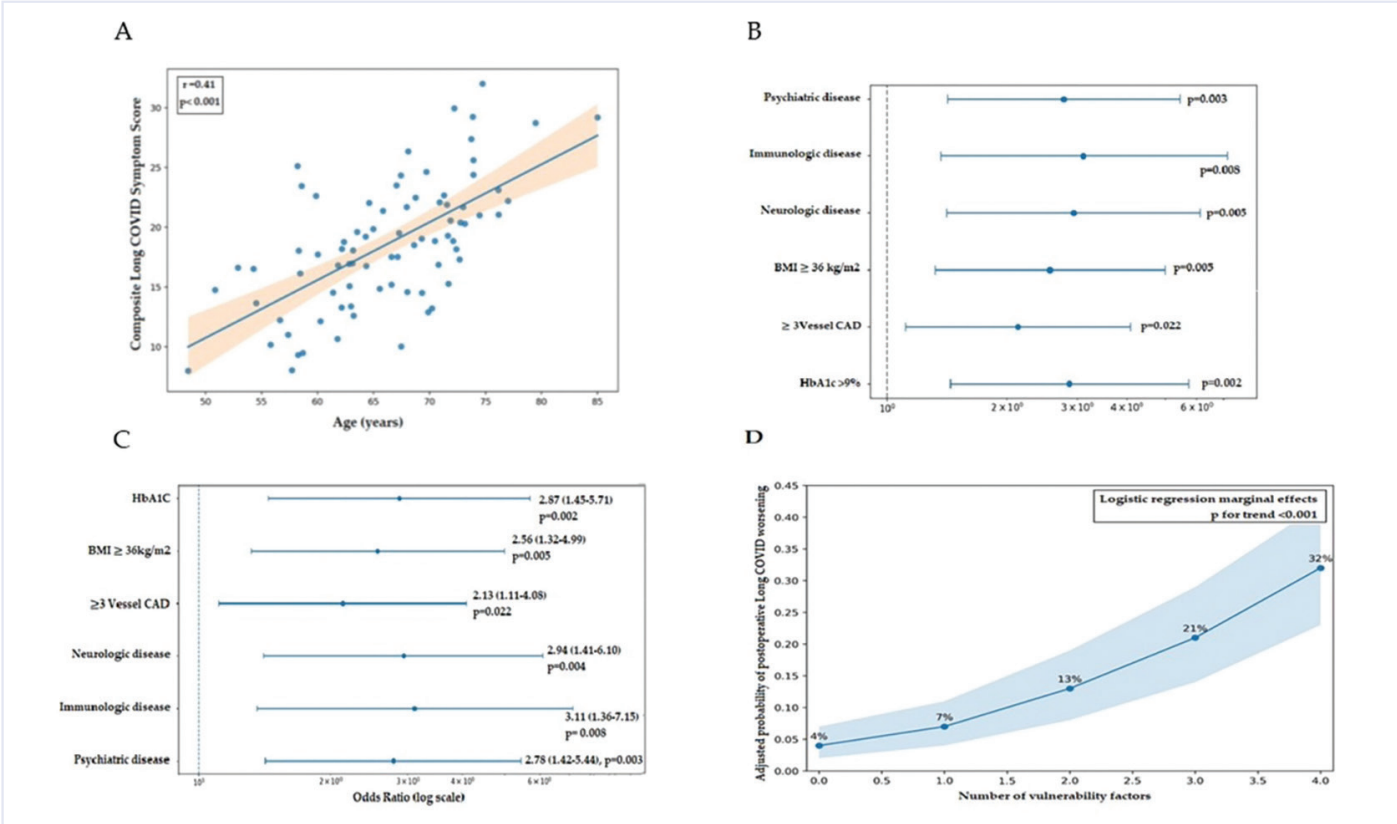

Figure 2. Longitudinal symptom burden and vulnerability subgroup analysis. (A) Distribution of change in composite long coronavirus (COVID) questionnaire (LCQ) scores between preoperative assessment and three-month follow-up. (B) Subgroup forest plot showing the association of predefined vulnerability characteristics with postoperative long COVID symptom worsening, ranked by effect size. (C) Forest plot showing adjusted odds ratios for independent predictors of clinically meaningful postoperative symptom worsening derived from multivariable logistic regression. (D) Adjusted probability of postoperative long COVID worsening according to the number of cumulative vulnerability factors, derived from logistic regression marginal effects analysis.

Table 5. Distribution of index SARS-CoV-2 infection according to pandemic variant period and association with long COVID prevalence

Variant period	Long COVID-19	No long COVID-19	p-value
2020-2021	29 (36.3%)	275 (20.5%)	0.002
2022-2023	39 (48.7%)	654 (48.8%)	0.98
2024-2025	12 (15.0%)	412 (30.7%)	0.004

COVID: Coronavirus; COVID-19: Coronavirus disease-2019; SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2.

Table 6. Markers of SARS-CoV-2 exposure severity and infection recency in patients with and without long COVID undergoing cardiac surgery

Variable	Long COVID-19	No long COVID-19	p-value
Reinfection count	1.88±0.91	1.36±0.71	<0.001
Last infection <6 months	26 (32.5%)	200 (14.9%)	<0.001
COVID-19 ICU admission	7 (8.8%)	41 (3.1%)	0.008
Mechanical ventilation history	4 (5.0%)	17 (1.3%)	0.01
Vaccination doses	2.3±1.2	2.8±1.1	0.002

Values are presented as mean ± standard deviation or number(percentage). ICU: Intensive care unit; COVID: Coronavirus; COVID-19: Coronavirus disease-2019; SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2.

The present findings support a phenotype-based interpretation of perioperative long COVID risk. Patients with poor glycemic control, severe obesity, advanced coronary artery disease, frailty, neuropsychiatric or immunologic comorbidities, and recent infection were most likely to experience worsening of symptoms. These features define a clinically recognizable vulnerability pattern that may assist in preoperative counseling, optimization of metabolic parameters, and structured postoperative follow-up. Such an approach may be more informative than considering long COVID as a uniform perioperative condition.

Several limitations should be acknowledged. The study represents a retrospective analysis of prospectively collected registry data and therefore cannot establish causality. The absence of an off-pump comparator group limits the evaluation of bypass-specific effects. The symptom assessment tool, although applied prospectively, has not undergone external validation. Biomarkers reflecting endothelial dysfunction or autonomic imbalance were not available for mechanistic analysis. Finally, follow-up was limited to three months, and longer-term symptom trajectories remain uncertain.

Long COVID is present in a meaningful proportion of patients undergoing CABG with CPB, who have heterogeneous postoperative trajectories. Symptom worsening appears to be driven primarily by metabolic and neuropsychiatric vulnerabilities rather than by procedural exposure alone. CPB is generally well tolerated, and risk stratification based on

Table 7. Multivariable logistic regression analysis identifying predictors of clinically meaningful postoperative worsening of long COVID symptoms

Variable	Univariable OR (95% CI)	p-value	Multivariable OR (95% CI)	p-value
Age ≥65 years	1.82 (1.01-3.29)	0.046	1.41 (0.74-2.68)	0.29
Female sex	2.12 (1.16-3.89)	0.014	1.76 (0.93-3.31)	0.08
BMI ≥36 kg/m²	3.89 (1.67-9.04)	0.002	3.21 (1.31-7.86)	0.011
HbA1c >9%	3.02 (1.54-5.92)	0.001	2.41 (1.32-4.38)	0.004
≥3-vessel coronary artery disease	2.27 (1.18-4.36)	0.014	1.94 (1.02-3.68)	0.043
Neurologic disease	3.18 (1.55-6.52)	0.002	2.48 (1.19-5.14)	0.016
Psychiatric disease	3.41 (1.73-6.72)	<0.001	2.63 (1.31-5.29)	0.006
Immunologic disease	3.72 (1.39-9.96)	0.009	2.71 (1.01-7.24)	0.047
Infection-to-surgery interval <6 months	3.05 (1.58-5.90)	0.001	2.36 (1.19-4.67)	0.014
CPB duration (per 10-min increase)	1.12 (1.01-1.25)	0.032	1.09 (1.00-1.21)	0.048
Frailty score ≥5	3.26 (1.68-6.32)	<0.001	2.58 (1.29-5.16)	0.007
Female sex × HbA1c interaction term	—	—	1.32 (0.74-2.36)	0.34

Clinically meaningful worsening was defined as an increase ≥5 points in the composite symptom score at three months. CPB duration was modeled per 10-minute increment.
OR: Odds ratio; CPB: Cardiopulmonary bypass; COVID: Coronavirus; BMI: Body mass index; CI: Confidence interval.

host-related factors may help guide perioperative management. Further multicenter studies incorporating objective neurocognitive assessment, biomarker profiling, and extended follow-up are warranted to refine perioperative risk stratification in patients with prior SARS-CoV-2 infection undergoing cardiac surgery.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Institutional Ethics Committee of Dr. İsmail Fehmi Cumalioğlu City Hospital (approval number: AN-261203-16, date: 12.03.2026).

Informed Consent: The ethics committee waived the requirement for informed consent because the study was observational.

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

Footnotes

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REFERENCES

1. Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, et al. Post-acute COVID-19 syndrome. Nat Med. 2021;27:601-15. doi: 10.1038/s41591-021-01283-z.
2. Davis HE, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine. 2021;38:101019. doi: 10.1016/j.eclinm.2021.101019.
3. Yong SJ. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. Infect Dis (Lond). 2021;53:737-54. doi: 10.1080/23744235.2021.1924397.
4. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. Nat Med. 2021;27:626-31. Erratum in: Nat Med. 2021;27:1116. doi: 10.1038/s41591-021-01361-2.
5. Carfì A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. JAMA. 2020;324:603-5. doi: 10.1001/jama.2020.12603.
6. Evans RA, McAuley H, Harrison EM, Shikotra A, Singapuri A, Sereno M, et al.; PHOSP-COVID Collaborative Group. Physical, cognitive, and mental health impacts of COVID-19 after hospitalisation (PHOSP-COVID): a UK multicentre, prospective cohort study. Lancet Respir Med. 2021;9:1275-87. Erratum in: Lancet Respir Med. 2022;10:e9. Erratum in: Lancet Respir Med. 2024;12:e41. doi: 10.1016/S2213-2600(24)00142-5.
7. Greenhalgh T, Knight M, A'Court C, Buxton M, Husain L. Management of post-acute covid-19 in primary care. BMJ. 2020;370:m3026. doi: 10.1136/bmj.m3026.
8. Paneroni M, Simonelli C, Saleri M, Bertacchini L, Venturelli M, Troosters T, et al. Muscle performance and physical function in patients with COVID-19-associated pneumonia at hospital discharge. Eur J Phys Rehabil Med. 2021;57:1-8.
9. Fedorchenko Y, Zimba O. Long COVID in autoimmune rheumatic diseases. Rheumatol Int. 2023;43:1197-207. doi: 10.1007/s00296-023-05319-0.
10. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020;395:1417-8. doi: 10.1016/S0140-6736(20)30937-5.
11. Xie Y, Xu E, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. Nat Med. 2022;28:583-90. doi: 10.1038/s41591-022-01689-3.

12. Puntmann VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5:1265-73. Erratum in: JAMA Cardiol. 2020;5:1308. doi: 10.1001/jamacardio.2020.4648.

13. Squiccimarro E, Labriola C, Malvindi PG, Margari V, Guida P, Visicchio G, et al. Prevalence and clinical impact of systemic inflammatory reaction after cardiac surgery. J Cardiothorac Vasc Anesth. 2019;33:1682-90. doi: 10.1053/j.jvca.2019.01.043.

14. McDonagh DL, Berger M, Mathew JP, Graffagnino C, Milano CA, Newman MF. Neurological complications of cardiac surgery. Lancet Neurol. 2014;13:490-502. doi: 10.1016/S1474-4422(14)70004-3.

15. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, et al.; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; Society of Cardiovascular Anesthesiologists; Society of Thoracic Surgeons. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2011;58:e123-210. doi: 10.1016/j.jacc.2011.08.009.

16. Dobbs TD, Gibson JAG, Fowler AJ, Abbott TE, Shahid T, Torabi F, et al. Surgical activity in England and Wales during the COVID-19 pandemic: a nationwide observational cohort study. Br J Anaesth. 2021;127:196-204. doi: 10.1016/j.bja.2021.05.001.

17. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The STROBE statement: guidelines for reporting observational studies. BMJ. 2007;335:806-8.

18. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis. 2022;22:e102-7. doi: 10.1016/S1473-3099(21)00703-9.

19. Predoi CE, Filipescu DC, Stefan MG, Iordache N. Elective cardiopulmonary bypass surgery after COVID-19: vasoactive needs and early complications. J Clin Med. 2025;14:8290. doi: 10.3390/jcm14238290.

20. Predoi CE, Dascalu A, Goicea R, Stefan M, Filipescu D, Iordache N, et al. Impact of COVID-19 history on perioperative outcomes: a systematic review. COVID. 2025;5:148. doi: 10.3390/covid5090148.

21. Şahin İ, Batur Ş, Üstündağ A, Arapi B, Tel Üstünışık Ç, Göksedef D, et al. The impact of COVID-19 on graft vasculopathy and postoperative thromboembolism in CABG patients: a prospective controlled study. Cardiovasc Toxicol. 2025;25:1123-38. doi: 10.1007/s12012-025-10017-3.