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Sex-Specific Differences in the Inflammatory Prognostic Index in Patients with Coronary Artery Disease Receiving Preoperative Intra-Aortic Balloon Pump Support

Izatullah Jalalzai

ijalalzai@gmail.com

Atatürk University

Ebubekir Sönmez

Kütahya City Hospital

Ümit Arslan

Atatürk University

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Abstract

Background/Objectives: Despite being constructed from polyurethane and establishing direct blood device interaction within the arterial circulation, the effect of intra-aortic balloon pump support on systemic inflammatory biomarkers remains incompletely defined. This study aimed to quantify the inflammatory response associated with preoperative IABP using the inflammatory prognostic index (IPI) and to determine whether this response differs according to sex**.**

Methods: After propensity score matching, 168 patients with preoperative IABP support (Group A: 63 women, 105 men) and 190 patients without IABP (Group B: 60 women, 130 men) were analyzed. The IPI, derived from C-reactive protein, serum albumin, neutrophil, and lymphocyte levels, was assessed at hospital admission and at 24 and 72 hours, and was evaluated between groups and in sex-stratified analyses. The IPI was calculated using the following formula: C-reactive protein-to-albumin ratio (CAR) × neutrophil-to-lymphocyte ratio (NLR).

Results: IPI values were consistently higher in the IABP group than in the non-IABP group, with the greatest difference observed at 24 hours ($r_{rb} = 0.62$; $p < 0.001$). Within the IABP group, women exhibited significantly higher IPI levels than men, reaching large effect sizes at 24 hours ($r_{rb} = 0.52$; $p < 0.001$) and 72 hours ($r_{rb} = 0.45$; $p < 0.001$), accompanied by higher CRP levels and neutrophil counts and lower lymphocyte counts and albumin levels. IABP support was associated with an approximately 34% greater increase in IPI in women at 24 hours and a 23% greater increase at 72 hours compared with men.

Conclusions: Preoperative IABP support is associated with a marked early increase in systemic inflammatory burden, particularly in women, followed by a more rapid subsequent decline over time. These findings support the value of early, sex-specific monitoring of integrated inflammatory indices in patients undergoing mechanical circulatory support.

Introduction

Mechanical circulatory support (MCS) devices play a central role in the management of hypoperfusion secondary to cardiac pathology by augmenting ventricular function and stabilizing systemic hemodynamics [1, 2]. The intra-aortic balloon pump (IABP) represents a well-established modality that increases diastolic pressure and coronary perfusion while reducing afterload and myocardial oxygen consumption, thereby providing modest yet clinically meaningful hemodynamic support [3, 4]. These hemodynamic benefits and their downstream physiological effects, together with lower invasiveness, procedural simplicity, and cost-effectiveness, have contributed to the sustained and widespread use of the IABP, with an estimated annual utilization exceeding 150,000 cases worldwide and continuous clinical application since the 1960s [5, 6]. Despite this extensive experience, IABP implantation is not without risk and has been associated with procedure-related complications such as bleeding, vascular injury, limb ischemia, and aortic dissection [7, 8]. The frequency and clinical spectrum of these mechanical and vascular complications have been comprehensively summarized by Motia et al. [9]. In

contrast, although the device is composed of polyurethane and directly interfaces with circulating blood elements, its impact on systemic inflammatory biomarkers remains incompletely elucidated.

In the early stages of its clinical development, the IABP balloon was manufactured from latex to withstand aortic pressure and minimize the risk of rupture; however, concerns regarding latex allergy, susceptibility to tensile stress, and the requirement for sustained durability during prolonged counterpulsation led to the subsequent adoption of polyurethane materials [5, 10, 11]. Although surface modifications have been developed to improve the biocompatibility of IABP balloons, blood contact with a foreign material result in the rapid adsorption of plasma proteins, thereby initiating a cascade of biological processes involving inflammation, coagulation, and platelet activation [12, 13]. In an experimental study by Segan et al. [14], immune cell adhesion to polyurethane surfaces was demonstrated using primary human peripheral blood mononuclear cells and macrophages derived from the human monocytic cell line THP-1, and subsequent cytokine analyses indicated a mild pro-inflammatory response after prolonged material contact.

Given this biological background, the evaluation of the systemic inflammatory response in patients receiving preoperative IABP support requires an integrated and clinically applicable biomarker. The inflammatory prognostic index (IPI), a composite parameter incorporating neutrophil and lymphocyte counts together with C-reactive protein (CRP) and albumin levels, has been used as a prognostic indicator in clinical conditions such as malignancy, aortic dissection, and coronary artery bypass grafting (CABG) [15–18]. However, despite its application in these settings, the behavior of IPI in patients supported with preoperative IABP—particularly with respect to potential sex-related differences—has not yet been systematically investigated. Accordingly, the present study aimed to evaluate the inflammatory status of patients with coronary artery disease (CAD) receiving preoperative IABP support using the IPI, with a specific focus on sex-related differences.

Materials and Methods

Study Design and Patient Selection

This study represents a post hoc secondary analysis of prospectively collected data derived from a registered observational cohort study (NCT06468982). Patient enrollment was continued in an integrated manner beyond the initial registration phase, allowing expansion of the study population within the same prospective framework. Among 340 patients who received IABP support, 215 met the predefined inclusion criteria. To establish a balanced comparison cohort, these patients were matched with 400 contemporaneous patients with CAD who were followed at our institution during the same period but did not receive IABP support. Propensity score matching was performed using a nearest-neighbor approach without replacement to reduce baseline differences between groups. Propensity scores were calculated based on clinically relevant covariates, including age, sex, left ventricular ejection fraction (LVEF%), EuroSCORE II, diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), presence of left main coronary artery disease (LMCA), prior percutaneous coronary intervention

(PCI), and acute myocardial infarction (AMI) without cardiogenic shock or mechanical complications. Matching resulted in two well-balanced groups comprising 168 patients receiving preoperative IABP support (Group A; 63 women and 105 men) and 190 patients without IABP support (Group B; 60 women and 130 men). Following the establishment of balanced cohorts, sex-stratified analyses were performed to explore potential differences in the IPI within the matched population.

Preoperative IABP support was used in patients with multivessel disease, left main coronary artery (LMCA) disease, recurrent or persistent chest pain at rest, or failed or infeasible percutaneous coronary intervention (PCI) due to diffuse and/or severely tortuous coronary anatomy. The IABP group comprised adult patients (≥ 18 years) with coronary artery disease (CAD) in whom preoperative IABP support was indicated and implanted by the cardiovascular surgery team. The IABP (Datascope® Medical Co., Ltd., Cambridgeshire, United Kingdom) was inserted percutaneously via the femoral artery.

Demographic characteristics, clinical variables, and daily laboratory data were prospectively recorded. Laboratory parameters were evaluated at three predefined time points: at hospital admission (baseline for both groups), and at 24 and 72 hours after IABP implantation in the IABP group, with corresponding time points applied to the matched control group. Serum albumin (g/dL), C-reactive protein (CRP) (mg/L), neutrophil count (×10³/μL), and lymphocyte count (×10³/μL) were measured from the same blood samples collected at each time point.

The C-reactive protein–to–albumin ratio (CAR) was calculated by dividing the CRP level by the serum albumin level. The neutrophil–to–lymphocyte ratio (NLR) was calculated as the ratio of neutrophil count to lymphocyte count. The inflammatory prognostic index (IPI) was subsequently derived using the following formula: IPI = CAR × NLR [15–19].

Exclusion Criteria

Patients presenting with cardiogenic shock; those requiring preoperative mechanical ventilation or resuscitation after cardiac arrest; those receiving extracorporeal membrane oxygenation or other forms of mechanical circulatory support; those with acute pulmonary edema; those undergoing emergency coronary artery bypass grafting within three days; those with peripheral arterial disease precluding femoral access; those with end-stage renal disease requiring dialysis; those with mechanical complications secondary to acute myocardial infarction; and those undergoing concomitant cardiac procedures other than isolated CABG were excluded to ensure cohort homogeneity. In addition, patients who declined the procedure were excluded from the final analysis..

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (version 28.0; IBM Corp., Armonk, NY, USA) and Jamovi (version 2.7.13; The Jamovi Project, Sydney, Australia). Continuous variables were expressed as mean ± standard deviation for normally distributed data and as median (interquartile range,

Q1–Q3) for non-normally distributed data, whereas categorical variables were presented as counts and percentages. Normality was assessed using the Shapiro–Wilk test, and homogeneity of variances was evaluated using Levene's test. Propensity score matching was applied to minimize baseline differences between patients receiving preoperative IABP support and those not receiving IABP. Propensity scores were estimated using a multivariable logistic regression model incorporating clinically relevant covariates, and matching was performed using a nearest-neighbor approach without replacement. Baseline characteristics were compared between female and male patients using Student's t-test for normally distributed continuous variables with homogeneity of variances. Variables that did not meet normality assumptions were compared using the Mann–Whitney U test, and the robustness of these comparisons was further evaluated using the Brunner–Munzel test in the presence of unequal variances or distributional differences. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. Changes over time (baseline, 24 hours, and 72 hours) were analyzed using the Friedman test for repeated measurements. Post hoc pairwise comparisons were performed using the Wilcoxon signed-rank test with Bonferroni correction. Effect sizes were reported as Cohen's d for parametric comparisons and as rank-based effect size (r) for non-parametric tests. Where appropriate, 95% confidence intervals were estimated using bootstrap resampling (5,000 iterations). To evaluate whether the effect of IABP on inflammatory response differed by sex, an interaction term (sex × IABP) was included in a generalized linear model using log-transformed IPI values. A two-sided p value < 0.05 was considered statistically significant.

Results

A total of 340 patients who received preoperative IABP support were screened for eligibility. Of these, 215 met the predefined inclusion criteria and constituted the pool for propensity score matching. During the same study period, 400 contemporaneous patients with CAD who were managed without IABP support were identified as potential controls. Propensity score matching yielded two well-balanced cohorts comprising 168 patients in the IABP group (Group A; 63 women and 105 men) and 190 patients in the non-IABP group (Group B; 60 women and 130 men). All baseline clinical covariates included in the propensity score model were adequately balanced after matching, with standardized mean differences (SMDs) below 0.10. Following the establishment of the matched cohorts, patients were stratified by sex, and demographic and clinical characteristics were analyzed separately for women and men. A post hoc power analysis performed using G*Power under a two-sided independent-samples framework ($\alpha = 0.05$) indicated that the final matched sample provided approximately 80% power to detect moderate effect sizes in both between-group comparisons and sex-stratified analyses.

Baseline demographic, clinical, and laboratory characteristics stratified by sex for each group are presented in Table 1. In both groups, most comorbidities and demographic variables were comparable between women and men. However, women consistently exhibited lower LVEF% and higher EuroSCORE II values. In addition, markers of metabolic and myocardial injury were more pronounced in women, as reflected by higher HbA1c and high-sensitivity troponin I levels. In contrast, men had a higher prevalence

of active smoking and a less favorable lipid profile, characterized by higher LDL cholesterol and triglyceride levels. The magnitude of these differences was in the moderate range.

Table 1
Baseline demographic, clinical, and laboratory characteristics stratified by sex in the IABP and non-IABP groups

	IABP group (n = 168)			Non-IABP group(n = 190)		
	Female (n = 63)	Male (n = 105)	p value	Female (n = 60)	Male (n = 130)	p value
Age, (years)	65.5 ± 9.2	63.5 ± 8.4	0.124	66.8 ± 8.5	63.9 ± 8.0	0.106
Hypertension, n (%)	43 (68.2)	73 (69.5)	0.863	38 (63.3)	85 (65.3)	0.783
Diabetes mellitus, n (%)	35 (55.5)	50 (47.6)	0.319	31 (51.6)	53 (40.7)	0.160
Smoker, n (%)	25 (39.6)	57 (54.2)	0.055	21 (35)	68 (52.3)	0.026
COPD, n (%)	29 (46.0)	54 (51.4)	0.604	22 (36.7)	43 (33.1)	0.636
LVEF%; median (Q1-Q3)	43.0 [35–50]	48.0 [40–55]	0.018	47 [40–55]	50 [45–60]	0.041
EuroScore II, %	2.2 ± 1.2	1.8 ± 1.1	0.020	1.9 ± 1.1	1.6 ± 1.2	0.151
PCI before CABG, n (%)	14 (22.2)	26 (24.7)	0.712	12 (20)	28 (21.5)	0.670
LMCA, n (%)	17 (27.0)	33 (31.4)	0.763	8 (13.3)	14 (10.7)	0.545
Hemoglobin, g/dL	13.3 ± 0.8	15.1 ± 0.5	< 0.001	14.0 ± 1.3	15.3 ± 1.5	< 0.001
Platelet count, 10^9/L; median [Q1-Q3]	220 [174–266]	243 [205–281]	0.072	235 [190–280]	255 [215–295]	0.095
HbA1c%[a]	7.4 ± 2.2	6.3 ± 1.6	< 0.001	6.8 ± 1.6	6.1 ± 1.3	0.002
LDL, mg/dL	124 ± 25	138 ± 23	< 0.001	115 ± 32	132 ± 35	< 0.001
Triglyceride, mg/dL	144 ± 41	177 ± 53	< 0.001	127 ± 45	158 ± 55	0.001
hsCTI; ng/m; median [Q1-Q3]	19.3 [11.5–32.0]	17.6 [9.8–27.5]	0.551	12.4 [7.2–18.9]	11.8 [6.5–17.6]	0.750

CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; hsCTI, high sensitivity cardiac troponin I; IABP, intra-aortic balloon pump; LDL, low-density lipoprotein LMCA, left main coronary artery disease; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention

Inflammation-related laboratory parameters, including complete blood count components, CRP, serum albumin levels, and composite inflammatory indices, were evaluated at three predefined time points (Table 2). At baseline, most inflammatory markers were comparable between the groups; however, the IPI was significantly higher in the IABP group. At 24 hours, patients receiving IABP support exhibited a pronounced inflammatory response, with significant increases in IPI, NLR, CAR, CRP levels, and neutrophil counts, accompanied by a marked reduction in lymphocyte counts and serum albumin levels compared with the non-IABP group. Although partial recovery was observed at 72 hours, IPI, NLR, CAR, CRP levels, and neutrophil counts remained significantly higher, and lymphocyte counts remained significantly lower in the IABP group. Overall, the non-IABP group demonstrated a more attenuated inflammatory trajectory, with earlier normalization of laboratory parameters over time.

Table 2
Temporal changes in inflammatory indices in IABP and non-IABP groups

Parameter	Time point	IABP (n = 168)	non-IABP (n = 190)	p-value*
IPI	Baseline	19.41 (9.98–30.13)	15.6 (10.8–22.4)	< 0.05
	24 h	181.39 (117.45–339.92)	78.9 (52.4–118.6)	< 0.001
	72 h	61.88 (38.88–116.95)	36.2 (24.9–58.3)	< 0.001
NLR	Baseline	2.93 (2.43–3.98)	2.61 (2.10–3.42)	NS
	24 h	7.74 (5.26–10.82)	5.63 (4.10–7.85)	< 0.001
	72 h	4.59 (3.54–6.10)	3.62 (2.85–4.92)	< 0.001
CAR	Baseline	6.33 (3.61–9.42)	5.10 (3.80–7.10)	NS
	24 h	24.87 (19.99–31.06)	14.6 (10.8–20.2)	< 0.001
	72 h	14.14 (10.47–17.79)	8.9 (6.9–12.8)	< 0.001
CRP (mg/L)	Baseline	25.79 (15.90–38.90)	22.1 (14.8–32.6)	NS
	24 h	95.68 (79.86–114.65)	57.4 (41.2–82.9)	< 0.001
	72 h	56.36 (39.47–69.87)	34.9 (25.6–52.8)	< 0.001
Albumin (g/dL)	Baseline	4.30 (4.16–4.45)	4.28 (4.10–4.42)	NS
	24 h	3.90 (3.54–4.10)	4.02 (3.78–4.25)	< 0.001
	72 h	4.03 (3.68–4.20)	4.15 (3.92–4.36)	NS
Neutrophils (×10⁹/L)	Baseline	6.50 (5.65–7.32)	6.05 (5.30–6.90)	NS
	24 h	10.10 (8.44–12.44)	8.25 (6.90–10.10)	< 0.001
	72 h	8.28 (7.22–9.48)	7.10 (6.25–8.45)	< 0.01
Lymphocytes (×10⁹/L)	Baseline	2.14 (1.86–2.37)	2.18 (1.92–2.48)	NS
	24 h	1.31 (1.08–1.66)	1.58 (1.32–1.96)	< 0.01
	72 h	1.86 (1.44–2.14)	2.05 (1.72–2.38)	< 0.05

CAR, C-reactive protein-to-albumin ratio; CRP, C-reactive protein; IABP, intra-aortic balloon pump; IPI, inflammatory prognostic index; NLR, neutrophil-to-lymphocyte ratio. * Wilcoxon rank-sum (Mann–Whitney U); Values are presented as median [Q1–Q3]; NS = Not Significant

Within the IABP group, clear sex-specific differences were observed across all inflammatory indices (Table 3). At baseline, women already had higher CAR, NLR, CRP, and IPI values together with lower serum albumin levels than men, with a moderate effect size for IPI (rank-biserial correlation $r_{rb} = 0.40$, 95% CI: 0.25–0.53; $p < 0.001$). These differences became more pronounced at 24 hours after IABP implantation. The between-sex separation was accompanied by concomitant increases in both NLR and CAR, with a greater contribution from CAR at this time point, reflecting marked CRP elevation and hypoalbuminemia. Accordingly, IPI values were significantly higher in women, reaching a large effect size ($r_{rb} = 0.52$, 95% CI: 0.39–0.65; $p < 0.001$). Although partial recovery was observed at 72 hours, inflammatory indices in women remained significantly different from those in men, and the effect size for IPI persisted in the moderate-to-large range ($r_{rb} = 0.45$, 95% CI: 0.30–0.58; $p < 0.001$), indicating a sustained inflammatory burden in female patients receiving IABP support.

Table 3
Sex-specific temporal changes in inflammatory indices in the IABP group

Parameter	Time point	Female (n = 63)	Male (n = 105)	p-value
IPI	Baseline	26.3 (14.8–46.5)	14.0 (8.3–25.5)	< 0.001
	24 h	323.9 (174.2–574.4)	160.8 (105.8–258.9)	< 0.001
	72 h	117.0 (54.7–194.8)	52.9 (36.3–76.4)	< 0.001
CAR	Baseline	7.1 (5.2–11.1)	5.4 (3.4–8.4)	< 0.01
	24 h	31.5 (23.6–41.0)	23.5 (19.7–27.3)	< 0.001
	72 h	19.9 (14.0–26.0)	12.8 (9.6–15.3)	< 0.001
NLR	Baseline	3.4 (2.9–4.6)	2.7 (2.3–3.4)	< 0.01
	24 h	10.3 (7.1–14.1)	6.9 (4.6–9.7)	< 0.001
	72 h	5.5 (4.4–8.0)	4.2 (3.3–5.3)	< 0.001
CRP (mg/L)	Baseline	28.0 (19.7–47.3)	23.5 (14.5–36.0)	< 0.05
	24 h	101.2 (82.9–129.8)	91.9 (79.9–103.3)	< 0.001
	72 h	69.9 (53.6–87.3)	51.4 (37.5–62.0)	< 0.001
Albumin (g/dL)	Baseline	4.10 (3.82–4.32)	4.34 (4.24–4.48)	< 0.01
	24 h	3.50 (3.10–3.90)	4.01 (3.80–4.17)	< 0.001
	72 h	3.65 (3.28–4.00)	4.11 (3.90–4.25)	< 0.01
Neutrophils (×10⁹/L)	Baseline	6.9 (6.1–8.4)	6.3 (5.4–7.1)	< 0.05
	24 h	11.3 (9.4–13.3)	9.6 (8.0–11.6)	< 0.001
	72 h	9.4 (8.1–10.3)	7.8 (7.0–8.6)	< 0.001
Lymphocytes (×10⁹/L)	Baseline	2.0 (1.7–2.2)	2.2 (2.0–2.5)	< 0.01
	24 h	1.1 (0.9–1.4)	1.4 (1.2–1.7)	< 0.001
	72 h	1.7 (1.2–1.9)	1.9 (1.6–2.2)	< 0.01

Values are presented as median [Q1–Q3]; CAR, C-reactive protein-to-albumin ratio; CRP, C-reactive protein; IABP, intra-aortic balloon pump; IPI, inflammatory prognostic index; NLR, neutrophil-to-lymphocyte ratio.

In Group B, sex-related differences in inflammatory indices were limited and transient (Table 4). At baseline, women had higher IPI values than men, with a small effect size ($r_{rb} = 0.20$, $p < 0.05$). This difference persisted at 24 hours, when IPI values remained significantly higher in women ($r_{rb} = 0.26$, 95% CI: 0.10–0.40; $p < 0.01$). However, by 72 hours, IPI values had converged between the sexes and the

between-sex difference was no longer statistically significant. A similar temporal pattern was observed for CAR, NLR, CRP levels, and neutrophil counts, with sex-related differences mainly evident at 24 hours and disappearing over time.

Table 4
Sex-specific temporal changes in inflammatory indices in the non-IABP group

Parameter	Time point	Female (n = 60)	Male (n = 130)	p-value
IPI	Baseline	17.0 (11.5–24.5)	13.9 (9.7–19.8)	< 0.05
	24 h	92.0 (62.0–140.0)	72.0 (50.0–105.0)	< 0.01
	72 h	39.0 (27.0–63.0)	34.0 (24.0–50.0)	NS
CAR	Baseline	5.6 (4.1–7.8)	4.8 (3.5–6.6)	NS
	24 h	16.2 (12.0–22.5)	13.8 (10.2–19.0)	< 0.05
	72 h	9.6 (7.3–13.8)	8.6 (6.7–12.1)	NS
NLR	Baseline	2.8 (2.2–3.7)	2.5 (2.0–3.2)	NS
	24 h	6.0 (4.5–8.4)	5.3 (3.9–7.2)	< 0.05
	72 h	3.8 (3.0–5.2)	3.5 (2.8–4.7)	NS
CRP (mg/L)	Baseline	23.8 (16.5–35.0)	21.2 (14.0–31.0)	NS
	24 h	62.0 (44.0–90.0)	54.0 (39.0–76.0)	< 0.05
	72 h	37.0 (27.0–56.0)	34.0 (24.0–49.0)	NS
Albumin (g/dL)	Baseline	4.22 (4.05–4.36)	4.30 (4.14–4.44)	< 0.05
	24 h	3.95 (3.70–4.15)	4.06 (3.82–4.28)	< 0.01
	72 h	4.08 (3.88–4.28)	4.18 (3.96–4.38)	< 0.05
Neutrophils (×10³/μL)	Baseline	6.2 (5.4–7.2)	5.9 (5.2–6.8)	NS
	24 h	8.6 (7.1–10.6)	8.0 (6.6–9.7)	< 0.05
	72 h	7.2 (6.3–8.7)	7.0 (6.2–8.3)	NS
Lymphocytes (×10³/μL)	Baseline	2.1 (1.8–2.4)	2.2 (1.9–2.5)	NS
	24 h	1.5 (1.2–1.9)	1.6 (1.3–2.0)	NS
	72 h	2.0 (1.6–2.3)	2.1 (1.7–2.5)	NS

Values are presented as median [Q1–Q3]; CAR, C-reactive protein-to-albumin ratio; CRP, C-reactive protein; IABP, intra-aortic balloon pump; IPI, inflammatory prognostic index; NLR, neutrophil-to-lymphocyte ratio. NS = Not Significant

Given the higher inflammatory burden observed in patients receiving IABP support compared with those managed without IABP, we further examined whether this effect differed according to sex. A significant sex × IABP interaction was identified for changes in IPI at both 24 and 72 hours, indicating that the relative increase in inflammatory burden associated with IABP support (on the log-transformed IPI scale) was significantly greater in women than in men. Specifically, IABP support was associated with an approximately 34% greater increase in IPI in women at 24 hours and a 23% greater increase at 72 hours compared with men (24 h: p = 0.002; 95% CI: 0.11–0.47; 72 h: p = 0.014; 95% CI: 0.05–0.37)..

Discussion

This study demonstrates that IABP support is associated with an increased early systemic inflammatory burden and that this response differs according to sex. Patients managed without IABP showed only modest and transient sex-related differences in inflammatory indices, whereas women receiving IABP support exhibited higher levels of inflammation than men. This pattern was consistently observed across multiple inflammatory markers, including IPI, CAR, NLR, CRP, neutrophil counts, and serum albumin levels, particularly during the first 24–72 hours of hospitalization. Notably, interaction analysis indicated that IABP modifies the relationship between sex and inflammation, suggesting that sex acts as a biological modifier of the early inflammatory response in patients receiving IABP support.

The IABP, the most widely used form of mechanical circulatory support, consists of a cylindrical polyurethane balloon positioned in the descending thoracic aorta, thereby creating a non-endothelialized artificial surface in direct contact with circulating blood [11, 20]. Polyurethane is designed to preserve structural integrity with minimal deformation under mechanical stress and offers improved biocompatibility compared with earlier latex-based materials, which were associated with hypersensitivity reactions and other material-related limitations [21]. Nevertheless, the implantation of any biomaterial inevitably elicits host responses, as blood–material interaction modulates leukocyte activity and innate immune signaling, leading to the initiation of acute inflammation [22]. Because no artificial surface can fully replicate the thromboresistant and immunologically quiescent properties of the native endothelium, recognition of these non-self structures by the innate immune system activates complement pathways and cellular inflammatory cascades, thereby precluding complete biocompatibility and promoting a systemic inflammatory response [23, 24]. During inflation, the IABP balloon transiently occupies a substantial portion of the aortic lumen, increasing blood–material contact and mechanical interaction with the vascular wall while altering local shear conditions. These factors may promote endothelial activation and contribute to the initiation of an inflammatory response [5, 25]. Bia et al. [26] demonstrated that IABP induces regionally heterogeneous vascular responses, including a mechanically driven reduction in aortic diameter and elasticity together with an apparent increase in vascular viscosity, reflecting complex interactions with vascular smooth muscle function. These alterations in aortic wall mechanics and shear conditions may influence both endothelial and adventitial biology and represent a plausible pathophysiological link through which IABP support contributes to inflammatory activation [27, 28].

These biomaterial- and hemodynamics-related mechanisms provide a biologically plausible explanation for the heightened systemic inflammatory response observed in patients receiving IABP support in the present study. To specifically delineate the inflammatory impact of IABP, a propensity score–matched comparison was performed with patients managed without mechanical support, and systemic inflammation was quantified using the inflammatory prognostic index (IPI). The IPI, derived from CRP, serum albumin levels, and neutrophil and lymphocyte counts, integrates key components of the acute-phase response, innate and adaptive immune activation, and immunonutritional status [29].

CRP–albumin and neutrophil–lymphocyte–based indices provide information on the degree of inflammation; however, composite markers such as the IPI allow a more integrated assessment of inflammatory status and are increasingly used in the cardiovascular setting [15, 16, 19]. The routine use of advanced molecular or metabolomic approaches in daily clinical practice remains limited by cost, availability, and technical requirements, making indices derived from standard biochemical and complete blood count parameters a pragmatic and widely accessible alternative. These readily obtainable indices may provide clinically meaningful insight into the severity of systemic inflammation and its potential adverse consequences [30, 31].

Despite the improved biocompatibility achieved with polyurethane-based IABP systems, evidence regarding the associated inflammatory burden remains limited. By comparing patients managed with and without IABP support, the present study provides additional insight into the potential prognostic relevance of integrated inflammatory markers in this setting. In the IABP group, IPI values—driven by marked increases in CRP levels and neutrophil counts at 24 hours—were significantly higher than in the non-IABP group (181.39 [117.45–339.92] vs. 78.9 [52.4–118.6]), with a Hodges–Lehmann estimated shift of 102.5 ($r_{rb} = 0.62$; 95% CI: 78.4–126.7; $p < 0.001$), indicating a large effect size and supporting a potential contribution of blood–device interaction to early inflammatory activation. Although higher troponin levels, lower left ventricular ejection fraction, and increased EuroSCORE II values in patients requiring IABP support may have contributed to a more pronounced inflammatory profile, these baseline differences were largely balanced by propensity score matching, allowing a more reliable evaluation of the device-related effect. In the matched non-IABP cohort, elevations in CRP levels and neutrophil counts were also observed, consistent with the inflammatory response accompanying acute coronary syndrome and PCI; however, the magnitude of this response remained clearly lower than that in the IABP group [32]. Collectively, these findings indicate that IABP support is associated with an additional early inflammatory burden beyond that attributable to baseline clinical severity alone [33, 34].

Sex-related differences in cardiovascular risk profile, clinical presentation, and outcomes have been consistently reported across a broad spectrum of coronary artery disease, and accumulating evidence suggests that inflammatory pathways contribute to these disparities [35–38]. Nevertheless, most inflammatory indices have historically been evaluated without adequate sex-specific stratification, despite well-recognized differences in immune regulation between women and men [39–41]. In the study by Bravo-Jaimes et al. [42], although women constituted nearly half as many patients as men in the IABP cohort ($p = 0.004$), they experienced a higher incidence of adverse events and an approximately 15%

greater mortality rate. This pattern may reflect a more pronounced inflammatory response in women that cannot be fully explained by differences in baseline clinical risk alone [43–45]. In this context, our findings extend the existing literature by demonstrating that the inflammatory response associated with IABP support differs significantly according to sex, with women exhibiting a greater early inflammatory burden despite comparable baseline characteristics after propensity score matching. These observations support the concept that biological sex acts as an important modifier of early inflammatory activation and may have direct implications for risk stratification and perioperative monitoring in this high-risk population.

In the non-IABP cohort, women exhibited a transient peak in IPI at 24 hours compared with men, primarily driven by increases in CRP levels and neutrophil counts ($r_{rb} = 0.26$, 95% CI: 0.10–0.40; $p < 0.01$). However, this sex-related difference was substantially greater in patients receiving IABP support ($r_{rb} = 0.52$, 95% CI: 0.39–0.65; $p < 0.001$). In contrast to the non-IABP group, the wider separation of IPI values in the IABP cohort was related not only to higher CRP levels and neutrophil counts but also to a more pronounced decline in serum albumin and lymphocyte counts in women (Tables 3 and 4). Although myocardial injury, PCI, and procedure-related stress are known to augment systemic inflammation [46–48], the percutaneous implantation of an IABP—introducing a non-endothelialized polyurethane surface into the arterial circulation—together with the close apposition of the 40-cc balloon to the aortic wall, particularly in women with a smaller aortic diameter, may have contributed to the early inflammatory activation in this group through increased blood–device interaction and mechanical endothelial perturbation [49–51].

From 24 to 72 hours, IPI declined significantly in both sexes in the IABP group (women: $Z = -6.901$, $p < 0.001$; men: $Z = -8.694$, $p < 0.001$), indicating a rapid attenuation of the early inflammatory surge. A similar but less pronounced reduction was observed in the non-IABP cohort (women: $Z = -5.12$, $p < 0.001$; men: $Z = -6.03$, $p < 0.001$). Despite higher peak levels at 24 hours, the IABP group demonstrated a steeper decline in IPI, largely driven by the marked decrease in CRP concentrations by 72 hours. Consistent with these findings, Gu et al. [52] reported that CRP levels were substantially reduced by the third day in patients with acute myocardial infarction treated with IABP compared with those managed without mechanical support. This temporal reduction in inflammatory activity may be related to the well-established hemodynamic effects of IABP, including enhanced coronary perfusion, improved myocardial blood flow, and partial restoration of pulsatile arterial flow, which collectively improve tissue oxygenation and may contribute to the attenuation of the inflammatory response over time [53, 54].

Another plausible mechanism underlying the higher IPI values observed in women relates to the age and menopause-associated decline in the anti-inflammatory and vasoprotective effects of estrogen. In a cohort with a mean age of approximately 65 years, this hormonal transition is accompanied by a shift toward a more proinflammatory state, characterized by increased acute-phase reactants, including CRP, together with altered immune cell regulation and enhanced innate immune activation [55]. These age-related changes in immune and metabolic regulation have been associated with lower serum albumin levels and relative lymphopenia, both of which directly contribute to higher IPI values. Within this

framework, the more pronounced reductions in albumin levels and lymphocyte counts observed in women may represent a biologically plausible substrate for the greater inflammatory burden identified in this group [56, 57].

Given the distinct pathophysiological features of coronary artery disease in women, the identification of sex-specific inflammatory profiles and risk determinants is of particular clinical relevance [58]. Variations in metabolic and nutritional status, age- and menopause-related immune modulation, and the persistent underrepresentation of women in studies of mechanical circulatory support have limited the understanding of device-related inflammatory responses in this population [59–61]. In line with the life-course approach proposed by Sambola et al. [62], the present findings underscore that women should not be evaluated within a uniform disease framework and that preventive and therapeutic strategies need to incorporate sex-specific biological differences. Notably, our results demonstrate that IABP support is associated with a more pronounced inflammatory burden in women, highlighting the potential clinical importance of inflammatory monitoring in this subgroup. These data indicate that the inflammatory response to mechanical circulatory support is not sex-neutral and should be integrated into risk stratification and management strategies, particularly in women undergoing IABP therapy [63].

Limitations

This study has several limitations that should be acknowledged. Although the data were collected prospectively using a standardized protocol, the single-center design may limit the generalizability of the findings. Inflammatory biomarkers are subject to biological and clinical variability and may be influenced by factors that were not fully captured in the study dataset; therefore, residual confounding cannot be entirely excluded despite the use of propensity score matching. The analysis focused on the early inflammatory phase and does not provide information on the long-term trajectory of inflammatory markers or their direct relationship with clinical outcomes. In addition, detailed cytokine or molecular inflammatory profiling was not performed; therefore, the mechanistic pathways underlying the observed inflammatory patterns cannot be fully clarified. The observational design also precludes causal inference. Further studies with longitudinal follow-up and more comprehensive inflammatory assessment may help to better define the clinical implications of these findings.

Conclusions

In this propensity score–matched prospective cohort of patients with coronary artery disease requiring preoperative support, IABP implantation was associated with a marked early increase in systemic inflammatory burden, particularly in women, followed by a more rapid decline over time. This response was most prominent at 24 hours and was characterized by concurrent increases in CRP levels and neutrophil counts together with reductions in lymphocyte count and serum albumin levels. These findings identify biological sex as an important modifier of the inflammatory response to IABP and support the clinical value of early, sex-specific monitoring using integrated inflammatory indices for risk stratification and periprocedural management in patients undergoing mechanical circulatory support.

Abbreviations

CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CAR	C-reactive protein to albumin ratio
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
IABP	Intra-aortic balloon pump
IPI	Inflammatory prognostic index
LEVF%	Left ventricular ejection fraction
MCS	Mechanical circulatory support
NLR	Neutrophil-to-Lymphocyte Ratio
PCI	Percutaneous coronary intervention

Declarations

Ethics approval and consent to participate: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Atatürk University Faculty of Medicine (Protocol Code:11/44, Date of Approval: 26.12.2025). Written informed consent was obtained from all participants in this study.

Consent for publication: Not applicable, as no individual patient data are presented.

Data Availability Statement: All data generated or analyzed during this study, including laboratory findings, and statistical data, are securely stored within the authors' archives. No data were obtained from external sources or previously published materials. These datasets are available from the corresponding author upon reasonable request.

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References

1. Crimi E, Rajkumar K, Coleman S, Fernando R, Marchant B, Garner C, Gaillard J, Hicks MH, Maves RC, Khanna AK. Cardiovascular Physiology During Mechanical Circulatory Support: Implications for Management and Monitoring. J Clin Med. 2025;14:6935. https://doi.org/10.3390/jcm14196935.
2. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary. Circulation. 2022;145(18):E876–94. https://doi.org/10.1161/CIR.0000000000001062.
3. Khan TM, Siddiqui AH. Intra-Aortic Balloon Pump. In StatPearls [Internet]; StatPearls Publishing: Treasure Island, FL, 2025. (accessed on December 2025). https://www.ncbi.nlm.nih.gov/books/NBK542233/
4. Annamalai SK, Buiten L, Esposito ML, Paruchuri V, Mullin A, Breton C, Pedicini R, O'Kelly R, Morine K, Wessler B, et al. Acute Hemodynamic Effects of Intra-Aortic Balloon Counterpulsation Pumps in Advanced Heart Failure. J Card Fail. 2017;23(8):606–14. https://doi.org/10.1016/j.cardfail.2017.05.015.
5. Parissis H, Graham V, Lampridis S, Lau M, Hooks G, Mhandu PC. IABP: History–Evolution–Pathophysiology–Indications: What We Need to Know. J. Cardiothorac. Surg. 2016, 11 (1), 122. https://doi.org/10.1186/s13019-016-0513-0
6. Market Reports World. Intra-Aortic Balloon Pump (IABP) Market Report; Market Reports World. January 2026. https://www.marketreportsworld.com/market-reports/intra-aortic-balloon-pump-iabp-market-14716268 (accessed on January 2026).
7. de Jong MM, Lorusso R, Al Awami F, Matteucci F, Parise O, Lozekoot P, Bonacchi M, Maessen JG, Johnson DM, Gelsomino S. Vascular Complications following Intra-Aortic Balloon Pump Implantation: An Updated Review. Perfusion 2018, 33 (2), 96–104. https://doi.org/10.1177/0267659117727825
8. Morici N, Sacco A, Frea S, Rota M, Villanova L, Gravinese C, Dini CS, D'Ettore N, Maj G, De Lio G, et al. Early Intra-Aortic Balloon Support for Heart Failure-Related Cardiogenic Shock: A Randomized Clinical Trial. J Am Coll Cardiol. 2025;85(16):1587–97. https://doi.org/10.1016/j.jacc.2025.03.003.
9. Motia N, Marko V, Karlsen MW. Complications Associated with Intra-Aortic Balloon Pump Treatment in Critically Ill Patients: A Systematic Review. Nurs Crit Care. 2024;29(6):1768–80. https://doi.org/10.1111/nicc.13163.
10. Taylor JS, Erkek E. Latex Allergy: Diagnosis and Management. Dermatol Ther. 2004;17(4):289–301. https://doi.org/10.1111/j.1396-0296.2004.04024.x.
11. Burke JF, Didisheim P, Goupil D, Heller J, Kane JB, Katz JL, Kim SW, Lemons JE, Refojo MF, Robblee LS, et al. Application of Materials in Medicine and Dentistry. In: Ratner BD, Hoffman AS, Lemons JE,

editors. Biomaterials Science: An Introduction to Materials in Medicine. San Diego, CA: Academic; 1996. pp. 283–388. https://doi.org/10.1016/B978-0-08-050014-0.50012-2.

12. Intra-Aortic Balloon Pump Device. WO1995017219A1. 1995. Google Patents. https://patents.google.com/patent/WO1995017219A1/en (accessed January 2026).
13. Coronel-Meneses D, Sánchez-Trasviña C, Ratera I, Mayolo-Deloisa K. Strategies for Surface Coatings of Implantable Cardiac Medical Devices. Front Bioeng Biotechnol. 2023;11:1173260. https://doi.org/10.3389/fbioe.2023.1173260.
14. Segan S, Jakobi M, Khokhani P, Klimosch S, Billing F, Schneider M, Martin D, Metzger U, Biesemeier A, Xiong X et al. Systematic Investigation of Polyurethane Biomaterial Surface Roughness on Human Immune Responses in vitro. Biomed. Res. Int. 2020, 2020, 3481549. https://doi.org/10.1155/2020/3481549
15. 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 (8), e20230226. https://doi.org/10.1590/1806-9282.20230226
16. 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(1):25–32. https://doi.org/10.9739/tjvs.2024.12.060.
17. Ma F, Li L, Xu L, Wu J, Zhang A, Liao J, Chen J, Li Y, Li L, Chen Z, et al. The Relationship between Systemic Inflammation Index, Systemic Immune-Inflammatory Index, and Inflammatory Prognostic Index and 90-Day Outcomes in Acute Ischemic Stroke Patients Treated with Intravenous Thrombolysis. J Neuroinflammation. 2023;20(1):220. https://doi.org/10.1186/s12974-023-02890-y.
18. Ekinci F, Erdogan AP, Yildirim S, Bulut G, Yilmaz C, Barutca S. Inflammatory Prognostic Index in Metastatic Renal Carcinoma Treated with Nivolumab. J Coll Physicians Surg Pak. 2022;32(10):1288–94. https://doi.org/10.29271/jcpsp.2022.10.1288.
19. Oflar E, Kalyoncuoğlu M, Koyuncu A, Yıldız Erbaş C, Sinoplu HA, Katkat F, Durmuş G. The Role of the Inflammatory Prognostic Index in Patients with Non-ST Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention. J Clin Med. 2025;14:4491. https://doi.org/10.3390/jcm14134491.
20. Limbert VM, Amiri AM. Intra-Aortic Balloon Pump for Patients with Cardiac Conditions: An Update on Available Techniques and Clinical Applications. *Reports* 2019, *2*, 19. https://doi.org/10.3390/reports2030019
21. Adrian K. Origins of Intraaortic Balloon Pumping. Ann Thorac Surg. 1990;50:672–4. https://doi.org/10.1016/0003-4975(90)90220-Z.
22. Anderson JM, Rodriguez A, Chang DT. Foreign Body Reaction to Biomaterials. Semin Immunol. 2008;20(2):86–100. https://doi.org/10.1016/j.smim.2007.11.004.
23. Nilsson B, Ekdahl KN, Mollnes TE, Lambris JD. The Role of Complement in Biomaterial-Induced Inflammation. Mol Immunol. 2007;44(1–3):82–94. https://doi.org/10.1016/j.molimm.2006.06.020.

24. Mollnes TE, Complement. Biocompatibility Vox Sang. 1998;74(Suppl 2):303–7. https://doi.org/10.1111/j.1423-0410.1998.tb05435.x.
25. Gorbet MB, Sefton MV, Biomaterial-Associated, Thrombosis. Roles of Coagulation Factors, Complement, Platelets and Leukocytes. Biomaterials. 2004;25(26):5681–703. https://doi.org/10.1016/j.biomaterials.2004.01.023.
26. Bia D, Zócalo Y, Armentano R, Camus J, Forteza ED, Cabrera-Fischer E. Increased Reversal and Oscillatory Shear Stress Cause Smooth Muscle Contraction-Dependent Changes in Sheep Aortic Dynamics: Role in Aortic Balloon Pump Circulatory Support. Acta Physiol (Oxf. 2008;192(4):487–503. https://doi.org/10.1111/j.1748-1716.2007.01765.x.
27. Bia D, Cabrera-Fischer EI, Zócalo Y, Armentano RL. The Endothelium Modulates the Arterial Wall Mechanical Response to Intra-Aortic Balloon Counterpulsation. Vivo Stud Artif Organs. 2011;35(9):883–92. https://doi.org/10.1111/j.1525-1594.2011.01320.x.
28. Cabrera-Fischer EI, Bia D, Zócalo Y, Wray S, Armentano R. The Adventitia Layer Modulates the Arterial Wall Elastic Response to Intra-Aortic Counterpulsation: In Vivo Studies. Artif Organs. 2013;37(12):1041–8. https://doi.org/10.1111/aor.12111.
29. Jiang Y, Luo B, Chen Y, Peng Y, Lu W, Chen L, Lin Y. Predictive Value of Inflammatory Prognostic Index for Contrast-Induced Nephropathy in Patients Undergoing Coronary Angiography and/or Percutaneous Coronary Intervention. Sci Rep. 2024;14(1):15861. https://doi.org/10.1038/s41598-024-66880-7.
30. Özmen M. The Role of C-Reactive Protein:Albumin Ratio and Neutrophil:Lymphocyte Ratio in Predicting Coronary Artery Disease. Cardiovasc J Afr. 2024;34:1–4. https://doi.org/10.5830/CVJA-2024-004.
31. Dirican N, Dirican A, Anar C, Atalay S, Ozturk O, Bircan A, Akkaya A, Cakir MA. New Inflammatory Prognostic Index, Based on C-Reactive Protein, the Neutrophil-to-Lymphocyte Ratio and Serum Albumin, Is Useful for Predicting Prognosis in Non-Small Cell Lung Cancer Cases. Asian Pac. J Cancer Prev. 2016;17(12):5101–6. https://doi.org/10.22034/APJCP.2016.17.12.5101.
32. Kofos C, Papazoglou AS, Fyntanidou B, Samaras A, Stachteas P, Nasoufidou A, Apostolopoulou A, Karakasis P, Arvanitaki A, Bantidos MG, et al. The Prognostic Gender-Related Value of the Systemic Immune-Inflammation Index in Patients with Acute Coronary Syndrome. Rev Cardiovasc Med. 2026;27(1):44305. https://doi.org/10.31083/RCM44305.
33. Theofilis P, Oikonomou E, Chasikidis C, Tsioufis K, Tousoulis D. Pathophysiology of Acute Coronary Syndromes—Diagnostic and Treatment Considerations. Life (Basel). 2023;13(7):1543. https://doi.org/10.3390/life13071543.
34. Potapov E, Schweiger M, Lehmkuhl E, Vierecke J, Stepanenko A, Weng G, Pasic M, Huebler M, Regitz-Zagrosek V, Hetzer R, Krabatsch T. Gender Differences during Mechanical Circulatory Support. ASAIO J. 2012;58(4):320–5. https://doi.org/10.1097/MAT.0b013e318251cdf9.
35. Henein MY, Vancheri S, Longo G, Vancheri F. The Role of Inflammation in Cardiovascular Disease. Int J Mol Sci. 2022;23:12906. https://doi.org/10.3390/ijms232112906.

36. Prabhavathi K, Selvi KT, Poornima KN, Sarvanan A. Role of Biological Sex in Normal Cardiac Function and in Its Disease. Outcome—A Rev J Clin Diagn Res. 2014;8(8):BE01–4. https://doi.org/10.7860/JCDR/2014/9635.4771.
37. Klein SL, Flanagan KL. Sex Differences in Immune Responses. Nat Rev Immunol. 2016;16(10):626–38. https://doi.org/10.1038/nri.2016.90.
38. Subramanian G, Muthusamy P, Kaliyamurthy T, Ganesan M. Difference of Coronary Artery Disease in Women and Men in Recent Trials. Indian J Cardiovasc Dis Women. 2025;10:131–7. https://doi.org/10.25259/IJCDW_62_2024.
39. Mazhar F, Faucon A-L, Fu EL, Szummer KE, Mathisen J, Gerward S, Reuter SB, Marx N, Mehran R, Carrero J-J, et al. Systemic Inflammation and Health Outcomes in Patients Receiving Treatment for Atherosclerotic Cardiovascular Disease. Eur Heart J. 2024;45(44):4719–30. https://doi.org/10.1093/eurheartj/ehae557.
40. Kim HL. Sex Differences in Coronary Atherogenesis: A Narrative Review. Ewha Med J. 2024;47(2):e15. https://doi.org/10.12771/emj.2024.e15.
41. Sobhani K, Nieves Castro DK, Fu Q, Gottlieb RA, Van Eyk JE. Noel Bairey Merz, C. Sex Differences in Ischemic Heart Disease and Heart Failure Biomarkers. Biol Sex Differ. 2018;9(1):43. https://doi.org/10.1186/s13293-018-0201-y.
42. Bravo-Jaimes K, Mejia MO, Abelhad NI, Zhou Y, Jumean MF, Nathan S, Dhoble A. Gender Differences in the Outcomes of Cardiogenic Shock Requiring Percutaneous Mechanical Circulatory Support. Am J Cardiol. 2022;174:20–6. https://doi.org/10.1016/j.amjcard.2022.03.033.
43. Luczak ED, Leinwand LA. Sex-Based Cardiac Physiology. Annu Rev Physiol. 2009;71:1–18. https://doi.org/10.1146/annurev.physiol.010908.163156.
44. Sakkers TR, Mokry M, Civelek M, Erdmann J, Pasterkamp G, Diez Benavente E, den Ruijter HM. Sex Differences in the Genetic and Molecular Mechanisms of Coronary Artery Disease. Atherosclerosis. 2023;384:117279. https://doi.org/10.1016/j.atherosclerosis.2023.117279.
45. Lansky AJ, Ng VG, Maehara A, Weisz G, Lerman A, Mintz GS, De Bruyne B, Farhat N, Niess G, Jankovic I, et al. Gender and the Extent of Coronary Atherosclerosis, Plaque Composition, and Clinical Outcomes in Acute Coronary Syndromes. JACC Cardiovasc Imaging. 2012;5(3 Suppl):S62–72. https://doi.org/10.1016/j.jcmg.2012.02.003.
46. Sullivan S, Young A, Hammadah M, Lima BB, Levantsevych O, Ko YA, Pearce BD, Shah AJ, Kim JH, Moazzami K, et al. Sex Differences in the Inflammatory Response to Stress and Risk of Adverse Cardiovascular Outcomes among Patients with Coronary Heart Disease. Brain Behav Immun. 2020;90:294–302. https://doi.org/10.1016/j.bbi.2020.09.001.
47. Buzle AM, Matache P, Moisi MI, Ghitea MC, Ghitea EC, Gîtea MF, Ghitea TC, Popescu MI. Early Post-PCI Inflammatory Risk Score for Diastolic Dysfunction: Development and Internal Validation (TRIPOD-Compliant). Appl Sci. 2025;15:10018. https://doi.org/10.3390/app151810018.
48. Brunetti ND, Troccoli R, Correale M, Pellegrino PL, Di Biase M. C-Reactive Protein in Patients with Acute Coronary Syndrome: Correlation with Diagnosis, Myocardial Damage, Ejection Fraction and

Angiographic Findings. Int J Cardiol. 2006;109(2):248–56. https://doi.org/10.1016/j.ijcard.2005.06.021.

49. Weber M, Steinle H, Golombek S, Hann L, Schlensak C, Wendel HP, Avci-Adali M. Blood-Contacting Biomaterials: In Vitro Evaluation of the Hemocompatibility. Front Bioeng Biotechnol. 2018;6:99. https://doi.org/10.3389/fbioe.2018.00099.
50. Rylski B, Desjardins B, Moser W, Bavaria JE, Milewski RK. Gender-Related Changes in Aortic Geometry throughout Life. Eur J Cardiothorac Surg. 2014;45(5):805–11. https://doi.org/10.1093/ejcts/ezt597.
51. Marois Y, Guidoin R. January. Biocompatibility of Polyurethanes. In: Madame Curie Bioscience Database [Internet]. Austin (TX): Landes Bioscience; 2000–2013. Available from: https://www.ncbi.nlm.nih.gov/books/NBK6422/?utm_source=chatgpt.com (accessed on 2026).
52. Gu J, Hu W, Xiao H, Feng X, Chen Y, Zhang D. Intra-Aortic Balloon Pump Improves Clinical Prognosis and Attenuates C-Reactive Protein Level in Acute STEMI Complicated by Cardiogenic Shock. Cardiology. 2010;117(1):75–80. https://doi.org/10.1159/000319618.
53. Zhang J, Zhang Y. The Clinical Effects of IABP Pumps Combined with Tirofiban in the Treatment of Acute Myocardial Infarction and on Patients' Serum Levels. Am J Transl Res. 2021;13(8):9796–801.
54. Onorati F, Santarpino G, Tangredi G, Palmieri G, Rubino AS, Foti D, Gulletta E, Renzulli A. Intra-Aortic Balloon Pump Induced Pulsatile Perfusion Reduces Endothelial Activation and Inflammatory Response following Cardiopulmonary Bypass. Eur J Cardiothorac Surg. 2009;35(6):1012–9. https://doi.org/10.1016/j.ejcts.2008.12.037.
55. Poznyak AV, Sukhorukov VN, Guo S, Postnov AY, Orekhov AN. Sex Differences Define the Vulnerability to Atherosclerosis. Clin Med Insights Cardiol. 2023;17:11795468231189044. https://doi.org/10.1177/11795468231189044.
56. Ilesanmi-Oyelere BL, Kruger MC. Associations between Dietary Patterns and an Array of Inflammation Biomarkers and Plasma Lipid Profile in Postmenopausal Women. BMC Womens Health. 2023;23(1):256. https://doi.org/10.1186/s12905-023-02417-w.
57. Bernier V, Chatelan A, Point C, Strauss M. Nutrition and Neuroinflammation: Are Middle-Aged Women. Red Zone? Nutrients. 2025;17:1607. https://doi.org/10.3390/nu17101607.
58. Kottilil S, Mathur P. The Influence of Inflammation on Cardiovascular Disease in Women. Front Glob Womens Health. 2022;3:979708. https://doi.org/10.3389/fgwh.2022.979708.
59. Dayanand S, Martinez JM, Figueredo VM, Gupta S. Mechanical Circulatory Support in Women. J Cardiol. 2021;77(3):209–16. https://doi.org/10.1016/j.jjcc.2020.07.012.
60. Stumpf F, Keller B, Gressies C, Schuetz P. Inflammation and Nutrition: Friend or Foe? *Nutrients* 2023, *15*, 1159. https://doi.org/10.3390/nu15051159
61. Tobb K, Kocher M, Bullock-Palmer RP. Underrepresentation of Women in Cardiovascular Trials—It Is Time to Shatter This Glass Ceiling. Am Heart J Plus. 2022;13:100109. https://doi.org/10.1016/j.ahjo.2022.100109.

62. Sambola A, Campuzano R, Castro A, Goya M, Coronado P, Fernández-Olmo R, María-Tablado MÁ, Ortiz-Cortés C, Ortolà X, Pallarés-Carratalá V, et al. Primary and Secondary Cardiovascular Prevention through Life Cycles in Women: Consensus Document of the SEC-GT CVD in Women, ACP-SEC, SEGO, AEEM, SEEN, semFYC, SEMERGEN. AEP AEM Rev Esp Cardiol (Engl Ed). 2025;78(7):639–51. https://doi.org/10.1016/j.rec.2025.01.005.
63. Wu L, Pamboukian SV. Women and Mechanical Circulatory Support. In: Arabía FA, editor. Mechanical Circulatory Support. Cham: Springer; 2025. Chap. 29. https://doi.org/10.1007/978-3-031-09048-6_29.