

Article

Relationship between Fibrinogen Values and Sensitivity and Specificity of STS Score, Euroscore for Patients Undergoing Open Heart Surgery

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Abstract

Background/Aim: Cardiovascular diseases are a leading cause of mortality worldwide, with surgical interventions playing a crucial role in outcomes. Despite technological advancements and improved operator experience, perioperative and postoperative risks remain significant, particularly for high-risk patients. Fibrinogen, an acute-phase reactant, increases during inflammation and plays a role in coagulation. This study investigates the prognostic impact of fibrinogen levels on the outcomes of cardiac surgery and evaluates its relationship with established risk classification systems. **Materials and Methods:** This observational cohort study included 105 patients who underwent cardiac surgery between May 2018 and December 2023. Patients with coronary bypass grafting and valve surgery were included, while those with transplantation, congenital heart surgery, or other significant conditions were excluded. Patient data, including demographic information, comorbidities, laboratory parameters, and surgical details, were collected. The fibrinogen cutoff value was determined using the Youden index. Statistical analyses were performed using SPSS 23.0, with p -values < 0.05 considered significant. **Results:** Of the 116 individuals screened, 105 were included in the study. The HighFib group (>3.8 g/dL) showed higher rates of complications, such as low cardiac output, prolonged mechanical ventilation, and atrial fibrillation, compared to the LowFib group (<3.8 g/dL). The HighFib group also had lower preoperative hemoglobin levels and higher Euroscore values. Logistic regression analysis demonstrated that both fibrinogen levels and established risk scores were significant predictors of postoperative complications. **Conclusion:** Elevated fibrinogen levels are associated with increased postoperative complications in cardiac surgery patients. Fibrinogen, alongside traditional risk scores, can be a valuable predictor of adverse outcomes. Prospective studies are needed to further validate these findings and establish optimal fibrinogen management strategies in cardiac surgery.

Keywords

fibrinogen; cardiac surgery; risk assessment; postoperative complications; prognosis

Introduction

Cardiovascular diseases are still the most important cause of mortality worldwide, and surgical interventions are important because of their outcomes. Technological developments and increased operator experience have reduced mortality and morbidity rates in patients undergoing cardiovascular surgery over the years, but peri- and postoperative risks remain high, especially for fragile patients. It is important to predict the complications that may be encountered in the preoperative period and to perform a risk assessment [1,2]. Various risk prediction models, such as the European Cardiac Operative Risk Assessment System and the Association of Thoracic Surgeons 2008 Cardiac Surgery Risk, Euroscore, have been used in cardiac surgery for decades [3–6].

Inflammation has been shown to trigger the formation of atherosclerotic plaques, increase platelet aggregation, and increase the risk of cardiovascular events [7]. Fibrinogen is a positive acute-phase reactant, and an increase in its serum level is observed during inflammation [7]. Fibrinogen also plays an active role in hemorrhage, and effective clot formation regulates the coagulation cascade [8].

Postoperative bleeding is the most common complication of cardiac surgery and is a significant cause of mortality and morbidity. Studies have shown different aggravating causes, such as thrombocytopenia, hyperfibrinolysis, platelet dysfunction and other coagulation factors, and antiplatelet agents [9]. Fibrinogen is used in some countries to reduce the incidence of bleeding events in the period after cardiac surgery, and there is also the opinion that it increases inflammation and cell damage, such as acute kidney injury [10]. Fibrinogen is a substrate and not an en-



zyme. However, excessive circulation may increase the risk of thrombosis [11].

Since data regarding the use of fibrinogen in the perioperative period are contradictory, the optimum fibrinogen level during the preoperative period has yet to be determined. In this study, we aimed to investigate the prognostic impact of fibrinogen levels and other factors on the outcomes of heart surgery.

Materials and Methods

This observational cohort study included 105 patients admitted to our cardiovascular surgery department between May 2018 and December 2023. Patients who underwent cardiac surgery, including coronary bypass grafting and valve surgery, were included in this study. The exclusion criteria were as follows: (1) transplantation, (2) congenital heart surgery, (3) left ventricular assist device, (4) extracorporeal membrane oxygenation, (5) liver and kidney disease, (6) coagulopathies, (7) heart failure (ejection fraction <30%), and (8) concomitant surgical procedures.

One of the risk scoring systems used to predict mortality in the preoperative period after cardiac surgery is the European System for Cardiac Operative Risk Evaluation (EuroSCORE) scoring system. The EUROSCORE accounts for patient demographic information, cardiac factors and surgery-related factors [3].

Like the Euroscore, the STS is a scoring system that evaluates operative risk factors in adult patients undergoing cardiac surgery, including patient demographic data, laboratory data, additional risk factors, procedures performed and cardiac status [4–6].

Patient information, such as demographic data, comorbidities, pre- and postoperative laboratory parameters, surgery type and duration, peri- and postoperative blood product transfusion and adverse events occurring in the postoperative period, were recorded. The fibrinogen cutoff value was determined with the Youden index formula [9]. The fibrinogen level at which the sensitivity and specificity values obtained via ROC analysis were closest to each other was determined as the area of the maximum potential effectiveness value. According to the Youden index calculation [12], the cutoff fibrinogen concentration was 3.8 g/dL, with 89.2% sensitivity and 69.6% specificity. Probability (p) values < 0.05 were considered statistically significant. Additionally, the perioperative predictors of blood loss and mortality endpoints were analyzed. The preoperative fibrinogen-to-albumin ratio (FAR) was hypothesized to be a composite mortality endpoint predictor.

Definitions

MI (Myocardial Infraction): Creatine kinase and troponin values above five times the 99th percentile of the

normal reference range during the first 72 hours following CABG (Coronary Artery Bypass Grafting) are considered diagnostic of CABG-related myocardial infarction when new pathological Q-waves, new left bundle branch block, angiographically documented new graft or native coronary artery occlusion are added. MI was considered a complication in patients who met these criteria in the postoperative period and required revascularization with surgical or percutaneous interventions.

Low flow rate: Complications were considered if cardiac index was below 2.2 L min⁻¹ m⁻² in postoperative follow-ups and clinical signs of hypoperfusion were present.

The study protocol was approved by the local ethics committee (ETHICS NO: 2022/03-09). The study was conducted in accordance with the ethical principles set up in the Declaration of Helsinki and Good Clinical Practice Guidelines. Informed consent was obtained from all participants enrolled in this study.

Statistical Analysis

Statistical analyses were performed with SPSS 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) software package. Continuous variables are presented as means ± standard deviations, and categorical variables are presented as percentages. Nonnormally distributed variables are presented as median (minimum–maximum) values. The distribution characteristics of the variables were determined using the Kolmogorov–Smirnov test and the Shapiro–Wilks test. Quantitative variables were compared with the Mann–Whitney U test, and for qualitative variables, the chi-square test was used. Changes observed in nonnormally distributed variables were analyzed with the Friedman test. To compare the fibrinogen and risk scores, a receiver operating characteristic (ROC) curve was used. The fibrinogen cutoff value was determined with the Youden index formula [13].

Results

A total of 116 individuals were screened in this study; however, 11 of them were excluded because of exclusion criteria. The demographic and clinical characteristics of the patients are presented in Table 1. Patients in both groups had similar demographic data except for age, previous extracardiac arteriopathy rate and hemoglobin levels. The highFib group was older than the LowFib group was ($p = 0.050$). Preoperative hemoglobin levels were significantly lower in the HighFib group than in the LowFib group ($p = 0.001$). There was no significant difference in the STS score between the groups. The Euroscore was higher in the HighFib group ($p = 0.007$). The incidence of postoperative

Table 1. Baseline demographics and procedural characteristics stratified by fibrinogen level (3.8 g/dL).

	HighFib, >3.8 g/dL (n: 79)	LowFib, <3.8 g/dL (n: 26)	<i>p</i> -values
Age, years	62.78 ± 9.93	57.76 ± 14.37	0.050
Height, cm	165.96 ± 7.88	167.69 ± 7.19	0.969
Weight, kg	75 (70–78)	76 (66–84)	0.324
Sex, male % (n)	64.6 (51)	84.6 (22)	0.054
DM, % (n)	48.1 (38)	30.8 (8)	0.122
Smokers, n (%)	70.9 (56)	69.2 (18)	0.872
HT, % (n)	65.8 (52)	50 (13)	0.150
Stroke, % (n)	1.3 (1)	0 (0)	0.564
COPD, % (n)	25.3 (20)	7.7 (2)	0.055
Extracardiac arteriopathy, % (n)	43 (34)	15.4 (4)	0.011
WBC	9.39 ± 5.09	8.28 ± 2.51	0.280
HGB, g/dL	12.81 ± 1.67	14.09 ± 1.47	0.001
PLT	268.43 ± 97.12	236.38 ± 83.13	0.134
GFR	93.85 (68.70–112.42)	99.25 (75.60–120.00)	0.156
Albumin	3.64 ± 0.50	3.72 ± 0.42	0.453
HS troponin	5740.87 ± 11,878.59	3942.30 ± 9594.76	0.486
LVEF, %	51 (50–66)	54 (52–67)	0.125
STS score	4.73 ± 2.11	3.99 ± 1.37	0.051
Euroscore	11.30 ± 9.19	6.07 ± 5.05	0.007
Total perfusion time	71.34 ± 29.93	68.00 ± 22.32	0.605
Crosstime	41.30 ± 20.19	39.26 ± 17.17	0.649
NT-ProBNP	2025.97 ± 3543.32	702.55 ± 945.92	0.554
IL-6	23.78 ± 93.94	12.16 ± 28.51	0.075
Fibrinogen	447.24 ± 108.31	274.93 ± 59.88	<0.001
CABG Surgery	86.0 (68)	84.6 (22)	0.128
Valve Surgery	1.4 (1)	3.8 (1)	0.245

DM, Diabetes Mellitus; HT, Hypertension; COPD, Chronic Obstructive Pulmonary Disease; WBC, White Blood Cell; PLT, Platelets; GFR, Glomerular Filtration Rate; LVEF, Left Ventricular Ejection Fraction; STS, Society of Thoracic Surgeons; IL-6, Interleukin-6; CABG, Coronary Artery Bypass Grafting.

in-hospital complications was higher in the HighFib group than in the other groups (Table 2). Although the frequencies of mortality, low cardiac output, mortality, mechanical ventilation duration, AF and postoperative MI were higher in the HighFib group, lower rates of bleeding events and revision surgery were observed. Low cardiac output, prolonged mechanical ventilation (MV), and atrial fibrillation (AF) were significantly more common in the HighFib group ($p = 0.006$, 0.008 , and 0.042 , respectively). However, bleeding events and revision surgery were more common in patients with low Fib ($p = 0.014$).

Univariate and multivariate analysis were performed to determine the independent predictors for postoperative complication (Table 3). According to univariate analysis, hemoglobin, STS score, Euroscore and fibrinogen levels were found statistically significant and with this variables multivariate model was performed. Multivariate analysis revealed STS score [Odds Ratio (OR): 1.455, 95% Confidence Interval (95% CI): 0.785–1.232, $p = 0.019$], Euroscore (OR: 1.763, CI 0.785–1.232, $p = 0.003$), fibrinogen (OR: 1.518, CI: 0.901–1.693, $p = 0.007$) as independent

predictors of postoperative complications including mortality, postoperative myocardial infarction, postoperative AF and revision surgery.

The ROC analysis was performed to determine the predictive power of STS score, Euroscore and fibrinogen (Fig. 1). According to STS score with a cut-off value of 4.1, area under curve (AUC) was 0.592, 95% CI: 0.456–0.727, $p = 0.186$. Euroscore with a cut-off value of 8.9 AUC was revealed 0.664, 95% CI: 0.541–0.787, $p = 0.018$ and fibrinogen the cut-off value of 3.8 AUC was 0.598, 95% CI: 0.464–0.732, $p = 0.157$.

Discussion

Fibrinogen is a positive acute-phase reactant, and an increase in its serum level is observed during inflammation [7]. Fibrinogen also plays an active role in hemorrhage, and effective clot formation regulates the coagulation cascade [8]. In our study, we aimed to examine the relationship between low and high fibrinogen levels and postoperative

Table 2. Postoperative complications according to fibrinogen levels.

Complications	HighFib	LowFib	<i>p</i> -values
Use of inotrope, % (<i>n</i>)	67.1 (53)	61.5 (16)	0.605
Low cardiac output, % (<i>n</i>)	11.4 (9)	3.8 (1)	0.006
Duration of MV (<i>h</i>)	7.43 ± 2.78	6.42 ± 1.30	0.008
Atrial fibrillation	24.1 (14)	19.2 (5)	0.042
Bleeding & Revision, % (<i>n</i>)	5.2 (3)	0 (0)	0.014
In hospital mortality, % (<i>n</i>)	3.4 (2)	0 (0)	0.199
Postoperative MI, % (<i>n</i>)	12.1 (7)	8.5 (4)	0.554

MV, Mechanical ventilation; MI, Myocardial infarction.

Table 3. Univariate and Multivariate analysis to analyze the predictors of postoperative complications.

Variable	Univariate			Multivariate		
	Exp (B)	Confidence Interval	<i>p</i> value	Exp (B)	Confidence Interval	<i>p</i> value
Sex	0.184	0.026–1.288	0.088			
Age	1.154	0.915–1.296	0.843			
External arteriopathies	1.049	0.221–4.978	0.352			
HGB	1.318	0.534–1.552	0.045	1.050	0.693–1.333	0.412
PLT	1.435	0.986–1.606	0.491			
GFR	1.015	0.887–1.117	0.184			
Albumin	1.410	0.067–2.520	0.334			
LVEF	1.053	0.955–1.162	0.207			
STS score	1.320	0.890–1.864	0.008	1.455	0.785–1.232	0.019
Euroscore	1.244	0.675–1.544	<0.001	1.763	0.876–1.501	0.003
IL-6	0.956	0.906–1.109	0.103			
Fibrinogen	1.202	0.866–1.264	0.028	1.518	0.901–1.693	0.007

Nagelkerke's R2 for model 1: 0.543 and mode 2: 0.668.

mortality and morbidity rates. Fibrinogen levels are similarly correlated with complications, as are the Euroscore and the STS score, which are risk classifications for cardiac surgery. Additionally, fibrinogen contributes to the formation of a clot. According to the guidelines, it is used in cardiac surgery to reduce the incidence of blood transfusions [13]. When preoperative fibrinogen levels are high, the incidence of postoperative bleeding events decreases [14]. Studies have indicated that although there is a decrease in the postoperative blood loss volume, there is an increase in the red blood cell transfusion rate in patients with high fibrinogen levels [15,16].

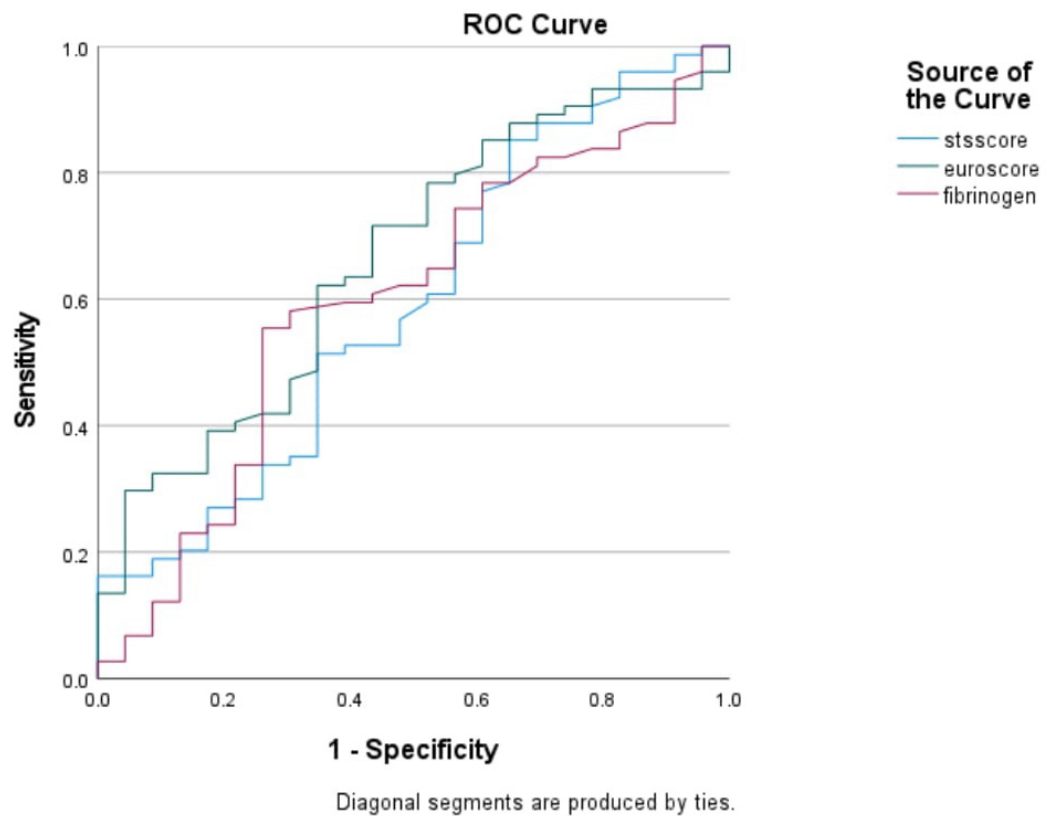
Many studies have shown that patients with low fibrinogen levels who undergo cardiac surgery experience more bleeding events [17–19]. On the basis of these findings, a randomized pilot study revealed that preoperative, prophylactic fibrinogen infusion in CABG patients significantly reduced the incidence of postoperative bleeding events, with no evidence of an increased incidence of thromboembolic events such as graft occlusion, myocardial infarction, or pulmonary embolism [20].

Additionally, another study evaluated the relationship between drainage volume and fibrinogen and found that preoperative and postoperative fibrinogen levels were clearly associated with the 24-hour mediastinal blood loss

volume, even when levels were within or above the normal reference range. Fibrinogen levels obviously modulate postoperative blood loss after CPB surgery [18]. However, when we look at studies that consider the relationship to be independent, it would be more accurate to evaluate fibrinogen in the preoperative period individually. It would incorrect to infer that patients with low fibrinogen alone are prone to bleeding events. Importantly, there are many variables here. Notably, cardiac surgery is a dynamic process. The patient's plasma cells, clotting factors, and the concentrations of both fibrinogen and other clotting factors in the plasma may affect these processes [21].

In our study, the rate of revision due to bleeding events during the postoperative period was 5.2% in the HighFib group. This value was significantly higher than that of the LowFib group ($p = 0.014$). Considering the difference here, the reason may be the decrease in antithrombin, which is an anticoagulant factor, and clotting factors during CPB. Our study also revealed that bleeding events are not only related to the fibrinogen level.

Studies have shown that fibrinogen is an inflammatory marker that increases with inflammation during CPB [7] and that off-pump surgery reduces the inflammatory response. Therefore, studies have shown that fibrinogen levels increase less in off-pump surgery [22]. In our study,



Variables	AUC	P value	% Confidence Interval	
			Lower Bound	Upper Bound
STS score	0.592	0.186	0.456	0.727
Euroscore	0.664	0.018	0.541	0.787
Fibrinogen	0.598	0.157	0.464	0.732

Fig. 1. ROC Curve and different risk scores and fibrinogen levels for predicting major adverse events after cardiac surgery.

there was no difference in postoperative mortality between the two different groups in terms of only fibrinogen level and no difference in other preoperative inflammatory parameters. However, atrial fibrillation more common in the HighFib group in patients with different values for fibrinogen but the same CPB time and the same cross-clamp time ($p = 0.042$).

Scoring systems such as the Euroscore and STS score have been used for many years to predict perioperative mortality associated with cardiac surgery [3–6]. In addition to these scoring systems, the EuroSCORE II has also started to be used. In some studies, the EuroSCORE II was not only superior to the EuroSCORE and STS score but also provided a very realistic estimate of mortality associated with aortic

valve replacement [23]. When the scores were compared in patients who underwent coronary artery bypass surgery, the Euroscore and STS score calculated the mortality risk more correctly than the Euroscore II did [24]. Therefore, it would be more appropriate to use the Euroscore for patients undergoing CABG. In our study, the Euroscore and STS score were good indicators for predicting hospital complications. In addition, fibrinogen values were also significant in predicting risk ($p = 0.035$).

In clinical practice, cardiac surgery risk models regarding the use of fibrinogen generally include factors such as age, gender, renal function, and pulmonary hypertension. Fibrinogen levels can be added as a hemostatic risk factor, allowing for a more precise estimation of postopera-

tive complication risks. Its use in perioperative care should be simple, and monitoring fibrinogen levels before, during, and after surgery may be critical for bleeding management. Low fibrinogen levels in preoperative significance are an indicator that requires particular attention, as they increase the risk of bleeding before surgery. Fibrinogen replacement can be started before surgery in these patients. Intraoperative management, fibrinogen levels may decrease rapidly during major cardiac surgery. Fibrinogen replacement should be considered using fresh frozen plasma (FFP), cryoprecipitate, or fibrinogen concentrates. Fibrinogen replacement can be optimized using coagulation tests such as ROTEM or TEG. Low fibrinogen levels in the postoperative period may be a sign of bleeding or the need for re-surgical intervention. Postoperative fibrinogen levels can be monitored for effective management of bleeding and fibrinogen supplementation can be administered if necessary. Various laboratory methods (such as the Clauss method) are used to measure fibrinogen levels. In addition, fibrinogen levels and function can be rapidly assessed intraoperatively with tests such as ROTEM/TEG. These tests may be critical during surgery to guide clinical decisions.

Limitation

This study was planned retrospectively and was conducted in a single center. Fibrinogen levels were not measured during the perioperative or postoperative periods. Additionally, other coagulant factors were not evaluated. All patients who underwent cardiac surgery were included in the study. It is not classified according to specific surgical procedures. Due to the limited number of patients, statistical differences were observed in some demographic characteristics between the groups on both sides of the fibrinogen cut-off value. The lack of propensity score matching is one of the statistical limitations of the study.

Conclusion

Low or high fibrinogen levels are not directly related to bleeding events. When evaluated alone, fibrinogen is not an indicator of bleeding after cardiac surgery. When we look at postoperative complications, the fibrinogen level as well as the Euroscore and the STS score may be predictors. Prospective studies will contribute more to the literature in the future.

Availability of Data and Materials

All authors declare the availability of data supporting the results or analyses presented in the article.

Author Contributions

BA, EET and MAY designed the research study. EET, DO, HO and MAY performed the research. DO and MAY analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The protocol of the study was approved by TC Firat University Non-Interventional Research Ethics Committee on 24.02.2022 (Approval Number: 2022/03-09). The study was conducted in accordance with the ethical principles set up in the Declaration of Helsinki and Good Clinical Practice Guidelines. Informed consent was obtained from all participants enrolled in this study.

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Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Adelborg K, Horváth-Puhó E, Schmidt M, Munch T, Pedersen L, Nielsen PH, *et al.* Thirty-Year Mortality After Coronary Artery Bypass Graft Surgery: A Danish Nationwide Population-Based Cohort Study. *Circulation. Cardiovascular Quality and Outcomes.* 2017; 10: e002708. <https://doi.org/10.1161/CIRCOUTCOMES.116.002708>
- [2] Park S, Nam K, Kim TK. Association Between Preoperative Fibrinogen-to-Albumin Ratio and All-Cause Mortality After Off-Pump Coronary Artery Bypass Grafting: A Retrospective Observational Study. *Anesthesia and Analgesia.* 2022; 134: 1021–1027. <https://doi.org/10.1213/ANE.0000000000005948>
- [3] Chalmers J, Pullan M, Fabri B, McShane J, Shaw M, Mediratta N, *et al.* Validation of EuroSCORE II in a modern cohort of patients undergoing cardiac surgery. *European Journal of Cardio-Thoracic Surgery.* 2013; 43: 688–694. <https://doi.org/10.1093/ejcts/ezs406>
- [4] Shahian DM, O'Brien SM, Filardo G, Ferraris VA, Haan CK, Rich JB, *et al.* The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1—coronary artery bypass grafting

- surgery. *The Annals of Thoracic Surgery*. 2009; 88: S2–S22. <https://doi.org/10.1016/j.athoracsur.2009.05.053>
- [5] O'Brien SM, Shahian DM, Filardo G, Ferraris VA, Haan CK, Rich JB, *et al*. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2—isolated valve surgery. *The Annals of Thoracic Surgery*. 2009; 88: S23–S42. <https://doi.org/10.1016/j.athoracsur.2009.05.056>
- [6] Shahian DM, O'Brien SM, Filardo G, Ferraris VA, Haan CK, Rich JB, *et al*. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 3—valve plus coronary artery bypass grafting surgery. *The Annals of Thoracic Surgery*. 2009; 88: S43–62. <https://doi.org/10.1016/j.athoracsur.2009.05.055>
- [7] Emerging Risk Factors Collaboration, Kaptoge S, Di Angelantonio E, Pennells L, Wood AM, White IR, *et al*. C-reactive protein, fibrinogen, and cardiovascular disease prediction. *The New England Journal of Medicine*. 2012; 367: 1310–1320. <https://doi.org/10.1056/NEJMoa1107477>
- [8] Szaba FM, Smiley ST. Roles for thrombin and fibrin(ogen) in cytokine/chemokine production and macrophage adhesion in vivo. *Blood*. 2002; 99: 1053–1059. <https://doi.org/10.1182/blood.v99.3.1053>
- [9] Dyke C, Aronson S, Dietrich W, Hofmann A, Karkouti K, Levi M, *et al*. Universal definition of perioperative bleeding in adult cardiac surgery. *The Journal of Thoracic and Cardiovascular Surgery*. 2014; 147: 1458–1463.e1. <https://doi.org/10.1016/j.jtcvs.2013.10.070>
- [10] Yang JJ, Lei WH, Hu P, Wu BB, Chen JX, Ni YM, *et al*. Preoperative Serum Fibrinogen is Associated With Acute Kidney Injury after Cardiac Valve Replacement Surgery. *Scientific Reports*. 2020; 10: 6403. <https://doi.org/10.1038/s41598-020-63522-6>
- [11] Ranucci M, Jeppsson A, Baryshnikova E. Pre-operative fibrinogen supplementation in cardiac surgery patients: an evaluation of different trigger values. *Acta Anaesthesiologica Scandinavica*. 2015; 59: 427–433.
- [12] Schisterman EF, Faraggi D, Reiser B, Hu J. Youden Index and the optimal threshold for markers with mass at zero. *Stat Med*. 2008; 30: 297–315. <https://doi.org/10.1002/sim.2993>
- [13] Ruopp MD, Perkins NJ, Whitcomb BW, Schisterman EF. Youden Index and optimal cut-point estimated from observations affected by a lower limit of detection. *Biometrical Journal*. 2008; 50: 419–430. <https://doi.org/10.1002/bimj.200710415>
- [14] Alagha S, Songur M, Avci T, Vural K, Kaplan S. Association of preoperative plasma fibrinogen level with postoperative bleeding after on-pump coronary bypass surgery: does plasma fibrinogen level affect the amount of postoperative bleeding? *Interactive Cardiovascular and Thoracic Surgery*. 2018; 27: 671–676. <https://doi.org/10.1093/icvts/ivy132>
- [15] Li B, Tan B, Chen C, Zhao L, Qin L. Is preoperative fibrinogen really not associated with blood transfusion? *The Annals of Thoracic Surgery*. 2014; 98: 1142–1143. <https://doi.org/10.1016/j.athoracsur.2014.04.019>
- [16] Fricault P, Piot J, Estève C, Savan V, Sebesteyn A, Durand M, *et al*. Preoperative fibrinogen level and postcardiac surgery morbidity and mortality rates. *Annals of Cardiac Anaesthesia*. 2022; 25: 485–489. https://doi.org/10.4103/aca.aca_103_21
- [17] Karlsson M, Ternström L, Hyllner M, Baghaei F, Nilsson S, Jeppsson A. Plasma fibrinogen level, bleeding, and transfusion after on-pump coronary artery bypass grafting surgery: a prospective observational study. *Transfusion*. 2008; 48: 2152–2158. <https://doi.org/10.1111/j.1537-2995.2008.01827.x>
- [18] Blome M, Isgro F, Kiessling AH, Skuras J, Haubelt H, Hellstern P, *et al*. Relationship between factor XIII activity, fibrinogen, haemostasis screening tests and postoperative bleeding in cardiopulmonary bypass surgery. *Thrombosis and Haemostasis*. 2005; 93: 1101–1107. <https://doi.org/10.1160/TH04-12-0799>
- [19] Liu G, McNicol PL, McCall PR, Bellomo R, Connellan J, McInnes F, *et al*. Prediction of the mediastinal drainage after coronary artery bypass surgery. *Anaesthesia and Intensive Care*. 2000; 28: 420–426. <https://doi.org/10.1177/0310057X0002800411>
- [20] Karlsson M, Ternström L, Hyllner M, Baghaei F, Flinck A, Skrtic S, *et al*. Prophylactic fibrinogen infusion reduces bleeding after coronary artery bypass surgery. A prospective randomised pilot study. *Thrombosis and Haemostasis*. 2009; 102: 137–144. <https://doi.org/10.1160/TH08-09-0587>
- [21] Erdoes G, Gerster G, Colucci G, Kaiser H, Alberio L, Eberle B. Prediction of Post-Weaning Fibrinogen Status during Cardiopulmonary Bypass: An Observational Study in 110 Patients. *PloS One*. 2015; 10: e0126692. <https://doi.org/10.1371/journal.pone.0126692>
- [22] Aljassim O, Karlsson M, Wiklund L, Jeppsson A, Olsson P, Berglin E. Inflammatory response and platelet activation after off-pump coronary artery bypass surgery. *Scandinavian Cardiovascular Journal*. 2006; 40: 43–48. <https://doi.org/10.1080/14017430500381307>
- [23] Holinski S, Jessen S, Neumann K, Konertz W. Predictive Power and Implication of EuroSCORE, EuroSCORE II and STS Score for Isolated Repeated Aortic Valve Replacement. *Annals of Thoracic and Cardiovascular Surgery*. 2015; 21: 242–246. <https://doi.org/10.5761/atcs.0a.14-00100>
- [24] Kunt AG, Kurtcepe M, Hidiröglü 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. *Interactive Cardiovascular and Thoracic Surgery*. 2013; 16: 625–629. <https://doi.org/10.1093/icvts/ivt022>