RESEARCH ARTICLE / ARAŞTIRMA MAKALESİ

DOI: 10.4274/atfm.galenos.2023.93899
Ankara Üniversitesi Tıp Fakültesi Mecmuası 2023;76(3):265-270

SURGICAL MEDICAL SCIENCES / CERRAHİ TIP BİLİMLERİ

Early Postoperative Thrombocytopenia Following Cardiac Surgery

Kardiyak Cerrahi Sonrası Erken Postoperatif Trombositopeni

Gülen Sezer Alptekin[1], Orkut Güçlü[2], Serhat Hüseyin[2], Volkan Yüksel[2], Suat Canbaz[2], Turan Ege[3]

[1]Kütahya University Faculty of Medicine, Department of Cardiovascular Surgery, Kütahya, Türkiye
[2]Trakya University Faculty of Medicine, Department of Cardiovascular Surgery, Edirne, Türkiye
[3]Kırklareli Medikent Hospital, Clinic of Cardiovascular Surgery, Kırklareli, Türkiye

Abstract

Objectives: There are various risk factors which make the cardiac surgery patients prone to thrombocytopenia such as the effects of cardiopulmonary bypass procedure, anticoagulant administration, bleeding diathesis, blood product transfusions and hypothermia. However the clinical and prognostic value of early thrombocytopenia soon after cardiac surgery is less studied previously and is the objective of our study.

Materials and Methods: In this cross-sectional study we evaluated cardiac surgery patients who were operated within 6 months period in our hospital electively. Thrombocytopenia was defined as a platelet count under 150,000/µL. The peroperative variables, prognostic scores according to the Sequential Organ Failure Assesment (SOFA), length of stay, mortality and adverse events during hospital stay were investigated.

Results: Thrombocytopenia was observed in 33.05% of all patients. The mean cross-clamping time was prolonged and the total mediastinal drainage volume was excessive in thrombocytopenia group. All-cause infection, pulmonary and renal dysfunction rates were higher, SOFA scores were increasing at 24th and 48th hours, and length of stay in hospital and intensive care unit were prolonged in this group.

Conclusion: Thrombocytopenia may be associated with multiple organ dysfunction and further infections; and may be regarded as a remarkable finding of poor prognosis and prolonged length of stay after cardiac surgery in early period. Hemorrhage and prolonged cross clamping time are the significant risk factors associated with thrombocytopenia in our study. Therefore an appropriate hemostatic approach and brief cross clamping time may be considered as preventive strategies to reduce thrombocytopenia following cardiac surgery.

Key Words: Thrombocytopenia, Coronary Artery Bypass, Postoperative Thrombocytopenia, Postoperative Prognosis

Öz

Amaç: Kardiyopulmoner baypas prosedürünün etkileri, antikoagülan uygulanması, kanama diyatezi, kan ürünü transfüzyonu ve hipotermi gibi çeşitli risk faktörleri kalp cerrahisi hastalarını trombositopeniye yatkın hale getirmektedir. Kalp cerrahisi sonrası erken trombositopeninin klinik ve prognostik önemi ise önceki çalışmalarda daha az incelenmiştir ve çalışmamızın temel konusunu oluşturmaktadır.

Gereç ve Yöntem: Bu kesitsel çalışmada 6 ay içerisinde hastanemizde elektif olarak kalp cerrahisi uygulanan hastalar incelendi. Trombosit sayısının 150.000/µL altında olması trombositopeni olarak kabul edildi. Peroperatif değişkenler, Ardışık Organ Yetmezliği Değerlendirmesi'ne (SOFA) göre prognostik skorlar, yatış süresi, hastane yatışı sırasındaki mortalite ve ek olaylar incelendi.

Bulgular: Hastaların %33,05'inde trombositopeni görüldü. Trombositopeni grubunda ortalama kros klemp süresi uzamış ve toplam mediastinal drenaj miktarı artmıştı. Bu grupta tüm nedenlere bağlı enfeksiyonlar, pulmoner ve renal disfonksiyon oranları fazla, SOFA skorları 24. ve 48. saatlerde yüksek, yoğun bakım ve hastane yatış süreleri daha uzun olmuştu.

Sonuç: Kalp cerrahisi sonrası erken dönemde trombositopeninin, multiorgan yetmezliği, gelişebilecek enfeksiyonlar, kötü prognoz ve uzamış yatış süresiyle ilişkili olabileceği gözlenmiştir. Çalışmamızda kanama ve uzamış kros klemp süresinin trombositopeniyle ilişkili anlamlı risk faktörleri olduğu saptanmıştır. Bu nedenle uygun hemostatik yaklaşım ve kros klemp süresinin kısa tutulmasının kalp cerrahisi sonrası trombositopeniyi azaltabilecek önlemler olabileceğini düşünmekteyiz.

Anahtar Kelimeler: Trombositopeni, Koroner Baypas, Postoperatif Trombositopeni, Postoperatif Prognoz

Yazışma Adresi/Address for Correspondence: Gülen Sezer Alptekin, Kütahya University Faculty of Medicine, Department of Cardiovascular Surgery, Kütahya, Türkiye
Tel.: +90 536 718 60 05 **E-posta:** gsezeralptekin@hotmail.com **ORCID ID:** orcid.org/0000-0003-2838-7828
Geliş Tarihi/Received: 22.09.2022 **Kabul Tarihi/Accepted:** 20.09.2023

Introduction

Platelets are strongly affected by cardiopulmonary bypass (CPB) using a pumpoxygenator (1). Hypothermia, anticoagulant administration and hemorrhage are many of the other risk factors for thrombocytopenia (TP) after cardiac surgery (2). Even among patients undergoing off-pump coronary artery bypass surgery, evidence of platelet dysfunction or lower platelet counts after surgical intervention were also noted (3). The incidence of TP is about 35% among high-risk surgical patients and it reaches to 65% among cardiac surgery patients (4). Herein we aimed to investigate the clinical and prognostic value of early TP after cardiac surgery.

Materials and Methods

Design of the Study

The patients who underwent cardiac surgery electively in six-months period between February and August 2013, in our institute were enrolled to this cross sectional study. The blood samples were obtained from the patients at 12th, 36th and 60th hours postoperatively according to our daily practice. The patients who had platelet count under 150,000/μL were enrolled to TP group. The control group were selected randomly as the same number of patients with TP group among the patients with normal platelet count. The complete blood cell analyses were performed with the same machine for all samples. The variables were compared between the TP and control groups. Exclusion criteria were preoperative TP, any disease which may lead to TP such as malignancy, age under 18 and urgent operations. The antiplatelet therapy was discontinued five days before surgery.

The study was approved by the local Ethics Commitee (TUTF-GOKAEK 2013/21).

Surgical Technique

All patients were operated via a median sternotomy incision under general anesthesia and underwent CPB procedure. In routine, the left internal thoracic artery was preferred for revascularization of the left anterior descending artery, double clamp technique was used for proximal anastomosis and normothermic cardiac arrest was applied among the coronary artery bypass graft (CABG) surgery patients whereas mild hypothermic (32-34 ^{o}C) and moderate hypothermic (28-32 ^{o}C) cardiac arrest was applied in valve replacement and aortic procedures respectively. Mechanical prosthesis were used for valve replacement.

Postoperative Evaluation

TP was defined as a platelet count <150,000/μL and was classified as mild (i.e. 100,000/μL to 149,000 /μL), moderate (i.e. 50,000/μL to 99,999/μL) and severe (i.e. <50,000/μL) (4-8). The patients were evaluated postoperatively according to the Sequential Organ Failure Assesment (SOFA) as a prognostic scoring system (9). 4Ts scoring test was performed to evaluate heparin induced TP (HIT) (4,10). The platelet replacement was administered postoperatively to the patients with excessive drainage and TP with platelet count under 100,000/μL (2). Informed consent was obtained from all individual participants included in the study.

Statistical Analysis

Statistical analysis was performed by using a Statistical Package For Social Sciences (SPSS) version 21. Once tested for the normality of distrubition of continuous variables by one sample Kolmogorov-Smirnov test, a t-test was applied following normal distrubition and Mann-Whitney U test was done for comparing the data with no specific distribution. Categorical variables were analyzed through Pearson χ^2 test, Fisher's exact χ^2 test and Kolmogorov-Smirnov two sample test. Descriptive data were defined as median (minimum-maximum) and arithmetic mean ± standard deviation. For all statistical tests p-values <0.05 were considered to be significant.

Results

Of 118 patients who were operated electively between February 2013 and August 2013 in our department, 39 developed TP (33.05%). Among the rest of the patients, 39 were randomly selected for control group. A total of 78 patients were enrolled to this study. Of 78 patients included in the study, 62.8% (n=49) were male and 37.2% (n=29) were female. The mean age was 61.82 (26-80). The mean platelet count was 115,580/μL (38,000-140,000/μL) among TP group. When the TP group was classified, 30 patients had mild (i.e. 100,000/μL to 149,000/μL), 7 patients had moderate (i.e. 50,000/μL to 99,999/μL), and 2 patients had severe (i.e. <50,000/μL) TP. None of the patients had score above low probability according to the 4Ts score.

The operations performed are reported on Table 1.

The preoperative and demographic data were not significantly different between the two groups.

The duration of CPB time was 112.58±43.39 minutes and 92.46±26.48 minutes (p=0.052) whereas the aortic cross-clamping time was 66.08±31.29 minutes and 50.59±19.37 minutes in TP and control groups respectively (p=0.034) (Figure 1). There was no significant difference between the two groups when we compared the hypothermia level, the volume of cardioplegic solution and the amount of heparine and protamine doses administered. The mediastinal drainage was increased in TP group (p=0.002) (Table 2). The unit of replaced fresh frozen plasma was significantly higher in TP group (p=0.001) (Figure 2).

Table 1: Operations performed

	Control (n%)	TP (n%)	Total (n%)
Isolated CABG	29 (74.4)	26 (66.7)	55 (70.5)
AVR	4 (10.3)	1 (2.6)	5 (6.4)
CABG + AVR	2 (5.1)	2 (5.1)	4 (5.1)
CABG + MVR	2 (5.1)	4 (10.3)	6 (7.7)
MVR + Tricuspid annuloplasty	1 (2.6)	0 (0.0)	1 (1.3)
CABG + CEA	1 (2.6)	0 (0.0)	1 (1.3)
Bentall procedure	0 (0.0)	2 (5.1)	2 (2.6)
Replacement of ascending aorta+ AVR + CABG	0 (0.0)	2 (5.1)	2 (2.6)
Mixoma resection + Mitral valve repair	0 (0.0)	1 (2.6)	1 (1.3)
CABG + VSR Repair	0 (0.0)	1 (2.6)	1 (1.3)

CABG: Coronary artery bypass graft, AVR: Aortic valve replacement, MVR: Mitral valve replacement, VSR: Ventricular septal rupture, CEA: Carotid endarterectomy, TP: Thrombocytopenia

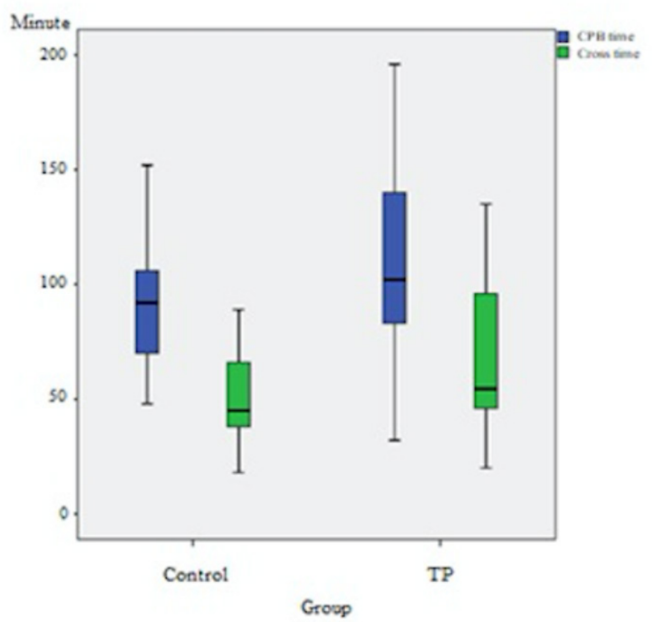

Figure 1: Cardiopulmonary bypass and aortic cross clamping times of TP and the control group

CPB: Cardiopulmonary bypass, TP: Thrombocytopenia

Table 2: The mediastinal drainage volumes in control and thrombocytopenia group

	Control (n=39) A. Mean ± SD Mean (Min.-Max.)	TP (n=39) A. Mean ± SD Mean (Min.-Max.)	p-value
Drainage (mL)	744.87±319.65 725 (300-1825)	1216.03±843.03 975 (375-3925)	0.002*

*: Mann-Whitney U test
TP: Thrombocytopenia, SD: Standard deviation, Min.-Max.: Minimum-maximum

SOFA scores were not significantly different between the groups at 12th hour whereas the 24th and the 48th hour scores were higher in TP group (p=0.137; p=0.001; p=0.001 respectively) (Figure 3).

The infection rates were increased in TP group (p=0.005) non-referred to the origin. The pulmonary (paO_2/FiO_2<200) and renal (creatinin >1.8 mg/dL or urine output <1000 mL/day) dysfunction rates were higher in TP group (p=0.006, p=0.038 respectively).

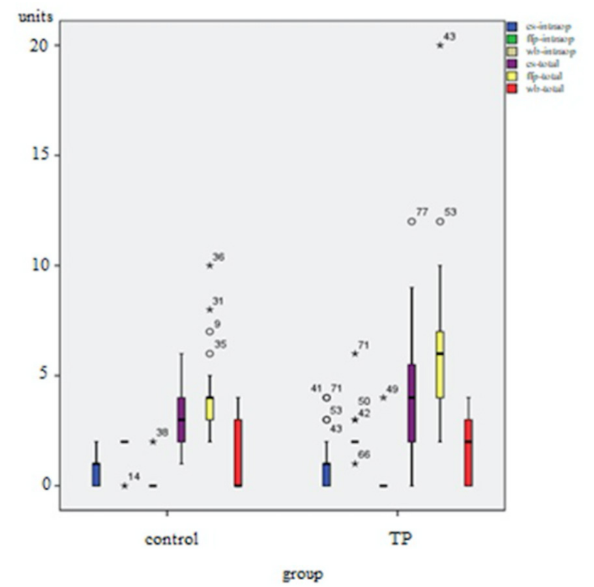

Figure 2: The distribution of the transfused blood products in both groups intraoperatively and in total.

TP: Thrombocytopenia, es: erythrocyte suspension, ffp: fresh frozen plasma, wb: whole blood

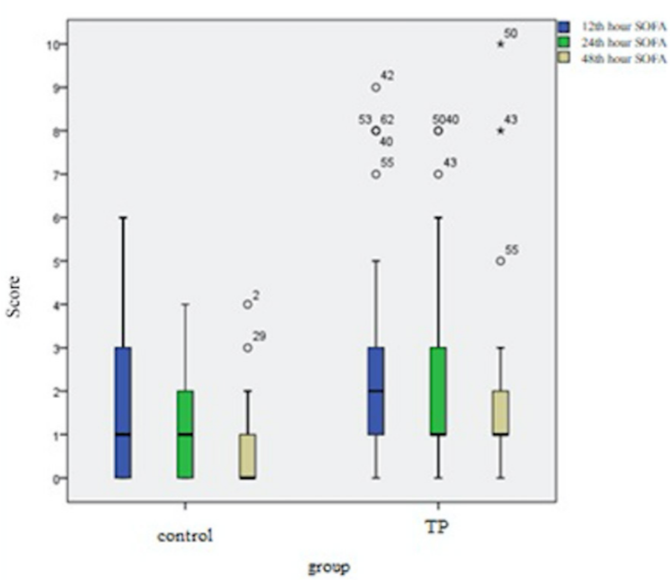

Figure 3: The distribution of the SOFA scores of the groups at the 12th, 24th, 48th hours

TP: Thrombocytopenia, SOFA: Sequential Organ Failure Assesment

Reexploration for hemorrhage was 2.6% in control group and 10.3% in TP group (p=0.358). The length of stay for hospital and intensive care unit were increased in TP group (respectively p=0.006; p=0.030) (Figure 4). All in hospital mortality rate was 2.6% in control group whereas it was 12.8% in TP group (p=0.200).

Discussion

TP after CPB was reported to be associated with increased postoperative mortality, infection, stroke rates and prolonged intensive care unit and hospital length of stay (8). Herein we investigated that the infection rates were increased in TP group, non-referred to the origin (p=0.005). Beside of an important role in hemostasis, platelets also play a relevant function in inflammation acting as proinflammatory cells (11). TP occurs in over 50% of patients with septic shock (12). Platelet mitochondrial membrane depolarization reflects disease severity in patients with sepsis and correlates with clinical outcome (13). Serial platelet monitoring may help identify patients at higher risk of postoperative complications such as infections.

In our findings pulmonary dysfunction was more often in TP group (p=0,006). TP is associated with an increased risk of acute respiratory distress syndrome (ARDS) and platelet count in combination with ARDS had a high predictive value for patient mortality (14). The pulmonary vasculature likely offers ideal shear and turbulence to promote individual platelet shedding from megakaryocytes and proplatelets (15). Accordingly the high TP incidence may be considered as related with respiratory failure in our study. The renal dysfunction rate was also higher in TP group (p=0.038) in our study. Platelet activation and

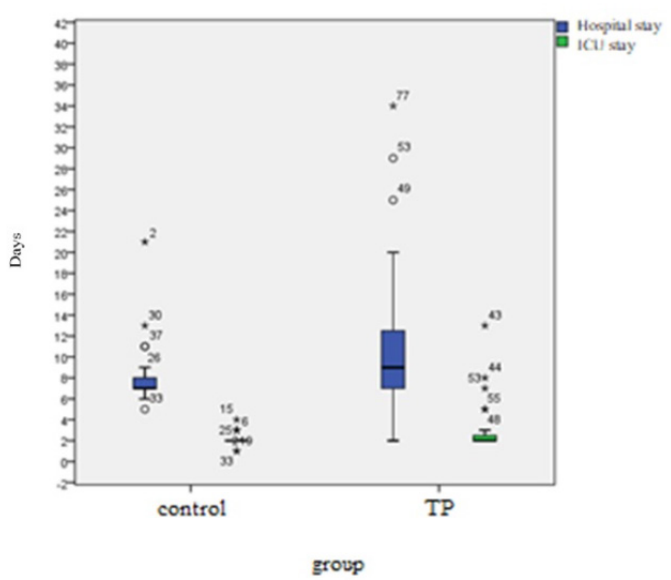

Figure 4: The length of stay in hospital and ICU in both group

TP: Thrombocytopenia, ICU: Intensive care unit

leukocyte inflammatory responses are important mediators of vascular microthrombosis and ischemic injury (16). The hemostatic balance during and after surgery may shift toward a hypercoagulable state and contribute to acute organ failure. The multiorgan failure concomitant with TP may be associated with the underappreciated microthrombosis after cardiac surgery (16). The limited use of perioperative antiplatelet therapy because of a culture of fear of bleeding, may be considered to be responsible for the issue (16).

TP is reported to reflect a physiologic imbalance and is accepted as an independent risk factor for poor outcome in patients who were supported with extracorporeal membrane oxygenation after cardiac surgery (17). Zhong et al. (18) developed a promising software model to realize and improve prognosis in ICU after open heart surgery. Patients who underwent coronary artery bypass surgery, aortic valve replacement, or other heart-related surgeries between 2001 and 2012 were analyzed and platelet count appeared to be an important predictor for outcomes (18). Early predicting comorbidities for critically ill patients after cardiac surgery is vital for patients' prognosis and doctors' decision making (18).

In our findings the mediastinal drainage (p=0.002) and the unit of replaced fresh frozen plasma (p=0.001) was higher in TP group. For its content of coagulant factors, fresh frozen plasma is often preferred to provide hemostasis in our daily practice. However the blood product transfusion is an independent risk factor of high mortality (2). The reexploration on time to prevent massive blood transfusion is important. The surgical hemostasis is vital as well as the hemostatic procedures administered in ICU so are (2).

Among our peroperative findings, the aortic cross-clamping time was longer in TP group (p=0.034) which also involves patients who were operated for more complicated surgeries such as aortic surgery. In recent data, combined cardiac surgeries were associated with higher requirement of platelet transfusion postoperatively (19). Further studies investigating strategies to reduce postoperative TP including reducing CPB time are recommended (8). Additionally cross-clamping time is significantly related with TP in our study.

Cardiovascular dysfunction is better related to outcome with the SOFA score than with the MODS (20). Using the cardiovascular components, outcome prediction was better for the SOFA score at all time intervals in our study. SOFA is applicable to cardiac surgery patients without any modification requirement (9). Accordingly we performed SOFA scoring system for postoperative risk assesment in our study. SOFA scores were not significant between the groups at 12^{th} hour whereas the scores were significantly higher in TP group at 24^{th} and 48^{th} hours (respectively p=0.137; p=0.001; p=0.001). Herein, platelet count, which is also a parameter of SOFA score, was also accomplished alone to predict poor outcome following cardiac surgery.

Although TP was not confirmed to be related significantly with mortality in our study, a higher number of patients who died in hospital were involved in TP group. A total of 30% decline in platelet count is related to mortality in many studies even if it is not under 150,000/µL (21-24).

Concomitant surgical procedures, red blood cell transfusion of >3 units were reported to be associated with prolonged hospital length of stay (25). TP is associated with prolonged lenght of stay both in hospital and intensive care unit following cardiac surgery (respectively p=0.030; p=0.006).

Hemorrhage and prolonged cross clamping time are the significant risk factors associated with TP in our study. Appropriate hemostatic approach begins preoperatively and lasts during intraoperative and postoperative processes (26,27). Principally it should be noted here that an optimal intraoperative surgical hemostasis even during exploration is substantial. To our opinion, an adequate side branch and leakage control, minimizing the tissue damage during the whole operation and spending enough time for bleeding control are considered to be the basic principles.

Optimal temperature, acidity level and appropriate heparin monitoring are some other hemostatic approaches which are called as coagulation-friendly enviroment, although these were not significant variables in our study as were managed in optimal levels in our surgical routine (26).

Minimally invasive extracorporeal circulation, autologous priming, ultrafiltration, cell salvage are some of the technical modifications and supportive methods for blood management (26).

As it is aferomentioned, longer CPB time decrease postoperative platelet count and function (27). Particularly, longer cross clamping time is associated with TP in our study. It was demonstrated that higher cross clamping leads to higher cardioplegia which may result in hemodilution and also platelet dysfunction (26). There are many options to avoid excessive cross-clamping time. On-pump beating heart and off-pump procedures may be beneficial to avoid unfavorable effects of cross-clamping on blood contents (26). Performing proximal anastomosis under side clamping, as double aortic clamping, may be considered as another procedural technique for reducing cross-clamping time (28).

Study Limitations

It was demonstrated that there are safe time limits of aortic cross clamping and CPB time in adult cardiac surgery (28). Consequently a complete or an incomplete revascularization for non-main branches in coronary bypass grafting, is a recent debate. Clinical features would rather influence the choice of a complete or an incomplete revascularization strategy in selected patient categories (29). Although it seems assertive, an incomplete revascularization that skips the non-main branches may be an option particularly when it has to be performed concomitantly with other complicated cardiac procedures and in selected patients to avoid excessive cross clampig time.

Conclusion

In conclusion, early TP may be associated with multiple organ dysfunction and infection; and may be regarded as a remarkable finding of poor prognosis and prolonged length of stay after cardiac surgery. We consider that daily platelet count evaluation in early period following cardiac surgery is an easy and applicable method for assessment of prognosis. Therefore an appropriate hemostatic approach and cross clamping time may be considered as preventive strategies to reduce TP and avoid its causations and consequences, following cardiac surgery.

Acknowledgement

The authors would like to thank F. Nesrin TURAN for her assistance in statistical analysis.

Ethics

Ethics Committee Approval: The study was approved by the local Ethics Commitee (TUTF-GOKAEK 2013/21).

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.S.A., O.G., S.H., V.Y., S.C., T.E., Concept: G.S.A., T.E., Design: G.S.A., T.E., Data Collection and Processing: G.S.A., O.G., S.H., V.Y., S.C., T.E., Analysis or Interpretation: G.S.A., T.E., Literature Search: G.S.A., O.G., T.E., Writing: G.S.A., O.G., S.H., V.Y., S.C., T.E.

Conflict of Interest: The authors declared that there was no conflict of interest during the preparation and publication of this article.

Financial Disclosure: This research received no specific grant from any funding agency or the public, commercial, or not-for-profit sectors.

References

1. Kirklin/Barrett-Boyes Cardiac Surgery. Hypothermia, Circulatory Arrest, and Cardiopulmonary Bypass. 4th ed. 2013. p. 90.
2. Bojar RM. Manual of Perioperative Care in Adult Cardiac Surgery. 5th ed. Wiley Blackwell: 2011;345-383.

3. Ballotta A, Saleh HZ, El Baghdady HW, et al. Comparison of early platelet activation in patients undergoing on-pump versus off-pump coronary artery bypass surgery. J Thorac Cardiovasc Surg. 2007;134:132-138.
4. Rezende E, Morais G, Silva Junior JM, et al. Thrombocytopenia in cardiac surgery: diagnostic and prognostic importance. Rev Bras Cir Cardiovasc. 2011;26:47-53.
5. Erkurt MA, Kaya E, Berbera I, et al. Thrombocytopenia in Adults: Review Article.J Hematol. 2012;1:44-53.
6. Marco-Schulke CM, Sánchez-Casado M, Hortigüela-Martín VA, et al. Trombocitopenia grave al ingreso en una unidad de cuidados intensivos en pacientes con disfunción multiorgánica [Severe thrombocytopenia on admission to the intensive care unit in patients with multiple organ failure]. Med Intensiva. 2012;36:185-192.
7. Jiménez-Zarazúa O, González-Carrillo PL, Vélez-Ramírez LN, et al. Survival in septic shock associated with thrombocytopenia. Heart Lung. 2021;50:268-276.
8. Griffin BR, Bronsert M, Reece TB, et al. Thrombocytopenia After Cardiopulmonary Bypass Is Associated With Increased Morbidity and Mortality. Ann Thorac Surg. 2020;110:50-57.
9. Ceriani R, Mazzoni M, Bortone F, et al. Application of the sequential organ failure assessment score to cardiac surgical patients. Chest. 2003;123:1229-1239.
10. Warkentin TE. Heparin-induced thrombocytopenia in the ICU: a transatlantic perspective. Chest. 2012;142:815-816.
11. Margetic S. Inflammation and haemostasis. Biochem Med (Zagreb). 2012;22:49-62.
12. Wang HL, Aguilera C, Knopf KB, et al. Thrombocytopenia in the intensive care unit. J Intensive Care Med. 2013;28:268-280.
13. Gründler K, Angstwurm M, Hilge R, et al. Platelet mitochondrial membrane depolarization reflects disease severity in patients with sepsis and correlates with clinical outcome. Crit Care. 2014;18:R31.
14. Wang T, Liu Z, Wang Z, et al. Thrombocytopenia is associated with acute respiratory distress syndrome mortality: an international study. PLoS One. 2014;9:e94124.
15. Lefrançais E, Looney MR. Platelet Biogenesis in the Lung Circulation. Physiology (Bethesda). 2019;34:392-401.
16. Raso Vasquez AO, Kertai MD, Fontes ML. Postoperative thrombocytopenia: why you should consider antiplatelet therapy? Curr Opin Anaesthesiol. 2018;31:61-66.
17. Opfermann P, Bevilacqua M, Felli A, et al. Prognostic Impact of Persistent Thrombocytopenia During Extracorporeal Membrane Oxygenation: A Retrospective Analysis of Prospectively Collected Data From a Cohort of Patients With Left Ventricular Dysfunction After Cardiac Surgery. Crit Care Med. 2016;44:e1208-e1218.
18. Zhong Z, Yuan X, Liu S, et al. Machine learning prediction models for prognosis of critically ill patients after open-heart surgery. Sci Rep. 2021;11:3384.
19. Yanagawa B, Ribeiro R, Lee J, et al. Platelet Transfusion in Cardiac Surgery: A Systematic Review and Meta-Analysis. Ann Thorac Surg. 2021;111:607-614.
20. Peres Bota D, Melot C, Lopes Ferreira F, et al. The Multiple Organ Dysfunction Score (MODS) versus the Sequential Organ Failure Assessment (SOFA) score in outcome prediction. Intensive Care Med. 2002;28:1619-1624.
21. Selleng S, Malowsky B, Strobel U, et al. Early-onset and persisting thrombocytopenia in post-cardiac surgery patients is rarely due to heparin-induced thrombocytopenia, even when antibody tests are positive. J Thromb Haemost. 2010;8:30-36.
22. Moreau D, Timsit JF, Vesin A, et al. Platelet count decline: an early prognostic marker in critically ill patients with prolonged ICU stays. Chest. 2007;131:1735-1741.
23. Olmez I, Zafar M, Shahid M, et al. Analysis of significant decrease in platelet count and thrombocytopenia, graded according to NCI-CTC, as prognostic risk markers for mortality and morbidity. J Pediatr Hematol Oncol. 2011;33:585-588.
24. Vanderschueren S, De Weerdt A, Malbrain M, et al. Thrombocytopenia and prognosis in intensive care. Crit Care Med. 2000;28:1871-1876.
25. Galas FR, Almeida JP, Fukushima JT, et al. Blood transfusion in cardiac surgery is a risk factor for increased hospital length of stay in adult patients. J Cardiothorac Surg. 2013;8:54.
26. Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA); Boer C, Meesters MI, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth. 2018;32:88-120.
27. Faggian G, Bernabei A, Tropea I, et al. Hemostasis during cardiopulmonary bypass. In: Kirali K, Coselli JS, Kalangos A editors. Cardiopulmonary Bypass. Academic Press; 2023. p. 295-309.
28. Nissinen J, Biancari F, Wistbacka JO, et al. Safe time limits of aortic cross-clamping and cardiopulmonary bypass in adult cardiac surgery. Perfusion. 2009;24:297-305.
29. Zimarino M, Calafiore AM, De Caterina R. Complete myocardial revascularization: between myth and reality. Eur Heart J. 2005;26:1824-1830.