ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ

ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ

ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ

Πρόγραμμα Μεταπτυχιακών Σπουδών (ΠΜΣ)

«Μεθοδολογία Βιοϊατρικής Έρευνας, Βιοστατιστική και Κλινική Βιοπληροφορική»

ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΕΤΟΣ 2021-22

Biomarkers and extracorporeal circulation as predictors of complications in cardiac surgery patients: a retrospective study.

Ο ρόλος των βιοδεικτών και της εξωσωματικής κυκλοφορίας στην πρόβλεψη επιπλοκών σε ασθενείς που υποβάλλονται σε καρδιοχειρουργικές επεμβάσεις: αναδρομική μελέτη.

ΑΝΝΑ ΓΚΙΟΥΛΙΑΒΑ

ΜΕΤΑΠΤΥΧΙΑΚΗ ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

Τριμελής Συμβουλευτική Επιτροπή

Δοξάνη Χρυσούλα

Αργυριάδου Ελένη

Ζιντζαράς Ηλίας

ΥΠΟΒΛΗΘΗΚΕ ΣΕΠΤΕΜΒΡΙΟ 2022

Table of contents

Abstract

Background

Biomarkers are increasingly used in cardiac surgery to predict morbidity and mortality in view of improving patient outcome. Minimal Invasive Extracorporeal Circulation (MiECC) has emerged as a promising perioperative strategy that minimizes disruption in perfusion and microcirculation over Conventional Extracorporeal Circulation (CECC).

Aim

Our aim is to investigate the role of biomarkers and extracorporeal circulation (EC) on the occurrence of adverse events in cardiac surgery.

Materials and Methods

The medical records of one hundred cardiac surgery patients were retrieved to equally represent MiECC(n=50) and CECC(n=50) patients. Demographic data, perioperative data including hemoglobin, Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte ratio, cardiopulmonary bypass duration, 12h drainage and transfusions were recorded. The presence of event was set as atrial fibrillation, myocardial infarction, stroke, need for revascularization, stage 3 acute kidney injury, prolonged ventilation or death occurring 30 days postoperatively.

Results

EC was found to be an independent predictor of adverse events following cardiac surgery. MiECC Patients had 60% lower risk of developing any complication (p=0.039, CI95% 0.18-0.9, AUC 0.61). Baseline parameters did not differ between MiECC and CECC patients.

Conclusion

EC is an independent predictor of adverse events in cardiac surgery when the perioperative strategy is also taken into account in regression models.

Keywords: biomarkers, cardiac surgery, extracorporeal circulation

Περίληψη

Εισαγωγή

Οι βιοδείκτες χρησιμοποιούνται συχνά για την πρόβλεψη νοσητότητας και θνητότητας στις καρδιοχειρουργικές επεμβάσεις με σκοπό τη βελτίωση της έκβασης των ασθενών. Η Ελάχιστα Επεμβατική Εξωσωματική Κυκλοφορία (ΕΕΕΚ) συνιστά υποσχόμενη διεγχειρητική στρατηγική που περιορίζει τη διαταραχή της μικροκυκλοφορίας σε σχέση με τη Συμβατική Εξωσωματική Κυκλοφορία (ΣΕΚ).

Στόχοι

Η διερεύνηση της επίδρασης τόσο των βιοδιεκτών όσο και της εξωσωματικής κυκλοφορίας (ΕΚ) στην εμφάνιση ανεπιθύμητων συμβάντων.

Μέθοδοι

Οι ιατρικοί φάκελοι 100 καρδιοχειρουργικών ασθενών συγκεντρώθηκαν με αντιπροσώπευση ισότιμα της ΕΕΕΚ(n=50) και της ΣΕΚ(n=50). Δημογραφικά και περιεγχειρητικά δεδομένα που περιελάμβαναν, την αιμοσφαιρίνη, τον Δείκτη Ουδετεροφίλων-Λεμφοκυττάρων, τον Δείκτη Αιμοπεταλίων-Λεμφοκυττάρων, τη διάρκεια εξωσωματικής κυκλοφορίας, τη μετεγχειρητική αιμορραφία και τις μεταγγίσεις καταγράφηκαν. Η σύνθετη μεταβλητή συμβάν ορίστηκε από την εμφάνιση κολπικής μαρμαρυγής, εμφράγματος μυοκαρδίου, εγκεφαλικού επεισοδίου, ανάγκης επαναιμάτωσης, στάδιου 3 νεφρική βλάβη, παρατεταμένου μηχανικού αερισμού ή θανάτου εντός 30 ημερών.

Αποτελέσματα

Η ΕΚ αποδείχθηκε ανεξάρτητος παράγοντας εμφάνισης ανεπιθύμητων συμβάντων. Ασθενείς της ΕΕΕΚ είχαν 60% χαμηλότερο κίνδυνο ($p=0.039$, CI95% 0.18-0.9, AUC 0.61). Από την ανάλυση σε ομάδες, δεν προκύπτει διαφορά στις προεγχειρητικές παραμέτρους.

Συμπέρασμα

Η ΕΚ αποδείχθηκε ανεξάρτητος προγνωστικός παράγοντας εμφάνισης ανεπιθύμητων συμβάντων σε καρδιοχειρουργικές επεμβάσεις.

Λέξεις-κλειδιά: βιοδείκτες, καρδιοχειρουργική επέμβαση, εξωσωματική κυκλοφορία

Introduction

According to the World Health Organization cardiovascular disease affects about 17.9 million people(1). Cardiopulmonary bypass (CPB) was developed in 1953 and marked the open-heart surgery era(2). Since then, advances in surgical technique, anaesthesia and intensive care management as well as CPB technology markedly improved clinical outcomes(3). However, cardiac surgery is still hampered by considerable morbidity and subsequent mortality, especially in complex procedures(4).

The European System for Cardiac Operative Risk Evaluation (EuroSCORE) is a logistic model used to predict mortality in cardiac surgery. The model merges patient, operation and specific cardiac related factors to estimate the risk of in hospital mortality(5). Meanwhile, full blood count is routinely used in the perioperative setting as part of the standard patient care. Anemia is a common finding in the preoperative setting affecting as much as 30% of patients and predisposes to adverse outcomes(6). In addition to this, combining two subpopulations of white blood cells has provided researchers and clinicians with an inexpensive, readily available index not only in cardiovascular patients but also cancer and autoimmune diseases(7–10)(11–13). The Neutrophil to Lymphocyte Ratio (NLR) is derived after dividing the absolute count of neutrophils to lymphocytes. The NLR represents the interaction between the innate and adaptive immune system and has been employed to estimate the degree of systemic inflammation and stress(7). Neutrophils are a major determinant of inflammation while lymphocytes are recognized as the regulators of these pathologic pathways and lymphopenia has been linked with increased morbidity after cardiovascular events(14). This interplay has also set the Platelet to Lymphocyte Ratio (PLR) as another potential tool of adverse outcomes in cardiac surgery patients. Looking into the PLR, platelets through the secretion of chemokines, growth factors and thromboxanes coordinate both inflammation and coagulation pathways(15).

Undoubtedly, the core triggers for postoperative morbidity and mortality are the inevitable pathophysiologic effects from the use of CPB. During Conventional Extracorporeal Circulation (CECC), which is still used in the majority of cardiac surgeries, surgical trauma, ischemia reperfusion injury and blood contact activation all add to coagulation disorders and inflammatory processes(2). However, contemporary advancements in CPB in line with applied cardiovascular physiology have led to the evolution of Minimal Invasive Extracorporeal Circulation (MiECC)(16). MiECC is emerging as a more ‘physiologic’ strategy, translated into improved end-organ protection, which depicts in its clinical benefits observed in multiple clinical trials and meta-analyses(17).

Even though many biomarkers have been investigated in cardiac surgery studies, no research has been conducted regarding their role when questioning the perioperative strategy applied during the operation. Taking into consideration the aforementioned, our aim is to describe the effect of MiECC or CECC in the occurrence of such events.

Materials and Methods

The medical records of patients who underwent cardiac surgery from January 2020 to July 2022 at the Cardiothoracic department of the University Hospital of AHEPA were retrieved after approval of the Institutional Review Board. All patients were adults scheduled for elective cardiac surgery. At total, 100 patients were selected to match the inclusion criteria. Patients were operated by the same surgical team under minimal invasive extracorporeal circulation or conventional CPB.

Anaesthesia

All patients had the same anaesthesia and perfusion team. All patients received a standardized anaesthetic protocol. General anaesthesia was induced with 3μg/kg fentanyl and 2–3 mg/kg propofol. Tracheal intubation was facilitated with 1 mg/kg rocuronium, which was also employed for intraoperative neuromuscular blockade as necessary. Perioperatively, anaesthesia and analgesia were maintained with Target-Controlled Infusion of propofol and remifentanil. Propofol was targeted to achieve a bispectral index of 40–45. All patients were monitored with near infrared spectroscopy for cerebral oximetry during the entire procedure. A dose of 15 mg/kg body weight tranexamic acid was given following induction of anaesthesia and after protamine administration in all patients. Antibiotic chemoprophylaxis was injected in every case. Weaning off form CPB, protamine was administered to reverse heparin action in a 0.75:1 ratio.

Surgical technique

Surgery was performed using a standard technique via median sternotomy. Surgery was generally performed under normothermia in CPB except in cases of aortic surgery. Transfusion-trigger of RBC was defined as hemoglobin value <8.0 g/dL.

CECC

An open bypass circuit, the Maquet HL 20 heart lung machine, consisting of uncoated PVC tubing, a hard-shell venous reservoir and a microporous membrane oxygenator (Affinity Fusion, Medtronic) was used. The circuit was primed with 1500 mL of a balanced crystalloid/colloid solution (1000 mL of Ringer's solution, 200 mL of mannitol 20% and 7500 IU unfractionated heparin. The ACT target was 480s.

MiECC

According to the Anastasiadis et al classification, a type IV modular Medtronic MiECC circuit was used in all cases. The ACT target was set at 300s for Coronary Artery Bypass Grafting (CABG) and 400s for all other cases. The prime solution consisted of 800 ml Ringer's Lactated, 200 mL of mannitol 20% and 7500 IU unfractionated heparin. In-line monitoring of metabolic parameters (System M, Spectrum Medical, FortMill, SC,USA) were continuously evaluated to achieve goal directed perfusion according to the institution's protocol(16).

Primary and secondary outcomes

The primary outcome was the event which was a composite of postoperative major adverse cardiac and cerebrovascular events, specifically: atrial fibrillation, myocardial infarction, stroke, need for repeat revascularization, stage 3 acute renal injury according to AKIN criteria(18), prolonged > 48 hours need for mechanical ventilation, death during the first 30 days postoperatively. Demographic data and pre-existing diseases were noted and the EuroSCORE was calculated. Blood for a full blood count was collected preoperatively and upon arrival at the ICU as a standard procedure in all cases. Hb, NLR, PLR, CPB duration were recorded along with postoperative bleeding at 12 hours, blood product transfusion, re-exploration for bleeding and total length of hospital stay. The total sample was divided in two Groups, MiECC and CECC as appropriate.

Statistical analysis

Continuous variables are presented as mean ± SD or medians and interquartile range depending on their distribution. Assessment of normality was performed though P-P, Q-Q diagrams and the Kolmogorov-Smirnov and Shapiro-Wilk tests. Categorical variables were summarized as absolute values and percentages. The independent samples t Test or the Mann- Whitney U test was used for between group comparisons of continuous data. For pairwise comparisons of proportions, the Chi-square or Fisher's exact test were used for pairwise comparisons of proportions, as appropriate, along with their 95% CIs were calculated. The degree of association between two variables was tested with the correlation coefficient. Partial correlation was used to control for the effect of Group. Logistic regression (backward, by likelihood ratios) was performed for the outcome of event, atrial fibrillation and event except for atrial fibrillation. Potential predictors included EuroSCORE; preoperative and postoperative values of Hb, NLR, PLR; CPB duration and Group marked as a categorical variable. For the model produced by logistic regression, predicted probabilities were used for the assessment of the accuracy, expressed by Receiver Operating Characteristics (ROC) curve and area under the curve (AUC). In all the above tests, a p-value of <0.05 was considered significant.

Classification and Regression Tree (CART)

Furthermore, a machine learning algorithm namely the Classification and Regression Tree (CART) was employed, in order to develop a predictive model for the occurrence of events including AF. Hb, Ht, NLR, PLR, CPB and Group were used as potential predictive factors and were included in the development of the regression tree. Accuracy was calculated using the confusion matrix of the test and predicted data.

The analyses were performed on SPSS (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.) and open source software R 4.2.1 (The R Foundation for Statistical Computing).

Results

One hundred patients were recorded overall. Patients were recorded to conform with the aforementioned perioperative strategy and were operated by the same surgical team.

Patients' characteristics and demographic data are provided in Table 1. Detailed statistical analysis is presented in the Appendix. Baseline conditions were similar among patients within each group as no statistically significant differences were detected.

	MiECC (n=50)	CECC (n=50)	p value
Age, years	65.7±10	65.6±9.6	>0.05
Male:Female, n, %	36,72%:14,28%	35,70%:15,30%	>0.05
Isolated CABG AVR MVR Complex surgery	27, 54% 11, 22% 2, 4% 10, 20%	24, 48% 16, 32% 5, 10% 5, 10%	>0.05
BMI, kg/m^2	28.1±4.7	28.6±5.4	>0.05
Euroscore, %	0.95, 0.71	0.93, 0.57	>0.05

Table 1. Patients' characteristics. Categorical data are presented as absolute values and frequencies. Continuous data are presented in mean±SD or median, IQR depending on the distribution of data. P value denotes statistical difference between groups. Independent samples T test, Mann-Whitney U test and chi-square test were used as appropriate.

Preoperative NLR and PLR values were calculated for all patients. Perioperative data including Hb, CPB and aortic cross clamp duration, intraoperative crystalloid infusion, chest tube drainage at 12 hours, Universal definition for perioperative bleeding class (UDPB) and the composite outcome of event were also recorded and processed (Table 2). Preoperative biomarkers' values did not differ between groups (p.0.05).

	MiECC (n=50)	CECC (n=50)	p value
Preoperative hemoglobin, mg/dl	13.5±1.6	13.4±1.5	>0.05
Postoperative hemoglobin, mg/dl	10.8±1.3	10.3±1.3	0.048
Preoperative platelet count, $10^3/mm^3$	237±66	237±72	>0.05
Postoperative platelet count, $10^3/mm^3$	202±66	189±68	>0.05
CPB duration, min	85±23	101±27	0.003
Aortic cross clamp duration, min	61±22	69±18	0.057
Intraoperative crystalloid infusion, ml	2340±714	3448±888	<0.001
UDPB Class 0 1 2 3	 39, 78% 7, 14% 3, 6% 1, 2%	 28, 59.6% 11, 23.4% 7, 14.9% 1, 2.1%	>0.05
Preoperative NLR	2.7, 1.6	2.6, 1.01	>0.05
Preoperative PLR	109, 63	109, 59	>0.05
Postoperative NLR	6.2, 6	6.1, 5.3	>0.05
Postoperative PLR	80, 106	96, 88	>0.05
Length of stay	11.3, 4	13.8, 6	0.002

Table 2. Perioperative data between the two Groups. Continuous data are presented in mean±SD or median, IQR depending on the distribution of data. P value denotes statistical difference between groups. Independent samples T test, Mann-Whitney U test and chi-square test were used as appropriate.

	MiECC (n=50)	CECC (n=50)	Chi-square test
Atrial fibrillation	12, 24%	16, 33%	>0.05
Postoperative Myocardial Infarction	0	1, 2%	>0.05
Stroke	1, 2%	2, 4%	>0.05
Need for revascularization	0	1, 2%	>0.05
Stage 3 AKI	1, 2%	2, 4%	>0.05
Prolonged mechanical ventilation	2, 4%	6, 12%	>0.05
Death	0	4, 8%	0.041
Event	13, 26%	23, 46%	0.037

Table 3. Outcomes between the two groups. Chi-square test was used to test for significant differences.

For the composite outcome event difference between frequencies among the two groups was significant, p =0.037.

Preoperative NLR or PLR were not associated with the EuroSCORE value or the 12h chest tube drainage. As for postoperative NLR or PLR, neither was associated with the 12h chest tube drainage or CPB duration. Controlling for Group and testing postoperative NLR and CPB duration, the partial correlation is significant (r=0.2, p= 0.04). Length of stay was significantly shorter for MiECC patients (Table 2).

Group, Euroscore, preoperative and postoperative Hb, CPB duration along with the NLR and PLR perioperative data were included in the logistic regression analysis for the binary outcome of event. The model results in Group being the only independent predictor of event (p=0.039, 95%CI 0.18-0.9). The possibility of event in patients undergoing cardiac surgery under MiECC is 60% less compared to CECC (the detailed steps are provided in the Appendix). After building a ROC curve with the predicted probabilities, the Area Under the Curve is 0.61 (Figure 7). After, computing for a variable Event_noaf, which comprises of all events except for AF, the variable Group is marginally not significant as a predictor (p=0.06, Table 35).

The CART for the binary outcome of the prediction of AF providing the GROUP and preoperative hemoglobin, NLR and PLR results in a model with 0.75 accuracy

(Figure1). Preoperative hemoglobin is the sole contributor to the model. The same model testing for the occurrence of event is characterised by an accuracy of 0.56 (Figure 2).

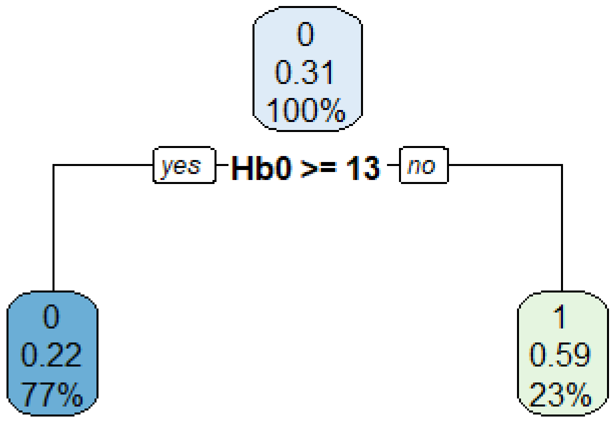

Figure 1. AF Classification Tree. Each leaf shows the probability of occurrence (equals 1) and the percentage denotes the patients included.

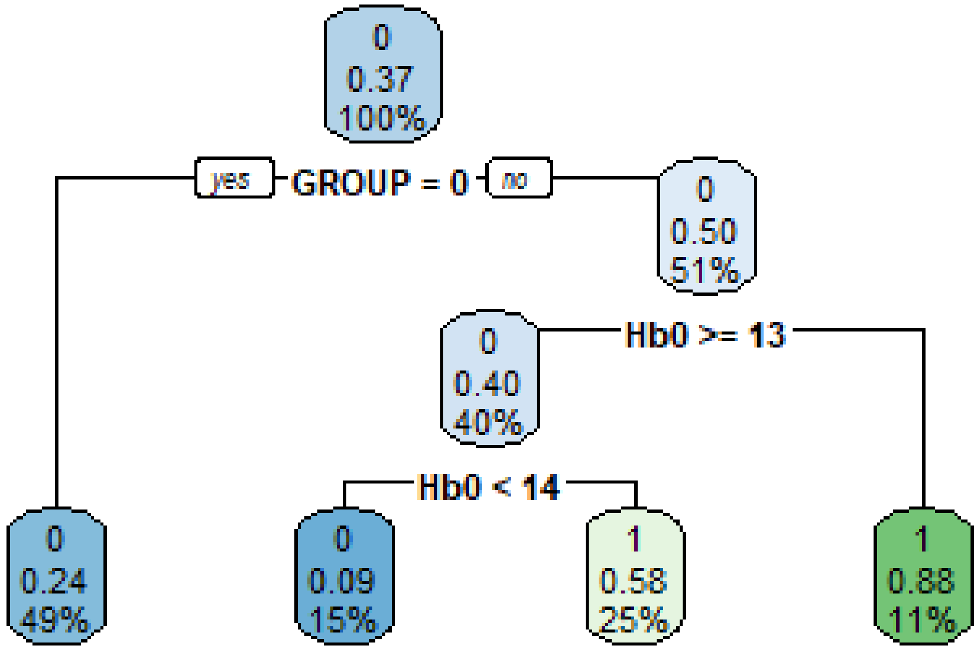

Figure 2. Event Classification Tree. Each leaf shows the probability of occurrence (equals 1) and the percentage denotes the patients included, MIECC is coded as Group equals 0.

Discussion

In this retrospective study, we found that undergoing cardiac surgery under MiECC is associated with a lower risk of developing an adverse event. The perioperative data of 100 patients undergoing all case mix cardiac surgery were collected along with short term outcomes of morbidity and mortality.

Regarding Hb, anemia has been identified in the literature as an index of complications pertaining to its impact on perfusion and the subsequent risk of transfusion, especially in CECC cases where hemodilution is unavoidable(19)(20). In our study, Hb was not significantly related to adverse outcomes in the logistic regression model. The classification tree of event in which it is the second contributor after MiECC, is of relatively low accuracy to allow for conclusions.

The NLR was also investigated as it has evolved as a valuable prognostic tool in cardiac surgery. Specifically, in a recent meta-analysis of over 13000 patients, elevated NLR was proved to be linked with both short- and long-term mortality(11). Furthermore, Tan et al performed a systematic review of patients undergoing CABG and found that both preoperative and postoperative NLR was accompanied with both increased atrial fibrillation occurrence and all-cause mortality(21). Currently, there is no meta-analysis over the role of PLR in cardiac surgery, although in cases of patients with acute coronary events it has been correlated with both morbidity and mortality indices(22). Based on our dataset, neither NLR nor PLR proved to be predictive of adverse outcomes.

The research question that triggered our hypothesis are the reported studies of the integrity of physiology during MiECC. Less blood air interaction, coated circuits and shorter connecting lines are all factors that limit inflammation in MiECC compared to CECC(23). Another core attribute is the reduced hemodilution as compared to CECC(24). These promising characteristics urged the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic

Anaesthesiology (EACTA) to support the use of MiECC into the Patient Blood Management Guidelines (Grade IIa) to reduce perioperative transfusions(25).

Overall, through this study we proved that the effect of the perioperative strategy may have a significant impact in postoperative outcomes and should be incorporated in future reviews or clinical trials looking into prediction tools. The retrospective design and sample size may have limited the identification of the other biomarkers, especially Hb. However, stratification of recruited patients may delineate the role of biomarkers before their integration in everyday clinical practice. Generalizing prediction models without taking into account all possible modifiers may lead to false results and disorientate clinicians. Parallel to this, MiECC should be the focus of upcoming studies to validate its clinical advantages in patient outcome and expand its implementation.

In conclusion, extracorporeal circulation is found to be an independent predictor of adverse outcomes in cardiac surgery.

References

1. WHO. Cardiovascular diseases (CVDs) Fact sheet [Internet]. Cardiovascular diseases. 2021 [cited 2022 Aug 26]. Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

2. Edmunds LH. Cardiopulmonary bypass after 50 years. N Engl J Med. 2004 Oct;351(16):1603–6.

3. Anastasiadis K, Argiriadou H, Deliopoulos A, Antonitsis P. Minimal invasive extracorporeal circulation (MiECC): the state-of-the-art in perfusion. Vol. 11, Journal of thoracic disease. 2019. p. S1507–14.

4. D'Agostino RS, Jacobs JP, Badhwar V, Fernandez FG, Paone G, Wormuth DW, et al. The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2019 Update on Outcomes and Quality. Ann Thorac Surg [Internet]. 2019;107(1):24–32. Available from: https://doi.org/10.1016/j.athoracsur.2018.10.004

5. Nashef SAM, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. EuroSCORE II†. Eur J Cardio-Thoracic Surg [Internet]. 2012 Apr 1;41(4):734–45. Available from: https://doi.org/10.1093/ejcts/ezs043

6. Miceli A, Romeo F, Glauber M, de Siena PM, Caputo M, Angelini GD. Preoperative anemia increases mortality and postoperative morbidity after cardiac surgery. J Cardiothorac Surg [Internet]. 2014;9(1):9050. Available from: https://doi.org/10.1186/1749-8090-9-137

7. Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. Bratisl Lek Listy [Internet]. 2021;122(7):474–88. Available from: https://europepmc.org/article/med/34161115

8. Josse JM, Cleghorn MC, Ramji KM, Jiang H, Elnahas A, Jackson TD, et al. The neutrophil-to-lymphocyte ratio predicts major perioperative complications in patients undergoing colorectal surgery. Color Dis. 2016;18(7).

9. Yoshida T, Kinoshita H, Yoshida K, Mishima T, Yanishi M, Komai Y, et al. Perioperative change in neutrophil-lymphocyte ratio predicts the overall survival of patients with bladder cancer undergoing radical cystectomy. Jpn J Clin Oncol. 2016;46(12).

10. Kubo T, Ono S, Ueno H, Shinto E, Yamamoto J, Hase K. Impact of the perioperative neutrophil-to-lymphocyte ratio on the long-term survival following an elective resection of colorectal carcinoma. Int J Colorectal Dis. 2014;29(9).

11. Perry LA, Liu Z, Loth J, Penny-Dimri JC, Plummer M, Segal R, et al. Perioperative Neutrophil-Lymphocyte Ratio Predicts Mortality After Cardiac Surgery: Systematic Review and Meta-Analysis. J Cardiothorac Vasc Anesth [Internet]. 2022;36(5):1296–303. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1053077021005735

12. Chung J, Bae J, Kwon Y, Yoon HK, Yoo S, Lee HJ, et al. Neutrophil/Lymphocyte Ratio in Patients Undergoing Noncardiac Surgery After Coronary Stent Implantation. J Cardiothorac Vasc Anesth. 2020;34(6).

13. Urbanowicz TK, Michalak M, Gąsecka A, Olasińska-Wiśniewska A, Perek B, Rodzki M, et al. A risk score for predicting long-term mortality following off-pump coronary artery bypass grafting. J Clin Med. 2021;10(14).

14. Azab B, Zaher M, Weiserbs KF, Torbey E, Lacossiere K, Gaddam S, et al. Usefulness of Neutrophil to Lymphocyte Ratio in Predicting Short- and Long-

Term Mortality After Non–ST-Elevation Myocardial Infarction. Am J Cardiol. 2010;106(4):470–6.

15. Larmann J, Handke J, Scholz AS, Dehne S, Arens C, Gillmann HJ, et al. Preoperative neutrophil to lymphocyte ratio and platelet to lymphocyte ratio are associated with major adverse cardiovascular and cerebrovascular events in coronary heart disease patients undergoing non-cardiac surgery. BMC Cardiovasc Disord. 2020;20(1).

16. Anastasiadis K, Murkin J, Antonitsis P, Bauer A, Ranucci M, Gygax E, et al. Use of minimal invasive extracorporeal circulation in cardiac surgery: principles, definitions and potential benefits. A position paper from the Minimal invasive Extra-Corporeal Technologies international Society (MiECTiS). Interact Cardiovasc Thorac Surg. 2016;22(5):647–62.

17. Anastasiadis K, Antonitsis P, Haidich A-B, Argiriadou H, Deliopoulos A, Papakonstantinou C. Use of minimal extracorporeal circulation improves outcome after heart surgery; a systematic review and meta-analysis of randomized controlled trials. Int J Cardiol. 2013 Apr;164(2):158–69.

18. Mehta RL, Kellum JA, Shah S V, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care [Internet]. 2007;11(2):R31. Available from: https://doi.org/10.1186/cc5713

19. Karkouti K, Wijeysundera DN, Beattie WS. Risk Associated With Preoperative Anemia in Cardiac Surgery. Circulation [Internet]. 2008 Jan 29;117(4):478–84. Available from: https://doi.org/10.1161/CIRCULATIONAHA.107.718353

20. Meybohm P, Westphal S, Ravn HB, Ranucci M, Agarwal S, Choorapoikayil S, et al. Perioperative Anemia Management as Part of PBM in Cardiac Surgery – A Narrative Updated Review. J Cardiothorac Vasc Anesth [Internet]. 2020;34(4):1060–73. Available from: https://www.sciencedirect.com/science/article/pii/S1053077019306391

21. Tan TP, Arekapudi A, Metha J, Prasad A, Venkatraghavan L. Neutrophil-lymphocyte ratio as predictor of mortality and morbidity in cardiovascular surgery: a systematic review. ANZ J Surg [Internet]. 2015;85(6):414–9.

Available from: https://onlinelibrary.wiley.com/doi/10.1111/ans.13036

22. Dong G, Huang A, Liu L. Platelet-to-lymphocyte ratio and prognosis in STEMI: A meta-analysis. Eur J Clin Invest [Internet]. 2021 Mar 1;51(3):e13386. Available from: https://doi.org/10.1111/eci.13386

23. Ranucci M, Balduini A, Ditta A, Boncilli A, Brozzi S. A systematic review of biocompatible cardiopulmonary bypass circuits and clinical outcome. Ann Thorac Surg. 2009 Apr;87(4):1311–9.

24. Yuruk K, Bezemer R, Euser M, Milstein DMJ, de Geus HHR, Scholten EW, et al. The effects of conventional extracorporeal circulation versus miniaturized extracorporeal circulation on microcirculation during cardiopulmonary bypass-assisted coronary artery bypass graft surgery. Interact Cardiovasc Thorac Surg. 2012 Sep;15(3):364–70.

25. Pagano D, Milojevic M, Meesters MI, Benedetto U, Bolliger D, von Heymann C, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. Eur J cardio-thoracic Surg Off J Eur Assoc Cardio-thoracic Surg. 2018 Jan;53(1):79–111.

Appendix

Descriptives

	GROUP			Statistic	Std. Error
age (years)	MiECC	Mean		65.71	1.441
		95% Confidence Interval for Mean	Lower Bound	62.82	
			Upper Bound	68.61	
		5% Trimmed Mean		66.06	
		Median		67.00	
		Variance		101.792	
		Std. Deviation		10.089	
		Minimum		43	
		Maximum		80	
		Range		37	

		Interquartile Range		19	
		Skewness		-.455	.340
		Kurtosis		-.830	.668
	CECC	Mean		65.64	1.434
		95% Confidence Interval for Mean	Lower Bound	62.75	
			Upper Bound	68.53	
		5% Trimmed Mean		66.07	
		Median		67.00	
		Variance		92.507	
		Std. Deviation		9.618	
		Minimum		43	
		Maximum		80	
		Range		37	
		Interquartile Range		13	
		Skewness		-.671	.354
		Kurtosis		-.146	.695
BMI (kg/m^2)	MiECC	Mean		28.1358	.68146
		95% Confidence Interval for Mean	Lower Bound	26.7656	
			Upper Bound	29.5060	
		5% Trimmed Mean		28.0003	
		Median		27.2817	
		Variance		22.755	
		Std. Deviation		4.77022	
		Minimum		20.06	
		Maximum		39.06	
		Range		19.00	
		Interquartile Range		5.91	
		Skewness		.493	.340
		Kurtosis		-.355	.668
	CECC	Mean		28.6065	.81270
		95% Confidence Interval for Mean	Lower Bound	26.9686	
			Upper Bound	30.2444	
		5% Trimmed Mean		28.2629	
		Median		28.0816	
		Variance		29.722	
		Std. Deviation		5.45177	
		Minimum		18.83	
		Maximum		48.83	
		Range		30.00	
		Interquartile Range		5.94	
		Skewness		1.212	.354

		Kurtosis		3.116	.695
Euroscore (%)	MiECC	Mean		1.0729	.10315
		95% Confidence Interval for Mean	Lower Bound	.8655	
			Upper Bound	1.2803	
		5% Trimmed Mean		.9726	
		Median		.9500	
		Variance		.521	
		Std. Deviation		.72206	
		Minimum		.50	
		Maximum		4.34	
		Range		3.84	
		Interquartile Range		.71	
		Skewness		2.561	.340
		Kurtosis		8.605	.668
	CECC	Mean		1.0278	.07241
		95% Confidence Interval for Mean	Lower Bound	.8818	
			Upper Bound	1.1737	
		5% Trimmed Mean		.9780	
		Median		.9300	
		Variance		.236	
		Std. Deviation		.48574	
		Minimum		.50	
		Maximum		2.62	
		Range		2.12	
		Interquartile Range		.57	
		Skewness		1.497	.354
		Kurtosis		2.457	.695
Preoperative hemoglobin (mg/dl)	MiECC	Mean		13.563	.2323
		95% Confidence Interval for Mean	Lower Bound	13.096	
			Upper Bound	14.030	
		5% Trimmed Mean		13.641	
		Median		13.700	
		Variance		2.645	
		Std. Deviation		1.6263	
		Minimum		9.6	
		Maximum		16.7	
		Range		7.1	
		Interquartile Range		2.1	
		Skewness		-.754	.340
		Kurtosis		.111	.668
	CECC	Mean		13.404	.2390

		95% Confidence Interval for Mean	Lower Bound	12.923	
			Upper Bound	13.886	
		5% Trimmed Mean		13.516	
		Median		13.600	
		Variance		2.570	
		Std. Deviation		1.6031	
		Minimum		8.1	
		Maximum		16.0	
		Range		7.9	
		Interquartile Range		2.0	
		Skewness		-1.114	.354
		Kurtosis		1.753	.695
Postoperative hemoglobin (mg/dl)	MiECC	Mean		10.829	.1845
		95% Confidence Interval for Mean	Lower Bound	10.458	
			Upper Bound	11.199	
		5% Trimmed Mean		10.813	
		Median		10.700	
		Variance		1.668	
		Std. Deviation		1.2913	
		Minimum		8.0	
		Maximum		14.0	
		Range		6.0	
		Interquartile Range		1.8	
		Skewness		.188	.340
		Kurtosis		-.241	.668
	CECC	Mean		10.373	.1979
		95% Confidence Interval for Mean	Lower Bound	9.975	
			Upper Bound	10.772	
		5% Trimmed Mean		10.390	
		Median		10.700	
		Variance		1.762	
		Std. Deviation		1.3272	
		Minimum		7.5	
		Maximum		13.5	
		Range		6.0	
		Interquartile Range		1.9	
		Skewness		-.285	.354
		Kurtosis		-.346	.695
Preoperative platelet count (10^3/mm^3)	MiECC	Mean		237.76	9.572
		95% Confidence Interval for Mean	Lower Bound	218.51	
			Upper Bound	257.00	

		5% Trimmed Mean		232.69	
		Median		236.00	
		Variance		4489.647	
		Std. Deviation		67.005	
		Minimum		141	
		Maximum		449	
		Range		308	
		Interquartile Range		85	
		Skewness		1.061	.340
		Kurtosis		1.646	.668
	CECC	Mean		245.22	10.714
		95% Confidence Interval for Mean	Lower Bound	223.63	
			Upper Bound	266.81	
		5% Trimmed Mean		246.00	
		Median		243.00	
		Variance		5165.268	
		Std. Deviation		71.870	
		Minimum		85	
		Maximum		372	
		Range		287	
		Interquartile Range		94	
		Skewness		-.037	.354
		Kurtosis		-.441	.695
Postoperative platelet count (10^3/mm^3)	MiECC	Mean		202.57	9.601
		95% Confidence Interval for Mean	Lower Bound	183.27	
			Upper Bound	221.88	
		5% Trimmed Mean		197.70	
		Median		194.00	
		Variance		4516.542	
		Std. Deviation		67.205	
		Minimum		83	
		Maximum		449	
		Range		366	
		Interquartile Range		70	
		Skewness		1.421	.340
		Kurtosis		3.222	.668
	CECC	Mean		194.76	10.302
		95% Confidence Interval for Mean	Lower Bound	173.99	
			Upper Bound	215.52	
		5% Trimmed Mean		193.27	
		Median		195.00	

		Variance		4776.098	
		Std. Deviation		69.109	
		Minimum		77	
		Maximum		338	
		Range		261	
		Interquartile Range		104	
		Skewness		.312	.354
		Kurtosis		-.506	.695
CPB duration (minutes)	MiECC	Mean		85.53	3.385
		95% Confidence Interval for Mean	Lower Bound	78.72	
			Upper Bound	92.34	
		5% Trimmed Mean		84.32	
		Median		84.00	
		Variance		561.504	
		Std. Deviation		23.696	
		Minimum		44	
		Maximum		169	
		Range		125	
		Interquartile Range		34	
		Skewness		.843	.340
		Kurtosis		2.092	.668
	CECC	Mean		100.24	4.220
		95% Confidence Interval for Mean	Lower Bound	91.74	
			Upper Bound	108.75	
		5% Trimmed Mean		100.04	
		Median		100.00	
		Variance		801.234	
		Std. Deviation		28.306	
		Minimum		29	
		Maximum		182	
		Range		153	
		Interquartile Range		34	
		Skewness		.191	.354
		Kurtosis		1.128	.695
Aortic cross clamp duration (minutes)	MiECC	Mean		61.29	3.192
		95% Confidence Interval for Mean	Lower Bound	54.87	
			Upper Bound	67.70	
		5% Trimmed Mean		59.83	
		Median		61.00	
		Variance		499.208	
		Std. Deviation		22.343	

		Minimum		27	
		Maximum		141	
		Range		114	
		Interquartile Range		27	
		Skewness		1.000	.340
		Kurtosis		2.256	.668
	CECC	Mean		67.93	2.846
		95% Confidence Interval for Mean	Lower Bound	62.20	
			Upper Bound	73.67	
		5% Trimmed Mean		67.94	
		Median		67.00	
		Variance		364.518	
		Std. Deviation		19.092	
		Minimum		18	
		Maximum		124	
		Range		106	
		Interquartile Range		22	
		Skewness		.192	.354
		Kurtosis		1.475	.695
Intraoperative crystalloid infusion (ml)	MiECC	Mean		2340.82	102.059
		95% Confidence Interval for Mean	Lower Bound	2135.61	
			Upper Bound	2546.02	
		5% Trimmed Mean		2311.22	
		Median		2000.00	
		Variance		510382.653	
		Std. Deviation		714.411	
		Minimum		1000	
		Maximum		4000	
		Range		3000	
		Interquartile Range		1000	
		Skewness		.691	.340
		Kurtosis		-.107	.668
	CECC	Mean		3448.89	132.521
		95% Confidence Interval for Mean	Lower Bound	3181.81	
			Upper Bound	3715.97	
		5% Trimmed Mean		3418.52	
		Median		3000.00	
		Variance		790282.828	
		Std. Deviation		888.979	
		Minimum		2000	
		Maximum		6000	

		Range		4000	
		Interquartile Range		1000	
		Skewness		.692	.354
		Kurtosis		.340	.695
12h chest tube drainage (ml)	MiECC	Mean		403.88	30.337
		95% Confidence Interval for Mean	Lower Bound	342.88	
			Upper Bound	464.87	
		5% Trimmed Mean		389.41	
		Median		380.00	
		Variance		45095.068	
		Std. Deviation		212.356	
		Minimum		80	
		Maximum		1140	
		Range		1060	
		Interquartile Range		250	
		Skewness		1.116	.340
		Kurtosis		1.979	.668
	CECC	Mean		420.00	35.458
		95% Confidence Interval for Mean	Lower Bound	348.54	
			Upper Bound	491.46	
		5% Trimmed Mean		396.67	
		Median		370.00	
		Variance		56577.273	
		Std. Deviation		237.860	
		Minimum		150	
		Maximum		1250	
		Range		1100	
		Interquartile Range		270	
		Skewness		1.595	.354
		Kurtosis		2.799	.695
Preoperative NLR	MiECC	Mean		2.7641	.20177
		95% Confidence Interval for Mean	Lower Bound	2.3584	
			Upper Bound	3.1698	
		5% Trimmed Mean		2.6524	
		Median		2.4855	
		Variance		1.995	
		Std. Deviation		1.41240	
		Minimum		.33	
		Maximum		7.08	
		Range		6.76	
		Interquartile Range		1.60	

		Skewness		1.261	.340
		Kurtosis		2.175	.668
	CECC	Mean		2.6020	.27857
		95% Confidence Interval for Mean	Lower Bound	2.0406	
			Upper Bound	3.1635	
		5% Trimmed Mean		2.3102	
		Median		2.3204	
		Variance		3.492	
		Std. Deviation		1.86872	
		Minimum		.94	
		Maximum		12.54	
		Range		11.60	
		Interquartile Range		1.01	
		Skewness		3.974	.354
		Kurtosis		19.056	.695
Preoperative PLR	MiECC	Mean		128.2104	9.82741
		95% Confidence Interval for Mean	Lower Bound	108.4511	
			Upper Bound	147.9698	
		5% Trimmed Mean		122.0499	
		Median		109.5745	
		Variance		4732.325	
		Std. Deviation		68.79189	
		Minimum		10.27	
		Maximum		404.50	
		Range		394.24	
		Interquartile Range		63.76	
		Skewness		1.787	.340
		Kurtosis		4.618	.668
	CECC	Mean		119.9683	7.96253
		95% Confidence Interval for Mean	Lower Bound	103.9209	
			Upper Bound	136.0158	
		5% Trimmed Mean		115.0662	
		Median		109.6234	
		Variance		2853.082	
		Std. Deviation		53.41425	
		Minimum		30.17	
		Maximum		379.10	
		Range		348.93	
		Interquartile Range		57.28	
		Skewness		2.682	.354

Kurtosis	12.009	.695

Table 4. Descriptive statistics of continuous variables between groups.

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	GROUP	Statistic	df	Sig.	Statistic	df	Sig.
age (years)	MiECC	.093	49	.200*	.946	49	.026
	CECC	.108	45	.200*	.950	45	.049
BMI (kg/m^2)	MiECC	.093	49	.200*	.963	49	.129
	CECC	.112	45	.198	.931	45	.010
Euroscore (%)	MiECC	.214	49	.000	.735	49	.000
	CECC	.151	45	.012	.863	45	.000
Preoperative hemoglobin (mg/dl)	MiECC	.120	49	.077	.940	49	.015
	CECC	.112	45	.193	.932	45	.011
Postoperative hemoglobin (mg/dl)	MiECC	.080	49	.200*	.988	49	.891
	CECC	.131	45	.053	.968	45	.253
Preoperative platelet count (10^3/mm^3)	MiECC	.090	49	.200*	.923	49	.003
	CECC	.061	45	.200*	.980	45	.608
Postoperative platelet count (10^3/mm^3)	MiECC	.124	49	.056	.904	49	.001
	CECC	.075	45	.200*	.968	45	.240
CPB duration (minutes)	MiECC	.080	49	.200*	.952	49	.043
	CECC	.076	45	.200*	.984	45	.799
Aortic cross clamp duration (minutes)	MiECC	.103	49	.200*	.935	49	.009
	CECC	.109	45	.200*	.974	45	.389
Intraoperative crystalloid infusion (ml)	MiECC	.316	49	.000	.864	49	.000
	CECC	.249	45	.000	.909	45	.002
12h chest tube drainage (ml)	MiECC	.109	49	.200*	.932	49	.008
	CECC	.161	45	.005	.855	45	.000
Preoperative NLR	MiECC	.129	49	.039	.909	49	.001
	CECC	.263	45	.000	.580	45	.000
Postoperative NLR	MiECC	.189	49	.000	.774	49	.000
	CECC	.126	45	.072	.888	45	.000
Preoperative PLR	MiECC	.195	49	.000	.848	49	.000
	CECC	.148	45	.015	.778	45	.000
Postoperative PLR	MiECC	.197	49	.000	.706	49	.000

CECC	.177	45	.001	.947	45	.040

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Table 5. Tests of normality.

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	.049[a]	1	.826	1.000	.500	
Continuity Correction[b]	.000	1	1.000			
Likelihood Ratio	.049	1	.826	1.000	.500	
Fisher's Exact Test				1.000	.500	
Linear-by-Linear Association	.048[c]	1	.826	1.000	.500	.170
N of Valid Cases	100					

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 14.50.

b. Computed only for a 2x2 table

c. The standardized statistic is .219.

Table 6. Chi-square test for the variable gender between groups

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	4.055[a]	3	.256	.276		
Likelihood Ratio	4.135	3	.247	.284		
Fisher's Exact Test	3.931			.280		
Linear-by-Linear Association	.137[b]	1	.712	.783	.391	.068
N of Valid Cases	100					

a. 2 cells (25.0%) have expected count less than 5. The minimum expected count is 3.50.

b. The standardized statistic is -.369.

Table 7. Chi-square test for the variable operation between groups.

Test Summary

Total N	99
Mann-Whitney U	1075.000
Wilcoxon W	2300.000
Test Statistic	1075.000
Standard Error	142.885
Standardized Test Statistic	-1.050
Asymptotic Sig.(2-sided test)	.294

Table 8. Independent-Samples Mann-Whitney U for the variable intraoperative crystalloid infusion

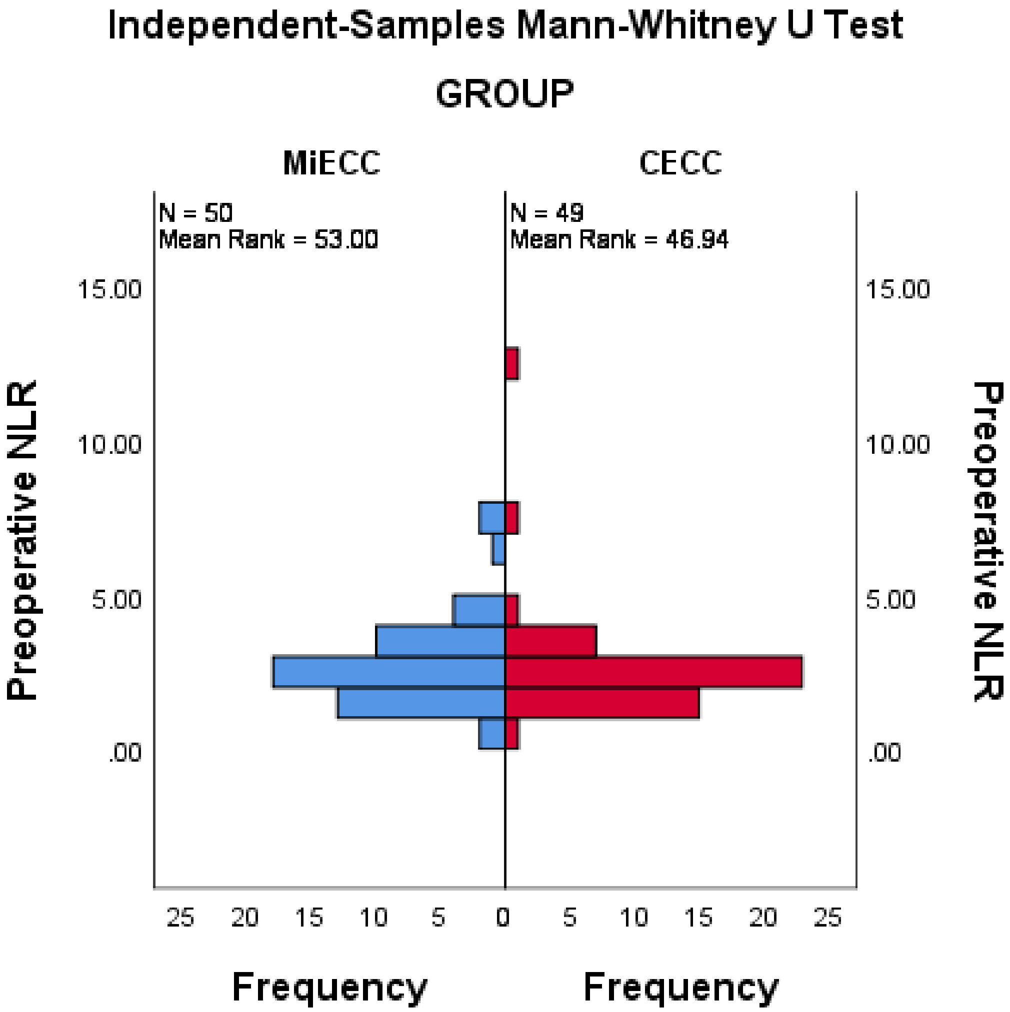

Figure 3. Independent-Samples Mann-Whitney U for the variable intraoperative crystalloid infusion. Graphic display.

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
age (years)	Equal variances assumed	.541	.464	-.317	98	.752	-.620	1.955	-4.500	3.260
	Equal variances not assumed			-.317	97.739	.752	-.620	1.955	-4.500	3.260
BMI (kg/m^2)	Equal variances assumed	.017	.895	-.444	98	.658	-.44629	1.00556	-2.44180	1.54922
	Equal variances not assumed			-.444	97.034	.658	-.44629	1.00556	-2.44204	1.54947
Preoperative hemoglobin (mg/dl)	Equal variances assumed	.131	.718	.313	98	.755	.1000	.3197	-.5344	.7344
	Equal variances not assumed			.313	97.874	.755	.1000	.3197	-.5344	.7344
Postoperative hemoglobin (mg/dl)	Equal variances assumed	.336	.564	2.000	97	.048	.5265	.2632	.0041	1.0489
	Equal variances not assumed			2.000	96.783	.048	.5265	.2633	.0039	1.0490
Preoperative platelet count (10^3/mm^3)	Equal variances assumed	1.202	.276	.033	98	.974	.460	13.932	-27.188	28.108
	Equal variances not assumed			.033	97.154	.974	.460	13.932	-27.191	28.111
Postoperative platelet count (10^3/mm^3)	Equal variances assumed	.999	.320	.948	97	.345	12.891	13.591	-14.083	39.864
	Equal variances not assumed			.948	96.735	.345	12.891	13.595	-14.093	39.874
CPB duration (minutes)	Equal variances assumed	.752	.388	-3.065	98	.003	-15.680	5.116	-25.833	-5.527
	Equal variances not assumed			-3.065	95.610	.003	-15.680	5.116	-25.836	-5.524
Aortic cross clamp duration (minutes)	Equal variances assumed	.833	.364	-1.923	98	.057	-7.920	4.118	-16.091	.251
	Equal variances not assumed			-1.923	95.591	.057	-7.920	4.118	-16.094	.254
12h chest tube drainage (ml)	Equal variances assumed	.138	.711	-.318	93	.751	-14.601	45.949	-105.847	76.645
	Equal variances not assumed			-.317	90.498	.752	-14.601	46.100	-106.180	76.979

Table 9. Independent Samples T Test of variable

Total N	99
Mann-Whitney U	1075.000
Wilcoxon W	2300.000
Test Statistic	1075.000
Standard Error	142.885
Standardized Test Statistic	-1.050
Asymptotic Sig.(2-sided test)	.294

Table 10. Independent-Samples Mann-Whitney U Test Summary for the variable preoperative NLR

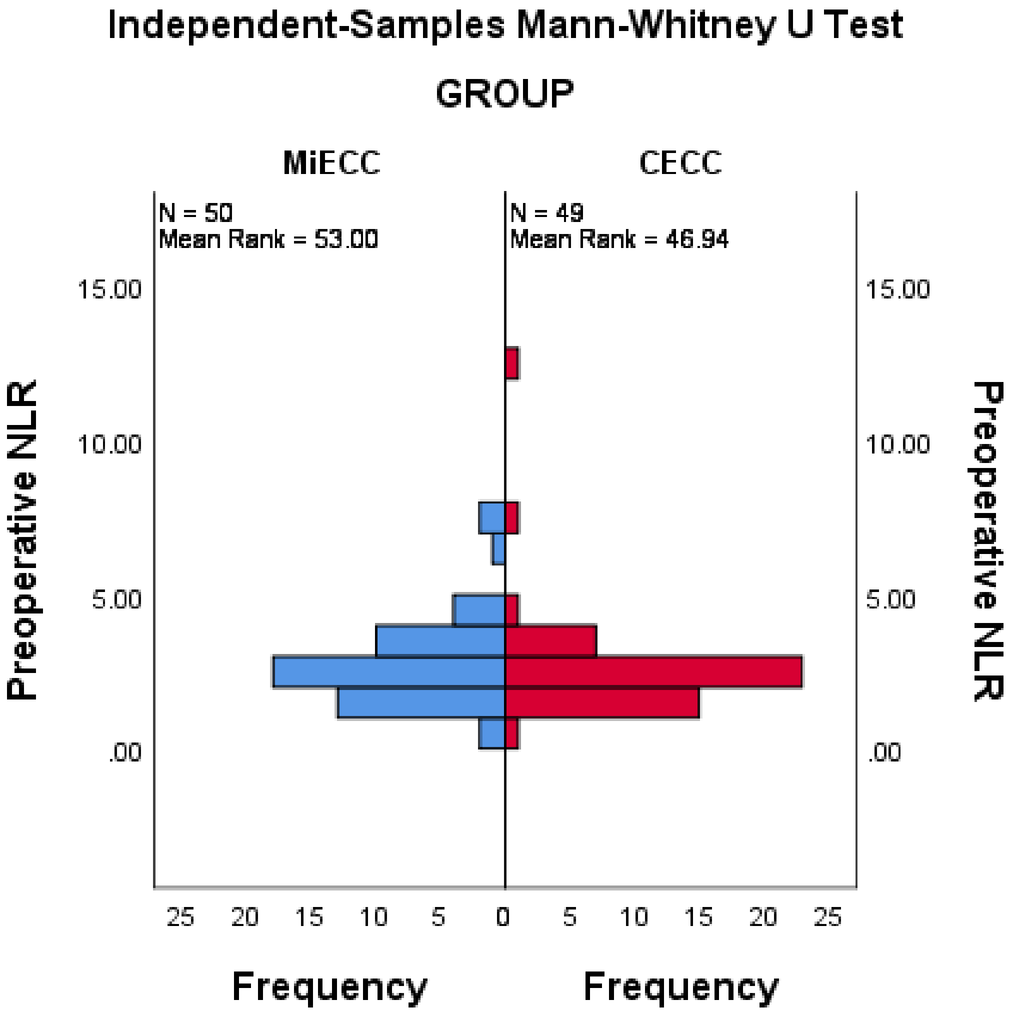

Figure 4. Independent-Samples Mann-Whitney U for the variable preoperative NLR. Graphic display.

Total N	99
Mann-Whitney U	1262.000
Wilcoxon W	2487.000
Test Statistic	1262.000
Standard Error	142.887
Standardized Test Statistic	.259
Asymptotic Sig.(2-sided test)	.796

Table 11. Independent-Samples Mann-Whitney U Test Summary for the variable preoperative NLR

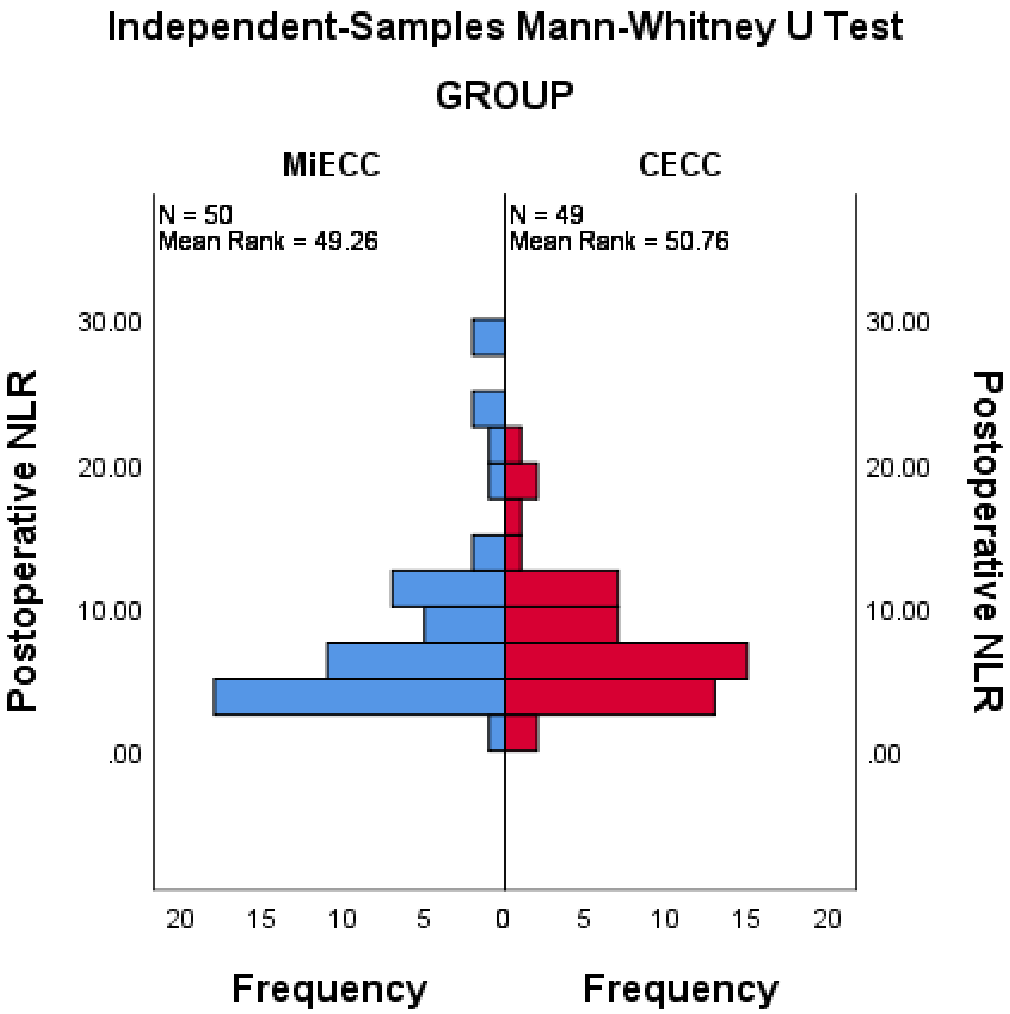

Figure 5. Independent-Samples Mann-Whitney U for the variable postoperative NLR. Graphic display.

Independent-Samples Mann-Whitney U Test Summary

Total N	99
Mann-Whitney U	1320.000
Wilcoxon W	2545.000
Test Statistic	1320.000
Standard Error	142.887
Standardized Test Statistic	.665
Asymptotic Sig.(2-sided test)	.506

Table 12. Independent-Samples Mann-Whitney U Test for the variable postoperative PLR.

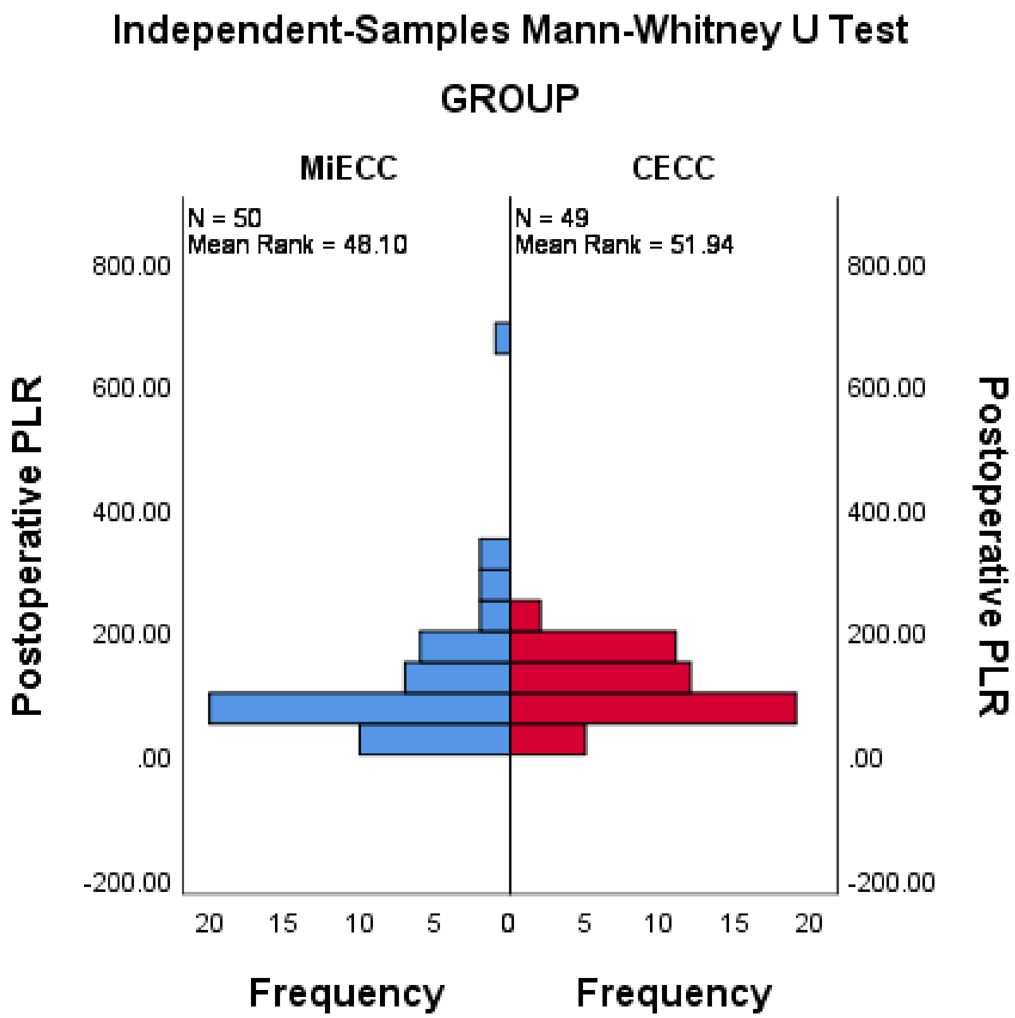

Figure 6. Independent-Samples Mann-Whitney U Test for the variable postoperative PLR. Graphic display.

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	.000[a]	1	1.000	1.000	.753	
Continuity Correction[b]	.000	1	1.000			
Likelihood Ratio	.000	1	1.000	1.000	.753	
Fisher's Exact Test				1.000	.753	
Linear-by-Linear Association	.000[c]	1	1.000	1.000	.753	.505
N of Valid Cases	100					

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.00.

b. Computed only for a 2x2 table

c. The standardized statistic is .000.

Table 13. Chi-Square Test for the variable IABP.

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	4.206[a]	3	.240	.238		
Likelihood Ratio	4.263	3	.234	.324		
Fisher's Exact Test	4.351			.180		
Linear-by-Linear Association	3.156[b]	1	.076	.084	.050	.022
N of Valid Cases	97					

a. 3 cells (37.5%) have expected count less than 5. The minimum expected count is .97.

b. The standardized statistic is 1.776.

Table 14. Chi-Square Test for the variable UDPB (Universal definition for perioperative bleeding class).

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1.366[a]	1	.242	.275	.172	
Continuity Correction[b]	.899	1	.343			
Likelihood Ratio	1.371	1	.242	.275	.172	
Fisher's Exact Test				.275	.172	
Linear-by-Linear Association	1.353[c]	1	.245	.275	.172	.090
N of Valid Cases	99					

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 14.35.

b. Computed only for a 2x2 table

c. The standardized statistic is 1.163.

Table 15. Chi-Square Test for the variable AF.

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1.010[a]	1	.315	1.000	.500	
Continuity Correction[b]	.000	1	1.000			
Likelihood Ratio	1.396	1	.237	1.000	.500	
Fisher's Exact Test				1.000	.500	
Linear-by-Linear Association	1.000[c]	1	.317	1.000	.500	.500
N of Valid Cases	100					

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .50.

b. Computed only for a 2x2 table

c. The standardized statistic is 1.000.

Table 16. Chi-Square Test for the variable postoperative MI.

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	.344[a]	1	.558	1.000	.500	
Continuity Correction[b]	.000	1	1.000			
Likelihood Ratio	.350	1	.554	1.000	.500	
Fisher's Exact Test				1.000	.500	
Linear-by-Linear Association	.340[c]	1	.560	1.000	.500	.379
N of Valid Cases	100					

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.50.

b. Computed only for a 2x2 table

c. The standardized statistic is .583.

Table 17. Chi-Square Test for the variable stroke.

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	1.010[a]	1	.315	1.000	.500	
Continuity Correction[b]	.000	1	1.000			
Likelihood Ratio	1.396	1	.237	1.000	.500	
Fisher's Exact Test				1.000	.500	
Linear-by-Linear Association	1.000[c]	1	.317	1.000	.500	.500
N of Valid Cases	100					

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .50.

b. Computed only for a 2x2 table

c. The standardized statistic is 1.000.

Table 18. Chi-Square Test for the variable need for revascularisation.

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	2.000[a]	1	.157	.495	.253	
Continuity Correction[b]	.490	1	.484			
Likelihood Ratio	2.773	1	.096	.495	.253	
Fisher's Exact Test				.495	.253	
Linear-by-Linear Association	1.980[c]	1	.159	.495	.253	.253
N of Valid Cases	99					

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .99.

b. Computed only for a 2x2 table

c. The standardized statistic is 1.407.

Table 19. Chi-Square Test for the variable stage 3 AKIN.

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	2.265[a]	1	.132	.160	.128	
Continuity Correction[b]	1.291	1	.256			
Likelihood Ratio	2.358	1	.125	.160	.128	
Fisher's Exact Test				.160	.128	
Linear-by-Linear Association	2.242[c]	1	.134	.160	.128	.100
N of Valid Cases	99					

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 3.96.

b. Computed only for a 2x2 table

c. The standardized statistic is 1.497.

Table 20. Chi-Square Test for the variable prolonged mechanical ventilation.

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	4.340[a]	1	.037	.060	.030	
Continuity Correction[b]	3.516	1	.061			
Likelihood Ratio	4.384	1	.036	.060	.030	
Fisher's Exact Test				.060	.030	
Linear-by-Linear Association	4.297[c]	1	.038	.060	.030	.019
N of Valid Cases	100					

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 18.00.

b. Computed only for a 2x2 table

c. The standardized statistic is 2.073.

Table 21. Chi-Square Test for the variable Event.

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	4.167[a]	1	.041	.117	.059	
Continuity Correction[b]	2.344	1	.126			
Likelihood Ratio	5.712	1	.017	.117	.059	
Fisher's Exact Test				.117	.059	
Linear-by-Linear Association	4.125[c]	1	.042	.117	.059	.059
N of Valid Cases	100					

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 2.00.

b. Computed only for a 2x2 table

c. The standardized statistic is 2.031.

Table 22. Chi-Square Test for the variable Death.

			Postoperative NLR	CPB duration (minutes)
Spearman's rho	Postoperative NLR	Correlation Coefficient	1.000	.163
		Sig. (2-tailed)	.	.106
		N	99	99
	CPB duration (minutes)	Correlation Coefficient	.163	1.000
		Sig. (2-tailed)	.106	.
		N	99	100

Table 23. Correlation coefficient, postoperative NLR and CPB duration.

Control Variables			CPB duration (minutes)	Postoperative NLR
GROUP	CPB duration (minutes)	Correlation	1.000	.202
		Significance (2-tailed)	.	.046
		df	0	96
	Postoperative NLR	Correlation	.202	1.000
		Significance (2-tailed)	.046	.
		df	96	0

Table 24. Partial Correlation, postoperative NLR and CPB duration controlling for Group.

Variables in the Equation

								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	GROUP(1)	-1.002	.488	4.211	1	.040	.367	.141	.956
	Euroscore (%)	.059	.382	.024	1	.877	1.061	.502	2.241
	Hb0	-.226	.171	1.753	1	.186	.798	.571	1.115
	Hb1	.226	.181	1.554	1	.213	1.253	.879	1.787
	CPB	.003	.010	.089	1	.765	1.003	.984	1.022
	NLR0	.238	.238	1.004	1	.316	1.269	.796	2.023
	NLR1	-.032	.098	.105	1	.746	.969	.799	1.174
	PLR0	.002	.007	.044	1	.834	1.002	.987	1.016
	PLR1	-.003	.007	.122	1	.727	.997	.983	1.012

	Constant	-.106	3.022	.001	1	.972	.900		
Step 2[a]	GROUP(1)	-.992	.483	4.212	1	.040	.371	.144	.956
	Hb0	-.237	.155	2.325	1	.127	.789	.582	1.070
	Hb1	.226	.181	1.554	1	.212	1.253	.879	1.787
	CPB	.003	.010	.106	1	.745	1.003	.984	1.022
	NLR0	.240	.238	1.019	1	.313	1.272	.798	2.028
	NLR1	-.034	.098	.119	1	.730	.967	.799	1.170
	PLR0	.001	.007	.036	1	.850	1.001	.987	1.016
	PLR1	-.002	.007	.111	1	.739	.998	.983	1.012
	Constant	.098	2.717	.001	1	.971	1.103		
Step 3[a]	GROUP(1)	-.984	.482	4.173	1	.041	.374	.145	.961
	Hb0	-.243	.153	2.535	1	.111	.784	.581	1.058
	Hb1	.227	.181	1.567	1	.211	1.254	.880	1.788
	CPB	.003	.010	.101	1	.751	1.003	.984	1.022
	NLR0	.268	.186	2.080	1	.149	1.308	.908	1.883
	NLR1	-.041	.090	.202	1	.653	.960	.804	1.146
	PLR1	-.002	.006	.077	1	.782	.998	.987	1.010
	Constant	.233	2.623	.008	1	.929	1.263		
Step 4[a]	GROUP(1)	-.968	.478	4.098	1	.043	.380	.149	.970
	Hb0	-.244	.152	2.581	1	.108	.783	.581	1.055
	Hb1	.227	.181	1.564	1	.211	1.254	.879	1.789
	CPB	.004	.009	.191	1	.662	1.004	.986	1.022
	NLR0	.268	.187	2.051	1	.152	1.307	.906	1.885
	NLR1	-.061	.052	1.372	1	.242	.940	.849	1.042
	Constant	.142	2.601	.003	1	.957	1.152		
Step 5[a]	GROUP(1)	-1.027	.460	4.979	1	.026	.358	.145	.883
	Hb0	-.236	.150	2.465	1	.116	.790	.589	1.060
	Hb1	.208	.176	1.393	1	.238	1.231	.872	1.737
	NLR0	.264	.188	1.983	1	.159	1.303	.902	1.882
	NLR1	-.057	.051	1.244	1	.265	.944	.854	1.044
	Constant	.606	2.373	.065	1	.799	1.832		
Step 6[a]	GROUP(1)	-1.025	.455	5.063	1	.024	.359	.147	.876
	Hb0	-.239	.148	2.598	1	.107	.787	.589	1.053
	Hb1	.187	.175	1.144	1	.285	1.205	.856	1.697
	NLR0	.177	.157	1.271	1	.260	1.194	.877	1.625
	Constant	.666	2.371	.079	1	.779	1.946		
Step 7[a]	GROUP(1)	-.932	.443	4.433	1	.035	.394	.165	.938
	Hb0	-.195	.141	1.922	1	.166	.823	.624	1.084
	NLR0	.170	.156	1.201	1	.273	1.186	.874	1.608
	Constant	2.024	1.994	1.030	1	.310	7.571		

Step 8[a]	GROUP(1)	-.891	.436	4.179	1	.041	.410	.175	.964
	Hb0	-.218	.137	2.529	1	.112	.804	.614	1.052
	Constant	2.769	1.865	2.204	1	.138	15.943		
Step 9[a]	GROUP(1)	-.886	.429	4.252	1	.039	.412	.178	.957
	Constant	-.160	.284	.319	1	.572	.852		

a. Variable(s) entered on step 1: GROUP, Euroscore (%), Hb0, Hb1, CPB, NLR0, NLR1, PLR0, PLR1.

Table 25. Logistic regression for the binary outcome Event.

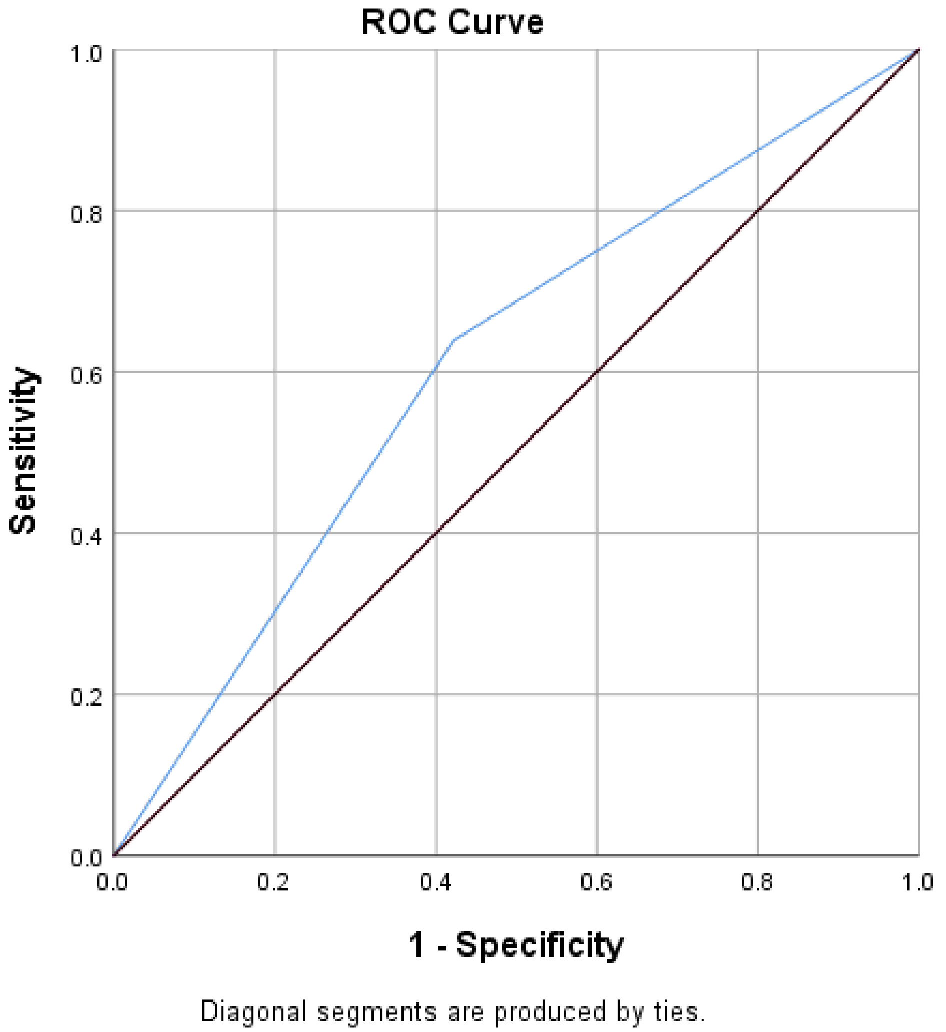

Figure 7. ROC Curve, AUC = 0.61.

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	GROUP(1)	-1.909	.916	4.342	1	.037	.148	.025	.893
	Euroscore (%)	-.041	.709	.003	1	.954	.960	.239	3.856

	Hb0	.150	.271	.306	1	.580	1.162	.683	1.976
	Hb1	-.056	.274	.042	1	.838	.946	.552	1.619
	CPB	-.008	.017	.250	1	.617	.992	.960	1.025
	NLR0	-.253	.375	.456	1	.500	.776	.372	1.619
	NLR1	.281	.171	2.715	1	.099	1.325	.948	1.851
	PLR0	.014	.014	1.089	1	.297	1.014	.988	1.042
	PLR1	-.031	.017	3.295	1	.070	.969	.937	1.003
	Constant	-2.189	4.944	.196	1	.658	.112		
Step 2[a]	GROUP(1)	-1.913	.915	4.370	1	.037	.148	.025	.888
	Hb0	.155	.257	.364	1	.547	1.168	.706	1.932
	Hb1	-.054	.272	.039	1	.843	.948	.556	1.614
	CPB	-.008	.017	.256	1	.613	.992	.960	1.024
	NLR0	-.251	.373	.453	1	.501	.778	.375	1.615
	NLR1	.281	.170	2.724	1	.099	1.324	.949	1.848
	PLR0	.014	.014	1.088	1	.297	1.014	.988	1.042
	PLR1	-.031	.017	3.324	1	.068	.969	.937	1.002
	Constant	-2.322	4.370	.282	1	.595	.098		
Step 3[a]	GROUP(1)	-1.933	.912	4.491	1	.034	.145	.024	.865
	Hb0	.140	.244	.330	1	.565	1.151	.713	1.856
	CPB	-.008	.016	.229	1	.633	.992	.961	1.025
	NLR0	-.248	.374	.441	1	.506	.780	.375	1.623
	NLR1	.275	.167	2.714	1	.099	1.317	.949	1.827
	PLR0	.014	.014	1.054	1	.305	1.014	.987	1.042
	PLR1	-.031	.017	3.323	1	.068	.970	.938	1.002
	Constant	-2.708	3.905	.481	1	.488	.067		
Step 4[a]	GROUP(1)	-1.811	.874	4.290	1	.038	.164	.029	.907
	Hb0	.132	.243	.294	1	.588	1.141	.709	1.837
	NLR0	-.273	.377	.524	1	.469	.761	.363	1.594
	NLR1	.254	.162	2.450	1	.118	1.289	.938	1.771
	PLR0	.015	.014	1.179	1	.278	1.015	.988	1.042
	PLR1	-.029	.017	3.058	1	.080	.971	.940	1.004
	Constant	-3.408	3.641	.876	1	.349	.033		
Step 5[a]	GROUP(1)	-1.746	.857	4.148	1	.042	.174	.032	.936
	NLR0	-.310	.376	.679	1	.410	.733	.351	1.533
	NLR1	.245	.163	2.268	1	.132	1.278	.929	1.758
	PLR0	.014	.013	1.069	1	.301	1.014	.988	1.041
	PLR1	-.028	.016	2.857	1	.091	.973	.942	1.004
	Constant	-1.521	1.073	2.008	1	.156	.219		
Step 6[a]	GROUP(1)	-1.654	.840	3.876	1	.049	.191	.037	.993

	NLR1	.164	.129	1.633	1	.201	1.179	.916	1.517
	PLR0	.006	.009	.427	1	.513	1.006	.988	1.023
	PLR1	-.021	.014	2.289	1	.130	.979	.953	1.006
	Constant	-1.448	.971	2.224	1	.136	.235		
Step 7[a]	GROUP(1)	-1.606	.832	3.724	1	.054	.201	.039	1.025
	NLR1	.138	.121	1.307	1	.253	1.148	.906	1.454
	PLR1	-.017	.012	2.040	1	.153	.984	.961	1.006
	Constant	-1.031	.752	1.876	1	.171	.357		
Step 8[a]	GROUP(1)	-1.546	.826	3.505	1	.061	.213	.042	1.075
	PLR1	-.007	.007	1.044	1	.307	.993	.980	1.006
	Constant	-.961	.749	1.646	1	.200	.383		
Step 9[a]	GROUP(1)	-1.520	.818	3.449	1	.063	.219	.044	1.088
	Constant	-1.658	.386	18.478	1	.000	.190		

a. Variable(s) entered on step 1: GROUP, Euroscore (%), Hb0, Hb1, CPB, NLR0, NLR1, PLR0, PLR1.

Table 26. Logistic regression for the binary outcome Event_noaf