The Association of Blood Transfusion with the Development of Post-operative Complications in Patients after Cardiac Surgery

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Key Words: *cardiac surgery, coronary artery bypass, bleeding, blood transfusion, patient's course.*

Summary. *The aim of this study was to analyse the association between blood transfusions and the development of post-operative complications in patients after cardiac surgery.*

Methods. Retrospective data analysis was conducted with purposive sample selection employed. The target group included patients who underwent planned or urgent cardiac surgery under cardiopulmonary bypass (CPB) at the university hospital during 2018–2019. The sample size was calculated by applying 95% of probability and 0.5 error. The retrospective analysis of 282 patients' files was performed during the period from June to October, 2019.

Results. A strong positive correlation between blood transfusion and post-operative complications was determined in patients after cardiac surgery under cardiopulmonary bypass. A significantly higher number of patients after blood transfusions experienced delirium (P < 0.001), anemia (P < 0.001), pneumonia (P < 0.001), renal function failure (P < 0.001), sepsis (P < 0.001), atrial fibrillation (P = 0.002) and death (P = 0.031).

Conclusions. Blood transfusion can save lives, but there is a strong positive correlation between blood transfusions and post-operative complications. Blood transfusion can result in some serious complications after cardiac surgery, such as delirium, anaemia, pneumonia, renal failure, sepsis, atrial fibrillation and death.

Nurses play an important role in this life-saving process. It is the nurses' task to perform blood transfusion to a patient when it is needed. At the same time, nurses may be the first ones to identify active or suspected bleeding to prevent massive blood transfusion requirement.

Introduction

Cardiovascular diseases are the main cause of death in the world; each year, more than 17 million people die because of this type of ailments, and it constitutes more than 30% of all causes of death (1). In Europe, this number is close to 1.8 million people or 36% of death causes (2). In Lithuania, approximately 22 thousand people die because of cardiovascular diseases each year and it makes 39% of all deaths in the country (3).

Approximately two thousand cardiac surgeries of various complexity are carried out in Lithuania each year (4). Just as in many other countries, these surgeries are usually performed to older patients; however, not taking age into account, the main reasons of cardiac surgeries and the whole treatment itself are life retention and maximum health restoration (5).

Bleeding in cardiac surgery is an extremely important problem and one of the most common complications met when the artificial blood circulation system (ABCS) is used (5). Bleeding is defined as a process during which a patient loses more than 500 mL of blood within the first 24 post-operational hours (6). Quite many patients experiencing cardiac surgeries with the supplement of the ABCS, face a great risk of bleeding due to coagulation system disturbances or surgical reasons. This complication is not dependent on the complexity and the character of a cardio-surgical operation, or a pre-operative condition of the patient's coagulation system, duration of the ABCS, but is influenced by disturbances in haemostasis (5, 7).

Bleeding and further usage of blood components in cardiac surgery remain an unsolved problem so far, despite the progress in science, innovations and applications of new biomaterials, improvement of medical devices, success in discovering and in grafting of new methods of extravasation diminution (5, 8, 9). A huge demand of blood components also causes difficulties to hospital administration, because expenses on allogeneic blood component preparation rises every year, as well as costs of blood bank administration (10, 11).

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Cardiac surgery, compared with other surgical treatments, requires greatest amounts of allogeneic transfusions of blood components (12). Usage of blood components in many cases causes additional problems, such as delirium, anaemia, myocardial infarction, stroke, pneumonia, renal failure, infection in the section site / mediastinitis, sepsis, death, re-sternotomy, atrial fibrillation, increased usage of antibiotics, and indicates usage of cell savers (13, 14). Due to these additional problems, prolonged patient's hospitalisation time is needed, and worse outcomes of the treatment are faced (15).

Nurses play an important role in bleeding treatment. They are the first ones who can notice bleeding, because they are 24/7 next to the patient. In order to save the patient's life after massive bleeding, a large proportion of patients receive blood transfusions. Nurses are the team members responsible for final verification of components before the transfusion and the ones who can cancel the procedure in case of component mismatch. It means that nurses must have a deep knowledge and understanding of pathophysiology of transfusion reactions and their treatment, be able to recognise symptoms in case of complications such as allergic reactions, fever, acute immune haemolytic reaction or blood-borne infection, thus ensuring the safe mode of performance of the transfusion procedure (16).

In Lithuania, blood transfusions are performed in accordance with the order of the Minister of Health of the Republic of Lithuania (17). In our healthcare system, the doctor gives a prescription to perform blood transfusion according to the condition of the patient, but the process is carried by a nurse. In some other countries around the world (e.g., Australia, the USA, the United Kingdom, the Netherlands, etc.), the competencies of nurses encompass much wider range of activities, including transfusions. While working in a team, specialists of blood transfusions cooperate and co-work with blood banks' representatives and consultants. This way the effective usage of blood components is ensured, and the practice of transfusions is improved (18). When transfusions are performed by a competent specialist, the risk of possible complications related with the transfusion technique or blood mismatch is reduced.

The aim of this study was to analyse the association between blood transfusions and the development of post-operative complications in patients after cardiac surgery.

Methods

Study Design and Sample. The study was performed at the Clinic of Cardiac, Thoracic and Vascular Surgery of the Hospital of Lithuanian University of Health Sciences, Kauno klinikos.

Sample selection was purposive and the target group included the patients who received a planned or urgent cardio-surgical operation with the supplied ABCS. The sample size was calculated with a 95% probability and a 5% error. The recommended sample size for this study was 273. The retrospective analysis of 282 patients' files was performed during the period from June to October, 2019.

Ethical Consideration. The study protocol was approved by the Centre of Bioethics at the Lithuanian University of Health Sciences (No. BEC-ISP(M)-240).

Confidentiality of patients was ensured, as investigation data were used only for the research purpose, data in a study protocol were anonymous, names and addresses of the participants were not recorded, and the results of the study were generalised. Only patients who gave written consent to use their data for scientific or educational purposes took place in this study.

Statistical Analysis. Statistical analysis was performed using SPSS 22.0 (Statistical Package for the Social Sciences) and MS Excel 2016 programmes: descriptive statistic was calculated, statistical hypotheses concerning differences in frequencies of means were verified, as well as medians with their quartiles and the interdependence of traits.

The statistical significance level was chosen to be 0.05; quantitative distributions of variables were evaluated using the Kolmogorov-Smirnov test. The parametric Student t or the Mann-Whitney test was used for the comparison of mean values of two independent groups. For the evaluation of associations of qualitative characteristics, the chi-squared (χ^2) criteria were applied: the exact criterion for small samples and asymptomatic χ^2 criterion for large samples. The associations among characteristics were assessed using Pearson and Spearman coefficients of correlation. For remarkable differences in comparative analysis, binary logistic regression was applied. The data were assumed to be statistically significant when $P < 0.05$.

Results

All developed post-surgical complications for bleeding (n = 122) and not bleeding patients (n = 160) were analysed. The results presented in Table 1 show that anaemia in 50 patients (41.0%), pneumonia in 28 (23%), renal failure in 11 (11.5%), re-sternotomy due to bleeding in 4 (3.3%), were developed for a significantly higher number of bleeding patients after cardio-surgical operations ($P < 0.05$); the need for antibiotic therapy due to subsequently occurring complications was relevant to 58 (47.5%) bleeding patients and 50 (31.3%) non-bleeding patients ($P = 0.005$).

Using binary logistic regression analysis, we could forecast that bleeding patients had a higher risk of anaemia caused by bleeding (Hb < 90g/L), 1.721 [1.047–2.830] (odds ratio [95% confidence interval]), pneumonia 2.25 [1.231–4.488], renal failure 2.463 [0.998–6.076] and use of antibiotic therapy 1.994 [1.224–3.247].

When massive bleeding occurred, the cell saver system for allogeneic blood (when donor and recipient are not the same person) was used in 8 (6.6%) patients, and thus the need for allogeneic blood was reduced ($\chi^2 = 5.701$, $P = 0.017$). Using binary logistic regression analysis, we obtained that the chances to employ the cell saver system for bleeding patients were 5.544 [1.156–26.597]. For the development of other complications, listed in Table 1, bleeding did not have a significant impact.

After analysing the post-operative complications, we selected bleeding patients (n = 122) and divided them into two groups: (1) bleeding patients who received blood transfusions (n = 52) and (2) bleeding patients who did not receive blood transfusions (n = 70). The aim of such division was to determine if blood transfusions make influence on the development of post-operative complications in bleeding patients (Table 2). A significantly higher number of patients who received blood transfusions experienced the following complications: delirium – 30 (57.7%), anaemia due to bleeding (Hb < 90g/L) – 32 (61.5%), pneumonia – 22 (42.3%), renal failure – 14 (26.9%), sepsis – 8 (15.4%), death – 4 (7.7%), atrial fibrillation – 34 (65.4%) and need for antibiotics – 34 (6.4%) ($P < 0.05$).

Table 1. Distribution and Comparison of Complications in Post-operative Cardiac Surgery Bleeding and Non-bleeding Patients

Complications	All Patients (n = 282)	Secretion through Drain		Chi-squared criterion	P
		< 500 (n = 160)	⩾ 500 (n = 122)		
		n (%)			
Delirium	104 (36.9)	56 (35.0)	48 (39.3)	0.561	0.454
Bleeding caused anaemia (Hb < 90g/L)	96 (34.0)	46 (28.8)	50 (41.0)	4.614	0.032
Stroke	2 (0.7)	0	2 (1.6)	2.642	0.186
Pneumonia	46 (16.3)	18 (11.3)	28 (23)	6.942	0.008
Renal failure	22 (7.8)	8 (5.0)	11 (11.5)	4.035	0.045
Sepsis	12 (4.3)	4 (2.5)	8 (6.6)	2.797	0.094
Death	6 (2.1)	2 (1.3)	4 (3.3)	1.368	0.408
Re-sternotomy due to bleeding	4 (1.4)	0	4 (3.3)	5.321	0.034
Atrial fibrillation	124 (44.0)	64 (40.0)	60 (49.2)	2.368	0.124
Antibiotics	108 (38.3)	50 (31.3)	58 (47.5)	7.774	0.005

P – level of significance; values in bold – *P* < 0.05.

Table 2. Distribution and Comparison of Complications in Post-operative Bleeding Patients with and without Blood Transfusion Therapy

Complications	All Patients (n = 122)	Blood Transfusion		Chi-squared Criterion	P
		Applied (n = 52)	Not Applied (n = 70)		
		n (%)			
Delirium	48 (39.3)	30 (57.7)	18 (25.7)	12.785	< 0.001
Anaemia due to bleeding (Hb < 90g/L)	50 (41.0)	32 (61.5)	18 (25.7)	15.831	< 0.001
Stroke	2 (1.6)	2 (3.8)	0	2.737	0.180
Pneumonia	28 (23.0)	22 (42.3)	6 (8.6)	19.203	< 0.001
Renal failure	14 (11.5)	14 (26.9)	0	21.289	< 0.001
Sepsis	8 (6.6)	8 (15.4)	0	11.525	0.001
Death	4 (3.3)	4 (7.7)	0	5.567	0.031
Re-sternotomy due to bleeding	4 (3.3)	2 (3.8)	2 (2.9)	0.092	1.000
Atrial fibrillation	60 (49.2)	34 (65.4)	26 (37.1)	9.521	0.002
Antibiotics	58 (47.5)	34 (65.4)	24 (34.3)	11.570	0.001

P – level of significance; values in bold – *P* < 0.05.

By using binary logistic regression analyses, we forecasted that, for bleeding patients who received allogeneic blood transfusions, the odds ratio for the development of complications was as follows: delirium − 3.939 [1.827–8.492], anaemia − 4.622 [2.131–10.025], pneumonia − 7.822 [2.873–21.294], atrial fibrillation − 3.197 [1.511–6.768] and the need for antibiotic therapy − 3.62 [1.702–7.702].

Some complications in the group of bleeding patients developed only in those who received blood transfusions. Those who did not receive blood transfusions did not experience such complications as stroke, renal failure, sepsis and death.

In order to avoid the need for blood transfusions for massively bleeding patients 8 (15.4%), the cell saver system was used. This system of returning autologous blood (donor and recipient are the same person) back to the patient was used only for the patients who received transfusions of allogeneic blood.

Discussion

Bleeding and usage of blood components in cardiac surgery remain an unsolved problem so far, despite innovations and applications of new biomaterials, improvement of medical devices, success in discovering and in grafting of new methods of extravasation diminution. Nurses play a huge role in the successful resuscitation of a patient with critical bleeding in cardiac surgery. They may be the first ones to identify active or suspected bleeding because they are directly caring for these patients.

In this retrospective study of patients' who received cardio-surgical operations with the supply of the ABCS, case files were analysed. All patients were divided into two groups: the first group was composed of bleeding patients (their blood secretion through drains was more than 500 mL within the first 24 post-operational hours) and the second group was composed of non-bleeding patients (blood secretion through drains was less than 500 mL).

These two groups of the patients were investigated, and the development of post-operative complications was analysed. The results revealed that bleeding patients tended to have anaemia, pneumonia, renal function failure, and re-sternotomy more often; they also more frequently got antibiotics therapy due to adjacent complications. These complications make the condition of the patient worse and more severe. Bleeding itself is one of the greatest complications in cardiac surgery, followed by other complications, impeding the condition of the patient.

Due to the fact that the health condition of bleeding patients is more severe than that of non-bleeding ones, we came to the assumption that it would be irrational to compare the development of complications between these two groups. Thus, we divided the group of bleeding patients into two subgroups: (a) patients who received blood transfusion and (b) patients who did not receive blood transfusion.

Blood transfusion can save lives, but other studies show a strong correlation between blood transfusions and following complications, such as death, stroke, respiratory failure, renal failure, sepsis, myocardial infarction, surgical site infection and others (12, 20, 21). We found a strong positive correlation between blood transfusions and post-operative complications that developed in patients who received them. A significantly higher number of patients after blood transfusions experienced delirium, anaemia, pneumonia, renal function failure, sepsis, death and atrial fibrillation. These results are supported by other studies as well (22, 23).

The significant positive correlation between blood transfusions and the development of delirium was also determined during this study. Van der Zanden et al. (24) made a hypothesis that blood transfusion was an effective remedy for delirium prevention because anaemia is one of delirium causes. They also found a correlation between blood transfusions and delirium development. According to the authors, validity of their results, i.e., that delirium is a complication following blood transfusion, is questioned because the study methodology was not properly implemented; thus, it could not be assured if delirium developed before the blood transfusion or after this treatment. It could be concluded that more research work involving more precise investigation should be performed in the future to confirm or deny the association between blood transfusion and delirium (24).

Anaemia is another severe complication, mostly provoked by post-operational bleeding; it causes hypoxia and dysfunction of organs. Anaemia can be treated via blood transfusion, but this decision should be based on the guidelines and algorithms according to an individual condition of the patient. Quite often, only blood test results are the reason for the correction of anaemia, not the overall condition of the patient. As an outcome, patients more often experience blood transfusion–induced complications (25). Our investigation showed that anaemia developed in a significantly greater number of bleeding patients who received blood transfusion, compared with those who did not. Shander et al. (2017) investigated post-operative complications in patients who received blood transfusion and anaemia was found as a significantly developed one (8).

Pneumonia is also a very frequent complication after cardiac surgeries, despite a big number of protective measures used in practice (26). During

the cardiac surgery, significant changes in body liquids take place, including blood transfusions; all these actions may cause the development of lung oedema (26, 27, 28). The results of this study report that blood transfusions make a significant impact on the development of post-operative pneumonia.

Acute renal failure is one of the most often met complications in patients after cardiac surgeries with the supply of the ABCS. The influence of blood transfusion on the development of renal failure is widely discussed in scientific literature (22, 29). The results of this study support the conclusions made by other investigators. Additionally, we found that bleeding patients who did not receive blood transfusions did not tend to have a complication of renal failure.

In this study, sepsis developed only in the patients who received blood transfusions ($P < 0.001$). These results fell into agreement with the conclusions of other researchers who report that blood transfusion in patients after cardiac surgery enhances the risk of sepsis development (30, 31).

More patients who received blood transfusions died, compared with those who did not receive it (22). According to the results of this study, only the patients who received blood transfusion died and that is in agreement with the major amount of studies reporting that blood transfusion enhances the frequency of post-operative deaths (10, 21, 22, 29, 30, 32–34).

There is the evidence (35) that post-operative transfusion of blood components does not make any influence on the development of atrial fibrilla-tion, whereas others investigators conclude that such influence exists (36, 37). The results of our investigation showed that atrial fibrillation developed in a significantly greater number of patients with blood transfusion compared with those without it. Diminution of transfusions may improve the post-operative outcomes and decrease the costs of post-operative care, but does not decrease the risk of atrial fibrillation development.

The usage of antibiotics is correlated with comorbidity, developed after blood transfusion. The results of our study revealed a strong correlation between these occurrences: blood transfusion enhances the probability of antibiotic therapy a few times.

The cell saver system was used in order to reduce the demand of blood transfusions in massively bleed-ing patients. This system of autologous blood return only for bleeding patients who received additional allogenic blood transfusions was employed.

The evidence exists that when blood vessels are damaged in healthy women, fibrin threads form faster in their blood stream than in healthy men facing the same problem (19). Viscoelastic properties of blood vessels in women are also better due to a greater amount of pro-coagulants in their structure compared with men. This should bring us to the conclusion that men tend to bleed to a greater extent than women after the same type of cardio surgery. However, the results of our study showed that gender and age of patients did not have significant influence on post-operative bleeding intensity.

Conclusions

Bleeding in cardiac surgery is an extremely important problem and one of the most frequent complications met, when cardiopulmonary bypass is used. Our research shows that blood transfusion can result in some serious complications after cardiac surgery, such as delirium, anaemia, pneumonia, renal failure, sepsis, atrial fibrillation and death.

It is important to notice bleeding after surgery as fast as it is possible, and nurses with good know-ledge of blood transfusion side effects can observe it quickly and prevent some possible complications such as allergic reactions, fever, acute immune haemolytic reaction or blood-borne infection. By noticing bleeding at the right time, the amount of blood products reducing possible complications may be decreased. As the need for blood transfusions declines, the costs of hospital administration are also reduced, because expenses on preparation of allogeneic blood components, as well as blood bank administration costs, rise every year.

Statement of Conflict of Interest
The authors declare no conflict of interest.

References
1. Cardiovascular Diseases [Internet]. World Health Organi-zation [cited 2019 November 8]. Available from: URL: http://www.who.int/health-topics/cardiovascular-diseases/#tab=tab_1.
2. Causes and occurrence of deaths in the EU [Internet]. Eu-rostat. 2019 [cited 2019 November 8]. Available from: URL: http://www.ec.europa.eu/eurostat/web/products-eurostat-news/-/DDN-20190716-1.
3. Commission E [Internet]. State of Health in the EU: country healh profile 2017 – Lithuania [serial online] 2017 [cited 2019 November 8]. Available from: URL: http://www.euro.who.int/__data/assets/pdf_file/0010/355987/Health-Profile-Lithuania-Eng.pdf?ua=1&fbclid=IwAR0zn41pT8

iRT0SF8gG-_K3NAXN0C-2LO_MiVFpM1mKOLftyPY-Zryx4cbA.
4. Higienos institutas (Institute of Hygiene) 2018 [Internet]. [cited 2019 November 08]. Available from: URL: https://stat.hi.lt/default.aspx?report_id=261.
5. Veikutienė A. Autologinio kraujo, išsiliejusio po širdies op-eracijos, ankstyvos reinfuzijos įtaka ligonių pooperacinei eigai. (The influence of early reinfusion of autologous shed mediastinal blood on the postoperative course after cardiac surgery.) [dissertation]. Kaunas: Lithuanian University of Health Sciences; 2010.
6. Meesters MI, Burtman D, van de Ven PM, Boer C. Predic-tion of postoperative blood loss using thromboelastometry

in adult cardiac surgery: cohort study and systematic review. J Cardiothorac Vasc Anesth 2018;32(1):141-50.

7. Strueber M. VAD: Why does it bleed? JACC: Heart Fail 2016;4(12):971-3.

8. Shander A, Javidroozi M, Lobel G. Patient blood management in the intensive care unit. Transfus Med Rev 2017; 31(4):264-71.

9. Nwafor IA, Arua OA, Eze JC, Ezemba N, Nwafor MN. Utilisation of blood and blood products during open heart surgery in a low-income country: our local experience in 3 years. Cardiol Young 2018;28(11):1289-94.

10. Pearse BL, Smith I, Faulke D, Wall D, Fraser JF, Ryan EG, et al. Protocol guided bleeding management improves cardiac surgery patient outcomes. Vox Sang 2015;109(3):267-79.

11. Bolliger D, Tanaka KA. Point-of-care coagulation testing in cardiac surgery. Semin Thromb Hemost 2017;43(4):386-96.

12. Patel NN, Murphy GJ. Evidence-based red blood cell transfusion practices in cardiac surgery. Transfus Med Rev 2017;31(4):230-5.

13. Budak A, McCusker K, Gunaydin SA. Cardiopulmonary bypass based blood management strategy in adult cardiac surgery. Heart Surg Forum 2017;20(5):195.

14. Kapturauskas J. Krešėjimo sistemos sutrikimai, lemiantys padidintą kraujavimą perioperaciniu laikotarpiu pacientams po širdies operacijų, atliekamų dirbtinės kraujo apytakos sąlygomis. (Influence of coagulation disorders on excessive perioperative bleeding in patients recovering from cardiac surgery with cardiopulmonary bypass.) [dissertation]. Kaunas: Lithuaninian University of Health Sciences; 2015.

15. Biancari F, Brascia D, Onorati F, Reichart D, Perrotti A, Ruggieri VG, et al. Prediction of severe bleeding after coronary surgery: the WILL-BLEED Risk Score. Thromb Haemost 2017;117(03):445-56.

16. American Society of Registered Nurses. Blood transfusion error prevention – a nurses role. The Journal of Advanced Practice Nursing 2013.

17. Lietuvos Respublikos sveikatos apsaugos ministro įsakymas Nr. 174 „Dėl transfuzijos atlikimo metodikos patvirtinimo". 1999 m. balandžio 20 d. (Order No. 174 of the Minister of Health of the Republic of Lithuania of 20 April 1999 "Approving the transfusion methodology") Official Gazette [Internet]. 1999;36-1100. [cited 2019 November 31]. Available from: URL: http://anest-rean.lt/bandymas/wp-content/uploads/2018/06/De%CC%87l-sertifikato-transfuzijai-atlikti-is%CC%8Cdavimo-tvarkos-ir-transfuzijos-atlikimo-metodikos-patvirtinimo.pdf.

18. Royal College of Nursing. Right Blood, Right Patient, Right Time: RCN guidance for improving transfusion practice. RCN 2013.

19. Lopes CT, Dos Santos TR, Brunori EH, Moorhead SA, Lopes JDL, Barros AL. Excessive bleeding predictors after cardiac surgery in adults: integrative review. J Clin Nurs 2015;24(21-22):3046-62.

20. Tempe DK, Khurana P. Optimal blood transfusion practice in cardiac surgery. J Cardiothorac Vasc Anesth 2018;32(6):2743-5.

21. Rawn J. The silent risks of blood transfusion. Curr Opin Anesthesiol 2008;21(5):664-8.

22. Vivacqua A, Koch CG, Yousuf AM, Nowicki ER, Houghtaling PL, Blackstone EH, et al. Morbidity of bleeding after cardiac surgery: is it blood transfusion, reoperation for bleeding, or both? Ann Thorac Surg 2011;91(6):1780-90.

23. Laine A, Niemi T, Schramko A. Transfusion threshold of hemoglobin 80 g/L is comparable to 100 g/L in terms of bleeding in cardiac surgery: a prospective randomized study. J Cardiothorac Vasc Anesth 2018;32(1):131-9.

24. van der Zanden V, Beishuizen SJ, Swart LM, de Rooij SE, van Munster BC. The effect of treatment of anemia with blood transfusion on delirium: a systematic review. J Am Geriatr Soc 2017;65(4):728-37.

25. Dhir A, Tempe DK. Anemia and patient blood management in cardiac surgery – literature review and current evidence. J Cardiothorac Vasc Anesth 2018;32(6):2726-42.

26. Ailawadi G, Chang HL, O'Gara PT, O'Sullivan K, Woo YJ, DeRose Jr JJ, et al. Pneumonia after cardiac surgery: experience of the national institutes of Health/Canadian institutes of health research cardiothoracic surgical trials network. J Thorac Cardiovasc Surg 2017;153(6):1384-91.

27. Perrotti A, Chenevier-Gobeaux C, Ecarno, F, Bardonnet K, Barrucand B, Flicoteaux G, et al. Is endocan a diagnostic marker for pneumonia after cardiac surgery? The ENDOLUNG study. Ann Thorac Surg 2018;105(2):535-41.

28. Kilic A, Ohkuma R, Grimm JC, Magruder JT, Sussman M, Schneider EB, et al. A novel score to estimate the risk of pneumonia after cardiac surgery. J Thorac Cardiovasc Surg 2016;151(5):1415-21.

29. Purvis TE, Goodwin CR, De la Garza-Ramos R, Ahmed AK, Lafage V, Neuman BJ, et al. Effect of liberal blood transfusion on clinical outcomes and cost in spine surgery patients. Spine J 2017;17(9):1255-63.

30. Kristof K, Büttner B, Grimm A, Mewes C, Schmack B, Popov AF, et al. Anaemia requiring red blood cell transfusion is associated with unfavourable 90-day survival in surgical patients with sepsis. BMC Res Notes 2018;11(1): 1-7.

31. Dupuis C, Sonneville R, Neuville M, Vinclair C, Abid S, Papin G, et al. Transfusion for patients With Sepsis in 2018. Clin Pulmonary Med 2018;25(4):138-43.

32. Rao SV, Jollis JG, Harrington RA, Granger CB, Newby LK, Armstrong PW, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. JAMA 2004;292(13):1555-62.

33. Salisbury AC, Reid KJ, Marso SP, Amin AP, Alexander KP, Wang TY, et al. Blood transfusion during acute myocardial infarction: association with mortality and variability across hospitals. J Am Coll Cardiol 2014;64(8):811-9.

34. Abouarab AA, Leonard JR, Ohmes LB, Lau C, Rong LQ, Ivascu NS, et al. Posterior Left pericardiotomy for the prevention of postoperative Atrial fibrillation after Cardiac Surgery (PALACS): study protocol for a randomized controlled trial. Trials 2017;18(1):1-10.

35. Vlahou A, Diplaris K, Ampatzidou F, Karagounnis L, Drossos G. The role of blood transfusion in the development of atrial fibrillation after coronary artery bypass grafting. Thorac Cardiovasc Surg 2016;64(08):688-92.

36. Gillinov AM, Bagiella E, Moskowitz AJ, Raiten JM, Groh MA, Bowdish ME, et al. Rate control versus rhythm control for atrial fibrillation after cardiac surgery. N Engl J Med 2016;374(20):1911-21.

37. Gu J, Skals RK, Torp-Pedersen C, Lundbye-Christensen S, Jakobsen CJ, Bæch J, et al. Storage time of intraoperative transfused allogeneic red blood cells is not associated with new-onset postoperative atrial fibrillation in cardiac surgery. PloS One 2017;12(2):e0172726.