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Blood transfusion and risk of atrial fibrillation after coronary artery bypass graft surgery

A meta-analysis of cohort studies

Shengqun Liu, MS, Zhanwen Li, MS, Zhe Liu, MS, Zhenhua Hu, MS*, Gaifang Zheng, MS

Abstract

The aim of this study was to systematically evaluate the effect of blood transfusion (BT) on postoperative atrial fibrillation (AF) in adult patients who had undergone coronary artery bypass grafting (CABG) surgery.

PubMed, Embase, and Cochrane Library databases from inception to January 2017 were searched. Cohort studies were searched that evaluated the association between BT and the risk of postoperative AF in adult patients who had undergone CABG surgery. Study quality was assessed by using the Newcastle–Ottawa scale (NOS). A meta-analysis was performed with the random-effect model.

Eight cohort studies involving 7401 AF cases and 31,069 participants were identified and included in our data analysis. The pooled odds ratio of postoperative AF in patients with BT was 1.45 (95% confidence interval, 1.26–1.67), with significant heterogeneity ($P < .0001$, $I^2 = 79\%$). Excluding one study that had an off-pump CABG did not significantly impact this result (odds ratio, 1.36; 95% confidence interval, 1.23–1.50; n = 7). To examine the stability of the primary results, we performed subgroup analyses. The association between BT and the risk of postoperative AF was similar, as determined in the stratified analyses conducted according to study design, type of surgery, and country.

The findings of the present meta-analysis demonstrated a statistically significant increase in postoperative AF risk among adult patients with BT. Further prospective large-scale studies are needed to establish causality and to elucidate the underlying mechanisms.

Abbreviations: AF = atrial fibrillation, BT = blood transfusion, CABG = coronary artery bypass grafting, CIs = confidence intervals, CPB = cardiopulmonary bypass, MOOSE = Meta-Analysis of Observational Studies in Epidemiology, NOS = Newcastle–Ottawa scale, OR = odds ratio, RBC = red blood cells, TGF-β1 = transforming growth factor beta 1.

Keywords: blood transfusion, cardiac surgery, meta-analysis, postoperative atrial fibrillation

1. Introduction

Postoperative atrial fibrillation (AF) is a common postoperative arrhythmia in patients who have undergone all types of cardiac operations, including those with coronary artery bypass grafting (CABG).[1] Its incidence has been reported to be as high as 45% to 65%.[2,3] AF most often occurs from the second to the fourth postoperative day.[4] Although most cases are self-limiting, postoperative AF may cause serious complications, increased cost, and prolonged hospital stay.[5] The development of AF after CABG surgery increases the morbidity and mortality, length of hospital stay, and hospital costs.[6,7] Reduction in its occurrence may result in enormous savings; thus, interests in the identification of risk factors that may enable implementation of preventative strategies are increasing.

The pathophysiology of new-onset postoperative AF remains unclear. Recent evidence supports an inflammatory mechanism in the development of AF.[8–10] Transfused red blood cell (RBC) or whole blood transfusions (BT) modulate the inflammatory response to cardiac surgery by changing many inflammatory mediators and augmenting the inflammatory response.[11–13] In addition, the inflammation level is related to the preoperative status and triggers associated with cardiac surgery.

Previous studies assessed the association of RBC transfusion and the risk of postoperative AF after cardiac surgery.[8,14–20] However, these studies have a modest sample size and convey inconclusive results. To obtain a more comprehensive estimate of the association between BT and the risk of postoperative AF after cardiac surgery, we conducted a meta-analysis to systematically evaluate the association between BT and the risk of postoperative AF in adult patients who had undergone CABG surgery.

2. Methods

The present meta-analysis was conducted in accordance with the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines.[21] All analyses were based on previous published studies; thus, no ethical approval and patient consent were required.

2.1. Search strategy

We conducted an electronic search on PubMed, Embase, and Cochrane Library databases from their dates of inception to January 2017 for cohort studies published in English. The search

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terms "blood transfusion or red blood cell" and "postoperative atrial fibrillation or atrial fibrillation" were combined with "coronary artery bypass or coronary bypass or myocardial revascularization or aortic valve or mitral valve or ascending aorta or cardiac surgery" as both keywords and exploded medical subject headings. We restricted the search to human studies. In addition, we reviewed the reference lists of the obtained articles to identify additional relevant studies. If multiple published reports from the same study were available, we included only one of them that contained the most detailed information for both exposure and outcome.

2.2. Eligibility criteria

Studies that met the following criteria were included: cohort study with adult patients (i.e., 18 years or older) who underwent CABG surgery; reported outcomes of postoperative new-onset AF at least; the exposure of interest was BT or RBC; and reported adjusted risk estimates for the association between BT and/or RBC, and postoperative AF, or had reported data with which to calculate these. Studies were excluded if they met the following exclusion criteria: reported a cross-sectional, case-control, randomized controlled trial; reported only unadjusted or only age- and sex-adjusted odds ratios (OR); did not report 95% confidence intervals (CIs); the exposure of interest was not BT or RBC; and the outcome was not postoperative new-onset AF.

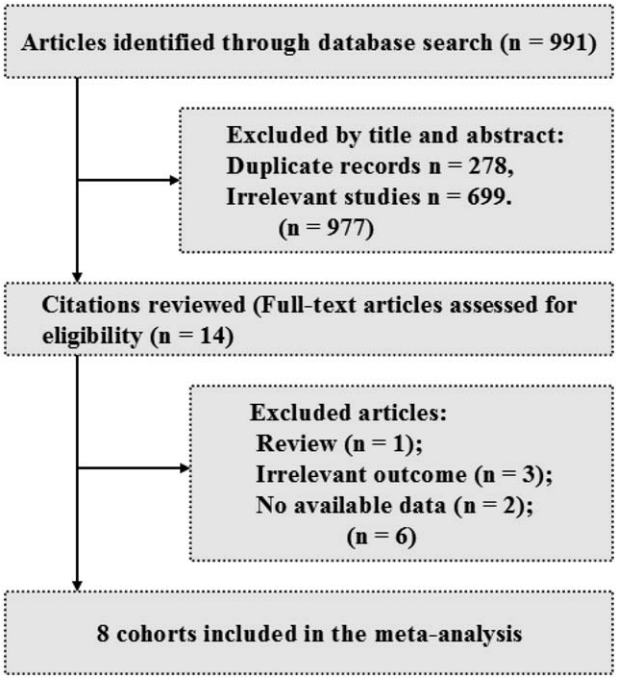

Figure 1. Flowchart of the literature search.

2.3. Data extraction

Data were extracted independently by 2 investigators and reviewed by a third investigator. The following data were extracted: first author's surname, year of publication, country, type of surgery, number of participants, number of AF cases, aortic cross-clamping time, and cardiopulmonary bypass (CPB) time, study period, type of blood products, and study design. A predesigned Excel (Microsoft Corporation) file was used to extract relevant information.

2.4. Quality assessment

The quality assessment of each study was conducted independently by 2 authors in accordance with the Newcastle–Ottawa scale for nonrandomized studies.[22] The NOS contains 3 categories (selection, comparability, and outcome) and eight items. In the selection and outcome categories, a quality research item received one star, and a comparable category could receive at most 2 stars. In the selection part, studies that precisely described the item (i.e., those drawn from the same community as the exposed cohort with secure records and a demonstration that outcome of interest was not present at start of the study) received one star. Regarding comparability, 2 items (i.e., study controls as the most important factor, and study controls as an additional factor) could receive a star if the study was eligible. In the outcome portion, various items (i.e., outcome assessments, a follow-up that was sufficiently long for outcomes to occur, and adequate follow up of cohorts) could elicit one star each if the study presented the corresponding details. The full score was 9 stars. We assigned scores of 0–3, 4–6, and 7–9 for low-, moderate-, and high-quality studies, respectively.[23,24]

2.5. Statistical analysis

The level of statistical significance for the two-tailed test of each hypothesis was 0.05. All statistical analyses were conducted using the Review Manager version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK) and Stata version 11.0 (Stata Corporation, College Station, TX). The measure of interest was the OR (odds ratio). When available, adjusted ratios were extracted. We combined these estimates by using a random-effects model, which takes into account both within- and between-study variabilities.[25] A P value of $<.10$ was used to indicate the lack of homogeneity (heterogeneity) among the effects. We also calculated the I^2 statistics, a quantitative measure of inconsistency across studies.[26] If evidence of heterogeneity was found, stratified syntheses and sensitivity analyses were performed to explain what contributed to the heterogeneity. We performed predefined stratified analyses in accordance with the study design (prospective cohort vs retrospective cohort), surgery type (CABG vs CABG ± valve replacement), and country (USA vs non-USA). We calculated linear P for trend and P for interaction for stratified analyses. Potential publication bias was assessed based on Begg's test and the symmetry of the funnel plot.[26–28]

3. Results

3.1. Literature search

In the electronic database searches, 991 unique records were identified. Of these records, 977 were excluded on the basis of the title and abstract content. Fourteen articles were subjected to full-length article review. Based on the abstract and full text, 6 of the records were excluded for clearly not fulfilling the inclusion criteria, which included article type, original data, population, or outcome of interest. Finally, 8 cohort studies (4 retrospective cohort studies and 4 prospective cohort studies) involving 7401 AF cases and 31,069 participants met the criteria for inclusion[8,14–20] (Fig. 1). The eligible studies were published between 2006 and 2016. The study characteristics and quality assessment scores are summarized in Table 1 and Supplementary Table 1, http://links.lww.com/MD/C145.

Table 1

Study characteristics.

First author, publication (year)	Country	Participants n (% male)	AF cases (n)	Type of surgery	Study period, years	Type of blood products	Cross-clamping time, minutes	CPB duration, minutes	Study design
Koch et al[11] (2006)	USA	5,841 (68.4)	2,305	CABG ± VR	2002–2005	RBC	75 ± 57.95 versus 69 ± 53.86	NA	PC
Whitson *et al.*[12] (2007)	USA	2,691 (68.6)	683	CABG ± VR	2002–2005	NA	88 versus 78	128 versus 114	PC
Choi et al[13] (2009)	Korea	315 (71.4)	66	CABG	2007–2008	RBC	NA	NA	PC
Topal et al[14] (2011)	Turkey	98 (55.1)	34	CABG	NA–2010	RBC	46.2 ± 37.7 versus 29.0 ± 13.9	74.5 ± 48.8 versus 48.7 ± 23.5	RC
Dorneles et al[15] (2011)	Brazil	4,028 (62.9)	309	CABG ± VR	1996–2009	RBC	NA	357 ± 11.5 versus 196 ± 21.4	RC
Paone et al[16] (2014)	USA	16,835 (78.6)	3,654	CABG	2008–2011	RBC	NA	NA	RC
Alameddine et al[17] (2014)	USA	815 (77.4)	239	CABG	2008–2010	RBC	82.1 ± 31.7 versus 78.2 ± 26.5	115.3 ± 37.2 versus 111 ± 32.8	RC
Vlahou et al[18] (2016)	Greece	446 (85)	111	CABG	2012–2014	RBC	69.1 ± 24.8 versus 65 ± 23.07	97.8 ± 36.1 versus 91.1 ± 34.1	PC

AF = atrial fibrillation, CABG = coronary artery bypass grafting, CPB = cardiopulmonary bypass, NA = not available, PC = prospective cohort, RBC = red blood cells, RC = retrospective cohort, VR = valve replacement.

3.2. Blood transfusion and postoperative atrial fibrillation risk

Pooling the results of individual studies, blood product transfusion in adult patients who underwent CABG surgery was associated with an increased risk of developing postoperative AF (OR, 1.45; 95% CI, 1.26–1.67; Fig. 2). Evidence of significant heterogeneity in the magnitude of the association across studies was found (P for heterogeneity $< .0001$, $I^2 = 79\%$). No evidence was detected for publication bias by inspection of the funnel plot and formal statistical tests (Begg's test, $P = .174$; Supplementary Fig. 1, http://links.lww.com/MD/C145).

3.3. Stratified analysis

The results of the stratified analyses are presented in Table 2. After stratification by surgery type, the associations between BT and risk of postoperative AF were established to be similar between the adult patients who underwent CABG surgery (OR, 1.59; 95% CI, 1.17–2.14; n = 5) and CABG ± VR (OR, 1.40; 95% CI, 1.17–1.69; n = 3). The pooled OR of AF were 1.34 (95% CI, 1.18–1.51; n = 4) for studies conducted in the United States and 1.82 (95% CI, 1.15–2.89; n = 4) for studies conducted in the non-United States countries. After stratification by study design, BT was associated with an increased risk of postoperative AF in both subgroups (prospective and retrospective cohorts).

3.4. Sensitivity analysis

The robustness of our results was evaluated by using sensitivity analysis. When studies included in the meta-analysis were deleted one at a time, the results remained largely unchanged, indicating that these results were stable (data not shown). Exclusion of studies that included off-pump CABG yielded a pooled OR of 1.36 (95% CI, 1.23–1.50; n = 7). Restricting analysis to studies that reported blood products yielded a pooled OR of 1.39 (95% CI, 1.21–1.61; n = 7), with substantial heterogeneity ($P = .0003$; $I^2 = 76\%$). Further analyses that examined the influence of a single study on the results by omitting a study at each turn yielded an OR ranging from 1.36 to 1.53.

4. Discussion

In this present meta-analysis, we reviewed eight cohort studies regarding the association between BT and risk of postoperative AF in adult patients who had undergone a CABG surgery. The pooled results using a random-effects model demonstrated a significant association between BT and postoperative AF with an overall 1.45-fold (95% CI, 1.26–1.67) increased risk in comparison with that in the non-BT participants. The increased risk was consistently observed across the studies but did not reach statistical significance in one study.[20]

4.1. Results in relation to other studies

To date, the relationship between BT and the risk of postoperative AF in adult patients who had undergone CABG surgery is controversial, and the results of the observational studies have been inconsistent. Similar to our findings, several studies have demonstrated an increased risk of postoperative AF in patients with BT.[8,14–20] In particular, a retrospective cohort study showed that BT was associated with the incidence of AF after CABG surgery (adjusted OR, 1.36; 95% CI, 1.11–1.68).[19] It is noteworthy that this risk increases with the increase in the

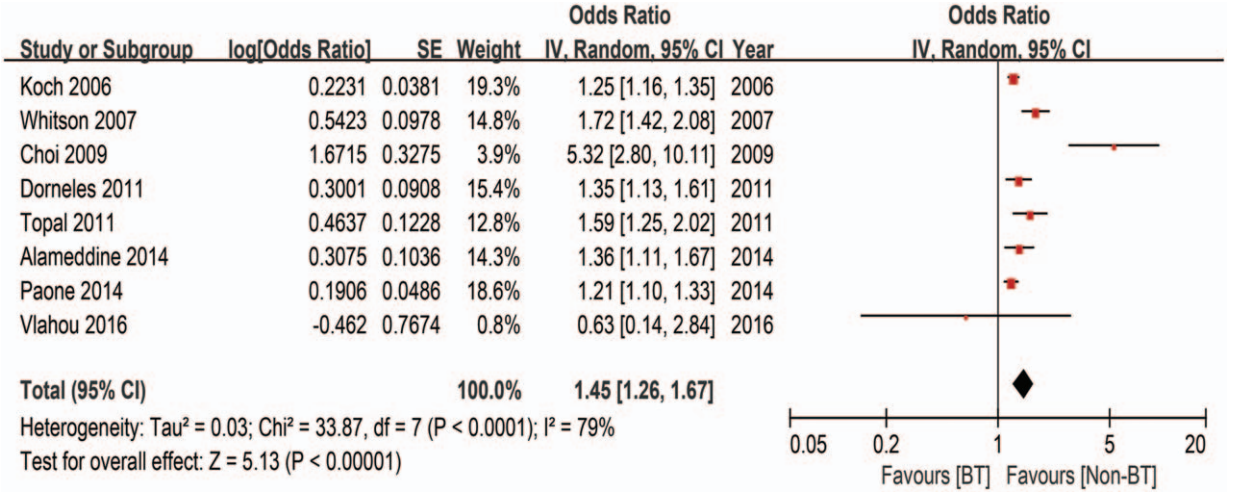

Figure 2. Forest plot showing the pooled odds ratio for postoperative AF after CABG. AF = atrial fibrillation, CABG = coronary artery bypass grafting, BT = blood transfusion.

number of BTs. Nevertheless, another study that investigated BT failed to demonstrate an association with postoperative AF.[20] Moreover, patients from this observational study did not receive transfusion regardless of hematocrit level and were probably predisposed to danger that would have been preventable. Hematocrit level has been shown to be a strong predictor of adverse outcomes in CABG surgery.[29] This may partly explain the inconsistency of the earlier findings. In addition, the authors also reported that this possible association was a result of the poor health status of the patients in the preoperative period and suggested the importance of a careful preoperative evaluation because it can reduce the risk of bleeding and the need for blood transfusion during the postoperative period.[17]

4.2. Potential mechanism

The increased risk of postoperative AF events in patients with BT is not well understood. A previous work that used animal models showed that when activated, neutrophils bind to cardiac myocytes, thereby causing changes in myocyte electrical activity that could be arrhythmogenic.[30] CPB can lead to the production of different proinflammatory mediators alongside widespread endothelial activation with increased expression of adhesion molecules and impaired release of nitric oxide. RBCs can be stored for up to 42 days before transfusion. Many biochemical and morphological alterations are progressively occurring during RBCs storage, such as impairment of nitric-oxide-mediated functions, depletion of adenosine triphosphate and 2,3-diphosphoglycerate, and increased lipid peroxidation. Moreover, the heart is exposed to proinflammatory cytokines invoked by heart ischemia or trauma, which triggers the release of oxygen radicals and depletion of plasma antioxidants. As a result, the inflammatory reaction leads to electrophysiological alterations in atrial myocytes. The increased levels of interleukin 6 (IL-6), tumor necrosis factor α (TNF-α), and C-reactive protein (CRP) have all been associated with postoperative AF.[31–33] Transforming growth factor beta 1 (TGF-β1) has also been implicated in the pathology of AF in animal models.

Table 2

Stratified analyses of blood transfusion and atrial fibrillation risk.

Group	No. of studies	Test of association		Heterogeneity test			
		OR (95% CI)	*P*-value	Q^2	*P*-value	I^2, %	P^* for interaction
All studies	8	1.45 (1.26–1.67)	<.00001	33.87	<.0001	79	
			Surgery type				<.00001
CABG	5	1.59 (1.17–2.14)	.003	24.46	<.0001	84	
CABG ± VR	3	1.40 (1.17–1.69)	.0003	9.38	.009	79	
			Study design				<.00001
PC	4	1.80 (1.17–2.76)	.007	28.41	<.00001	89	
RC	4	1.33 (1.19–1.48)	<.00001	5.13	.16	42	
			Country				<.00001
USA	4	1.34 (1.18–1.51)	<.00001	11.19	.01	73	
Non-USA	4	1.82 (1.15–2.89)	.01	17.78	.0005	83	
RBC transfusion							.08
Yes	7	1.39 (1.21–1.61)	<.00001	25.31	.0003	76	
No	1	1.72 (1.42–2.08)	<.00001	NA	NA	NA	

CABG = coronary artery bypass grafting, CI = confidence interval, NA = not applicable, OR = odds ratio, PC = prospective cohort, RBC = red blood cells, RC = retrospective cohort, VR = valve replacement.
P^* for interaction was utilized to assess the stratified differences.

The analysis of human right atrial tissue has demonstrated the presence of higher levels of total and active TGF-β1 in patients who developed postoperative AF than in patients who remained in sinus rhythm.[34] The impact of TGF-β1 on the development of postoperative AF may be related to the possibility that the factor can promote the expression of fibrosis-related genes in a Smad2-related pathway.[35] Furthermore, the renin-angiotensin-aldosterone (RAA) system may have a key role in the development of AF.[36,37] On the other hand, many preoperative and intraoperative factors, such as increased age, diabetes mellitus, kidney disease, central nervous system and lung diseases, atrial cannulation, CPB, type of cardioplegia, impaired left ventricular function, and peripheral vascular disease, have been associated with postoperative AF.[38,39]

4.3. Clinical implications

Nonetheless, we do not hesitate to suggest that aggressive attempts at BT are warranted. The measurements of serum iron and the preoperative administration of iron and preoperative erythropoietin may reduce the need for hemoderivatives.[40] Koch et al[8] demonstrated that the transfusions of fresh frozen plasma and platelets exerts the same effects in patients with CAGS. Based on our findings, we can conclude that if a patient requires a blood transfusion during or post-CAGS, the comprehensive strategy for BT should be evaluated regarding the development of other postoperative complications but not the new onset of postoperative AF.

Even though 8 included studies were of high quality, some limitations remained. Thus, the results of this research should be interpreted with caution. First, in all of the included studies, the patients received RBC transfusion, but the storage time of the transfused RBCs, and the volume and rate of transfusion were not considered. Second, this is a meta-analysis of observational studies that, at the best, can demonstrate an association but cannot establish cause and effect. Therefore, we cannot be certain that BT itself in comparison with other potential confounding factors (e.g., hemoderivatives, oxygen concentration, and temperature) was the cause of the increased postoperative AF risk. Furthermore, these studies were at risk of detection bias, as the patients in their cohorts, because of their myopathy, were exposed to more medical examinations and investigations, and thus to a higher likelihood of AF prevention. Finally, another possible limitation is due to language bias. We attempted to minimize this bias by searching 3 major electronic databases with no language restriction. However, some articles published in Chinese or other non-English languages might not have appeared in international journal databases and could have been missed by our searches.

5. Conclusion

The findings of the present meta-analysis demonstrate a statistically significant higher postoperative AF risk among adult patients with BT. Further prospective large-scale studies are needed to establish causality and to elucidate the underlying mechanisms.

Acknowledgments

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Appendix: PubMed search terms

#1: Search "Coronary Artery Bypass"[Mesh] Sort by: Relevance

#2: Search ((((((((((Artery Bypass, Coronary[Title/Abstract]) OR Artery Bypasses, Coronary[Title/Abstract]) OR Bypasses, Coronary Artery[Title/Abstract]) OR Coronary Artery Bypasses [Title/Abstract]) OR Coronary Artery Bypass Surgery[Title/Abstract]) OR Bypass, Coronary Artery[Title/Abstract]) OR Aortocoronary Bypasses[Title/Abstract]) OR Aortocoronary Bypass[Title/Abstract]) OR Bypass, Aortocoronary[Title/Abstract]) OR Bypasses, Aortocoronary[Title/Abstract]) OR Bypass Surgery, Coronary Artery[Title/Abstract]) OR Coronary Artery Bypass Grafting[Title/Abstract] Sort by: Relevance

#3: #1 OR #2

#4: Search "Atrial Fibrillation"[Mesh] Sort by: Relevance

#5: Search ((((((((((((((((((((((((Fibrillation, Atrial[Title/Abstract]) OR Fibrillations, Atrial[Title/Abstract]) OR Auricular Fibrillation[Title/Abstract]) OR Atrial Fibrillations[Title/Abstract]) OR Auricular Fibrillations[Title/Abstract]) OR Fibrillation, Auricular[Title/Abstract]) OR Fibrillations, Auricular[Title/Abstract]) OR Persistent Atrial Fibrillation[Title/Abstract]) OR Atrial Fibrillation, Persistent[Title/Abstract]) OR Atrial Fibrillations, Persistent[Title/Abstract]) OR Fibrillation, Persistent Atrial [Title/Abstract]) OR Fibrillations, Persistent Atrial[Title/Abstract]) OR Persistent Atrial Fibrillations[Title/Abstract]) OR Familial Atrial Fibrillation[Title/Abstract]) OR Atrial Fibrillation, Familial[Title/Abstract]) OR Atrial Fibrillations, Familial [Title/Abstract]) OR Familial Atrial Fibrillations[Title/Abstract]) OR Fibrillation, Familial Atrial[Title/Abstract]) OR Fibrillations, Familial Atrial[Title/Abstract]) OR Paroxysmal Atrial Fibrillation[Title/Abstract]) OR Atrial Fibrillation, Paroxysmal[Title/Abstract]) OR Paroxysmal Atrial Fibrillations[Title/Abstract]) OR Fibrillations, Paroxysmal Atrial[Title/Abstract]) OR Fibrillation, Paroxysmal Atrial[Title/Abstract]) OR Atrial Fibrillations, Paroxysmal[Title/Abstract] Sort by: Relevance

#6: #4 OR #5

#7: Search "Blood Transfusion"[Mesh] OR "Blood Component Transfusion"[Mesh] OR "Blood Transfusion, Autologous"[Mesh] OR "Blood Transfusion, Intrauterine"[Mesh] OR "Platelet Transfusion"[Mesh] Sort by: Relevance

#8: Search ((Transfusion, Blood[Title/Abstract]) OR Transfusions, Blood[Title/Abstract]) OR Blood Transfusions[Title/Abstract] Sort by: Relevance

#9: #7 OR #8

#10: Search "Erythrocyte Transfusion"[Mesh] Sort by: Relevance

#11: Search ((((((Erythrocyte Transfusions[Title/Abstract]) OR Transfusion, Erythrocyte[Title/Abstract]) OR Transfusions, Erythrocyte[Title/Abstract]) OR Red Blood Cell Transfusion [Title/Abstract]) OR Transfusions, Red Blood Cell[Title/Abstract]) OR Transfusion, Red Blood Cell[Title/Abstract]) OR Red Blood Cell Transfusions[Title/Abstract] Sort by: Relevance

#12: #10 OR #11

#13: #12 OR #9

#14: #13 AND #3 AND #6

References

[1] Tran DT, Perry JJ, Dupuis JY, et al. Predicting new-onset postoperative atrial fibrillation in cardiac surgery patients. J Cardiothorac Vasc Anesth 2015;29:1117–26.

[2] Hogue CW Jr, Hyder ML. Atrial fibrillation after cardiac operation: risks, mechanisms, and treatment. Ann Thorac Surg 2000;69:300–6.

[3] Lahtinen J, Biancari F, Salmela E, et al. Postoperative atrial fibrillation is a major cause of stroke after on-pump coronary artery bypass surgery. Ann Thorac Surg 2004;77:1241–4.
[4] Fuller JA, Adams GG, Buxton B. Atrial fibrillation after coronary artery bypass grafting. Is it a disorder of the elderly? J Thorac Cardiovasc Surg 1989;97:821–5.
[5] Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. Circulation 1996;94:390–7.
[6] Patel D, Gillinov MA, Natale A. Atrial fibrillation after cardiac surgery: where are we now? Indian Pacing Electrophysiol J 2008;8:281–91.
[7] Steinberg JS. Postoperative atrial fibrillation: a billion-dollar problem. J Am Coll Cardiol 2004;43:1001–3.
[8] Koch CG, Li L, Van Wagoner DR, et al. Red cell transfusion is associated with an increased risk for postoperative atrial fibrillation. Ann Thorac Surg 2006;82:1747–56.
[9] Purohit A, Rokita AG, Guan X, et al. Oxidized Ca(2+)/calmodulin-dependent protein kinase II triggers atrial fibrillation. Circulation 2013;128:1748–57.
[10] Xie W, Santulli G, Reiken SR, et al. Mitochondrial oxidative stress promotes atrial fibrillation. Sci Rep 2015;5:11427.
[11] Fransen E, Maessen J, Dentener M, et al. Impact of blood transfusions on inflammatory mediator release in patients undergoing cardiac surgery. Chest 1999;116:1233–9.
[12] Xiong Z, Cavaretta J, Qu L, et al. Red blood cell microparticles show altered inflammatory chemokine binding and release ligand upon interaction with platelets. Transfusion 2011;51:610–21.
[13] Belizaire RM, Prakash PS, Richter JR, et al. Microparticles from stored red blood cells activate neutrophils and cause lung injury after hemorrhage and resuscitation. J Am Coll Surg 2012;214:648–55. discussion 656-647.
[14] Whitson BA, Huddleston SJ, Savik K, et al. Bloodless cardiac surgery is associated with decreased morbidity and mortality. J Card Surg 2007;22: 373–8.
[15] Choi YS, Shim JK, Hong SW, et al. Risk factors of atrial fibrillation following off-pump coronary artery bypass graft surgery: predictive value of C-reactive protein and transfusion requirement. Eur J Cardiothorac Surg 2009;36:838–43.
[16] Topal AE, Eren MN. Predictors of atrial fibrillation occurrence after coronary artery bypass graft surgery. Gen Thorac Cardiovasc Surg 2011;59:254–60.
[17] Dorneles Cde C, Bodanese LC, Guaragna JC, et al. The impact of blood transfusion on morbidity and mortality after cardiac surgery. Rev Bras Cir Cardiovasc 2011;26:222–9.
[18] Paone G, Likosky DS, Brewer R, et al. Transfusion of 1 and 2 units of red blood cells is associated with increased morbidity and mortality. Ann Thorac Surg 2014;97:87–93. discussion 93-84.
[19] Alameddine AK, Visintainer P, Alimov VK, et al. Blood transfusion and the risk of atrial fibrillation after cardiac surgery. J Card Surg 2014;29: 593–9.
[20] Vlahou A, Diplaris K, Ampatzidou F, et al. The role of blood transfusion in the development of atrial fibrillation after coronary artery bypass grafting. Thorac Cardiovasc Surg 2016;64:688–92.
[21] Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008–12.
[22] Stang A. Critical evaluation of the Newcastle–Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25:603–5.
[23] Wang F, Zhou J, Zhang Y, et al. The value of MicroRNA-155 as a prognostic factor for survival in non-small cell lung cancer: a meta-analysis. PLoS One 2015;10:e0136889.
[24] Wells G, Shea B, O'Connell D. The Newcastle–Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Metaanalyses. Ottawa Hospital Research Institute, Ottawa (ON):2009.
[25] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.
[26] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.
[27] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.
[28] Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50:1088–101.
[29] Williams ML, He X, Rankin JS, et al. Preoperative hematocrit is a powerful predictor of adverse outcomes in coronary artery bypass graft surgery: a report from the Society of Thoracic Surgeons Adult Cardiac Surgery Database. Ann Thorac Surg 2013;96:1628–34. discussion 1634.
[30] Hoffman BF, Feinmark SJ, Guo SD. Electrophysiologic effects of interactions between activated canine neutrophils and cardiac myocytes. J Cardiovasc Electrophysiol 1997;8:679–87.
[31] Ucar HI, Tok M, Atalar E, et al. Predictive significance of plasma levels of interleukin-6 and high-sensitivity C-reactive protein in atrial fibrillation after coronary artery bypass surgery. Heart Surg Forum 2007;10:E131–135.
[32] Elahi MM, Flatman S, Matata BM. Tracing the origins of postoperative atrial fibrillation: the concept of oxidative stress-mediated myocardial injury phenomenon. Eur J Cardiovasc Prev Rehabil 2008;15:735–41.
[33] Wu N, Xu B, Xiang Y, et al. Association of inflammatory factors with occurrence and recurrence of atrial fibrillation: a meta-analysis. Int J Cardiol 2013;169:62–72.
[34] Polejaeva IA, Ranjan R, Davies CJ, et al. Increased susceptibility to atrial fibrillation secondary to atrial fibrosis in transgenic goats expressing transforming growth factor-beta1. J Cardiovasc Electrophysiol 2016;27: 1220–9.
[35] Rahmutula D, Marcus GM, Wilson EE, et al. Molecular basis of selective atrial fibrosis due to overexpression of transforming growth factor-beta1. Cardiovasc Res 2013;99:769–79.
[36] Hornero F, Rodríguez I, Bueno M, et al. Surgical ablation of permanent atrial fibrillation by means of maze radiofrequency: mid-term results. J Card Surg 2004;19:383–8.
[37] Kirchhof P, Schotten U. Hypertension begets hypertrophy begets atrial fibrillation? Insights from yet another sheep modelThe opinions expressed in this article are not necessarily those of the Editors of the European Heart Journal or of the European Society of Cardiology. Eur Heart J 2006;27:2919.
[38] Hakala T, Pitkanen O, Hartikainen J. Cardioplegic arrest does not increase the risk of atrial fibrillation after coronary artery bypass surgery. Eur J Cardiothorac Surg 2004;25:415–8.
[39] Helgadottir S, Sigurdsson MI, Ingvarsdottir IL, et al. Atrial fibrillation following cardiac surgery: risk analysis and long-term survival. J Cardiothorac Surg 2012;7:87.
[40] Souza HJBD, Moitinho RF. Estratégias para redução do uso de hemoderivados em cirurgia cardiovascular. Revista Brasileira De Cirurgia Cardiovascular 2008;23:53–9.