



# **Transfusion Strategy and Postoperative Complications in Adults Undergoing Cardiac and Vascular Surgery: Systematic Review and Meta-analysis**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. Authors LGL and GCRG performed conceptualization, methodology, investigation, writing – original draft, formal analysis, writing - review and editing. Author MP performed the statistical analysis. Author MMSN performed conceptualization, methodology, formal analysis, writing - review and editing. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Background:** Bleeding is frequent in cardiac and vascular surgery (CVS) having a greater need for transfusion. Studies have observed an increase in complications in transfused patients, and in this context the use of a liberal strategy (LS) was questioned, and a restrictive strategy (RS) gained space in the scientific environment. However, the effects of these strategies remain uncertain. This study aimed to verify if there is an association between the transfusion strategy and the occurrence of postoperative complications in adult patients undergoing CVS.

**Methodology:** Searches were performed in four databases and manually. The selection was made from studies with adult patients who underwent CVS that required transfusion, and the

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outcome variable was the complications arising from this procedure. The languages were restricted to Portuguese and English. The Stata software was used for meta-analysis.

**Results:** Six publications, involving 6,187 patients, were included. In four studies there was no evidence that the risk of mortality and adverse events differed among patients allocated to an RS transfusion versus an LS. On the other hand, two studies raised a possible RS inferiority, however, the meta-analysis demonstrated no statistically significant difference between the two strategies. Furthermore, another study also suggested that the number of red blood cell units transfused was an independent risk factor for the occurrence of complications.

**Conclusions:** RS is not inferior to LS in terms of postoperative complications in CVS, but other randomized clinical trials are necessary to better define the minimum allowed value for the RS.

*Keywords: Blood transfusion; liberal transfusion strategy; restrictive transfusion strategy; cardiac surgical procedures; vascular surgical procedures; postoperative complications; adult patients.*

## 1. INTRODUCTION

A rapid development in many different areas of medicine has been observed [1]. In this context, cardiac and vascular surgery (CVS) have been studied intensively, having in the present scenario a solid situation with great professionals and centers [2]. Moreover, the number of surgeries is increasing, having for example, the average from the reference center Heart Institute of the Clinical Hospital of the Medical School of the University of São Paulo (InCor-HCFMUSP), which is 2,971 operations/year [3]. However, despite all technological advances and the experience gathered from the scientific environment, [1] the mortality rate resulting from CVS has reduced but remains high (around 7.0% in Brazil) [3-6].

In this perspective, bleeding remains a frequent complication in CVS, [7,8] which is why this procedure is associated with a greater need for transfusion [9-11]. The rational use of blood components in situations of significant morbidity or mortality can save lives and improve patient's health; on the other hand, indiscriminate use can be deleterious and increase the costs of public and private health services [12-14].

In some transfusion safety and efficacy studies of patients undergoing CVS, a greater number of complications can be observed in transfused patients [11,15-17]. Among them are immunological and non-immunological transfusion reactions, transmission of viral infections, renal failure, atrial fibrillation, acute myocardial infarction, stroke, and even risk of death [13,14,16-20].

Given this scenario of unfavorable clinical outcomes in transfused patients, an increasing

amount of research on this practice is observed, implying a constant reassessment. A prospective randomized and controlled study by Hébert PC et al. which analyzed the use of a LS (Hemoglobin [Hb]. <10 g/dL) and an RS (Hb <7 g/dL) in a population of 838 critical ill patients, concluded that RS is as effective as and possibly superior than a LS [21]. Furthermore, it indicates that maintaining hemoglobin values in the range of 7–9 g / dL reduced the average number of red blood cells transfused by 54%, concluding that the strategies previously proposed lead to the abusive use of blood components [21].

Conversely, in the meta-analysis “*Restrictive versus Liberal Transfusion Strategy in the Perioperative and Acute Care Settings*” with randomized studies involving critically ill patients, Hovaguimian F. et al. demonstrated an increased trend towards mortality in the RS group [22]. Those with cardiovascular disease undergoing a cardiac or vascular procedure assigned to the RS group presented a higher number of events related to inadequate oxygen supply and a higher mortality rate [22].

The ideal practice of using blood components is still widely discussed and diverges in literature. Moreover, transfusion therapy should not be performed according to arbitrary values [23]. Clinical and laboratory parameters are necessary, and an individualized assessment is imperative [23] to decide the best surgical strategy and therefore, to obtain better results in terms of reducing the patient's morbidity and mortality after CVS. Thus, this study aims to verify whether there is an association between the transfusion strategy (liberal or restrictive) and the occurrence of postoperative complications in adult patients undergoing CVS.

## 2. METHODOLOGY

To describe the results of this systematic review and meta-analysis the recommendation of the Main Items for Reporting Systematic Reviews and Meta-analysis (PRISMA) was used [24]. This study is registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the number CRD42020195779.

Once it is a systematic review and meta-analysis, there is no conflict of interest and therefore, submission to the Research Ethics Committee (REC) is not required.

To standardize the careful evaluation of the methodological quality and risk of bias of the included studies, the instrument Joanna Briggs Institute - The University of Adelaide - was used [25]. All studies were independently scored by two researchers and in cases of discrepancy a third researcher was responsible for the final evaluation. The checklist for randomized clinical trial studies (13 items) was used. The item was not scored if the answer was "no", received 1 point when the answer was "not clear" and 2 points when the answer was "yes". A higher score indicated a better methodological quality, and a score above 70% of the maximum value to be reached [25] indicated a low risk of bias.

### 2.1 Eligibility Criteria

For the methodological basis, scientific articles were selected only from randomized clinical trials published between January 2000 and May 2020, which met the languages of Portuguese and English. There was no restriction on the minimum number of patients for each included study. The selection was made from studies with adult patients submitted to CVS who required blood transfusion and were allocated to groups of LS versus RS, and the outcome variable sought were the complications arising from this procedure.

In this systematic review and meta-analysis were excluded studies with patients under 18 years old, studies with titles not related to the subject of the research, studies that did not contain in the abstracts relevant data related to the research and duplicate studies.

### 2.2 Search Strategy

Researches were carried out in the following databases: PubMed (05/26/2020), Scielo

(05/27/2020), Cochrane (05/28/2020) and Lilacs (05/2/2020). They were performed using combined descriptors through Boolean operators present throughout the article. The terms used in this search are related to blood transfusion (blood transfusion OR red cell transfusion OR platelets transfusion OR plasma transfusion OR cryoprecipitate transfusion), transfusion strategy (AND liberal strategy OR restrictive strategy), complications (AND complications), cardiac and vascular surgery (AND cardiovascular surgery OR cardiac surgery OR vascular surgery) AND adult patients (appendix). In addition, in order to enrich the work and reduce the number of possible non-selected studies, there was a manual search from the references of the articles included in this systematic review.

### 2.3 Selection of Studies

The results of both searches were placed in a table in Excel to apply the eligibility criteria of this systematic review and meta-analysis. The first criteria evaluated was language and year, the second was duplicity of studies, the third was by the title of the study and the fourth was the summary of the study. All remaining studies were read thoroughly to check that they met all criteria and objective of this systematic review and meta-analysis.

### 2.4 Process of Data Collection

A table in Excel was used to standardize the important data for this systematic review and meta-analysis. In this table were included the identification, the design, the results, the conclusion and the quality of the study.

### 2.5 List of Data

The variables analyzed for this study were age, type of CVS, surgery status, transfusion threshold (RS or LS), transfused unit average, transfusion rate, hemoglobin or hematocrit concentration (preoperative and postoperative) and complications after transfusion. The PICO strategy [26] was applied: P - adult patient with some cardiac or vascular condition requiring surgery and transfusion; I - blood transfusion in the CVS according to RS; C - blood transfusion in the CVS according to LS; O - complications arising from the strategy used.

### 2.6 Statistical Analysis

The Stata software version 14.0 was used for meta-analysis. For each included study the

relative risk (RR) was calculated with 95% confidence intervals (CI) for dichotomous results. The RR calculation was LS/RS. The heterogeneity between studies was calculated with the Mantel-Haenszel chi-square test and the  $I^2$  test. Significant heterogeneity was defined as  $P < 0.10$  using the chi-square test, or an  $I^2 > 50%$  [27].

### 2.7 Summary of Results

The results were summarized in comparative figures and tables, in which the outcomes of adult patients submitted to CVS in which an RS was used versus the outcomes of LS, were analyzed.

### 3. RESULTS

The research strategy identified a total of 510 records. Two hundred and sixteen publications did not meet the inclusion criteria for the year of publication and language and eight were excluded for being duplicated publications. After screening the titles and abstracts, 16 articles were analyzed. Among them, 10 publications did not meet the eligibility criteria and therefore, were excluded. The remaining 6 publications were included in this systematic review and meta-analysis and have high methodological quality and low risk of bias (Fig. 1, Table 1, Table 2).

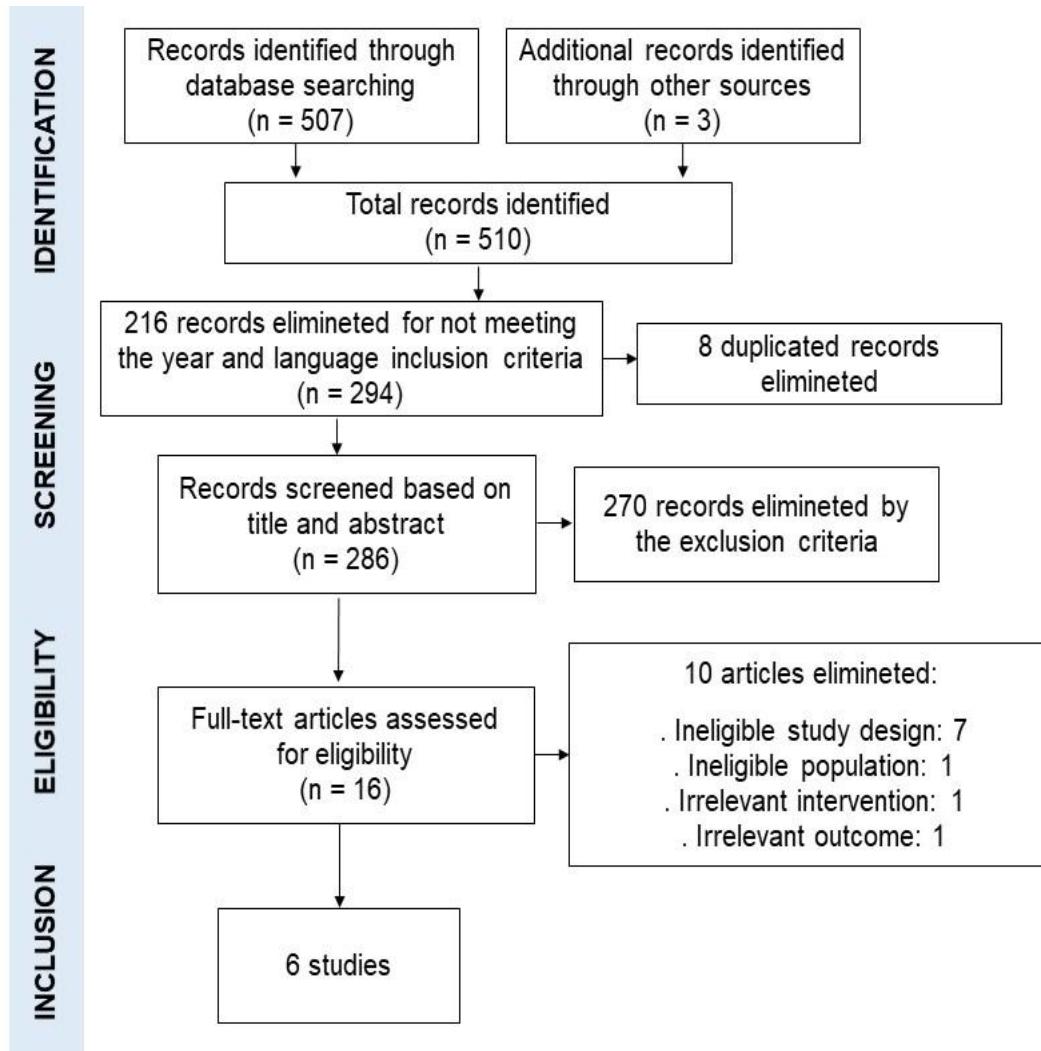


Fig. 1. Flowchart of selection of the studies

**Table 1. Studies included in the systematic review and meta-analysis**

Author and year of publication	Title of the article	Study type	Quality	Risk of bias
Hajjar LA et al. [11], 2010*	Transfusion requirements after cardiac surgery: the TRACS randomized controlled trial	Randomized clinical trial	24/26	Low
Shehata N et al. [28], 2012†	A randomized controlled pilot study of adherence to transfusion strategies in cardiac surgery	Randomized clinical trial	22/26	Low
Koch CG et al. [29], 2017†	A Randomized Clinical Trial of Red Blood Cell Transfusion Triggers in Cardiac Surgery	Randomized clinical trial	25/26	Low
Mazer CD et al. [30], 2017‡	Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery	Randomized clinical trial	24/26	Low
Mazer CD et al. [31], 2018‡	Six-Month Outcomes after Restrictive or Liberal Transfusion for Cardiac Surgery	Randomized clinical trial	22/26	Low
Møller A et al. [32], 2019*	Low vs high hemoglobin trigger for transfusion in vascular surgery: a randomized clinical feasibility trial	Randomized clinical trial	24/26	Low

\* Studies included by PubMed; † Studies included manually; ‡ Studies included by PubMed and Cochrane

### 3.1 Study Characteristics

The six records analyzed are randomized clinical trials that compared an RS to a LS in adult patients undergoing CVS [11,28-32]. The characteristics of the studies are represented in Table 3. The population studied are adult patients (>18 years old) who were scheduled to undergo an unit elective CVS; one article also used as inclusion criteria an “European System for Cardiac Operative Risk Evaluation” (EuroSCORE I) score of 6 or more [30], and another article, a “Cardiac Anesthesia Risk Evaluation” (CARE) score of 3 or 4 [28]. EuroSCORE I has a scale from 0 to 47 and higher scores indicate a higher risk of death after cardiac surgery [30]. CARE is a score for heart surgery patients used to predict both mortality and morbidity; CARE 3 is defined as patients with uncontrolled medical problems or patients in whom complex surgery is performed; CARE 4 is patients with any uncontrolled medical problem in whom complex surgery is performed [28].

In all studies, transfusion occurred intra and postoperatively, and there has been no report of transfusion reactions [11,28-32]. Moreover, in Shehata N et al. [28] and Moller A et al. [32] studies a lower percentage of transfusion adherence was reported in the LS group (41% adherence in the LS versus 84% in the RS [28]; 66% adherence in the LS versus 72% in the RS [32], respectively). Reasons for non-adherence included patient refusal, use of other parameters for transfusion other than the hemoglobin concentration [28] and failure to follow the

established transfusion threshold (transfusion occurred at a hemoglobin level above or below the allocated threshold or with undefined indications) [32].

### 3.2 Primary Outcomes

The studies by Hajjar LA et al. [11], Koch CG et al. [29] and Mazer CD et al. [30] determined as primary outcome a compound of death by any cause and severe morbidity occurring during hospitalization from the beginning of surgery until hospital discharge. The percentage of patients who had an event of the primary outcome varied from 11% to 16% in the RS group, compared to a variation of 10% to 19% in the LS group (Table 4) [11,29,30]. Mazer CD et al. [31] still in another study, evaluated the same primary outcomes after a period of six months after surgery, whose incidence was 17.4% in the RS group and 17.1% in the LS group (Table 4). There was no statistically significant difference between transfusion strategies in any of the other primary outcomes: non-fatal myocardial infarction, stroke, recent onset kidney failure with dialysis, cardiogenic shock, and adult respiratory distress syndrome [11,29-31].

The study by Moller A et al. [32] determined as primary outcome the mean hemoglobin after 15 days postoperatively and demonstrated a statistically significant difference between the means of the RS and the LS, being 9.46g/dL and 10.33g/dL, respectively. Moreover, the study also showed an increase in brain desaturation and vascular complications in patients undergoing an

RS, the latter occurring in 62% of patients in the RS group and 28% in the LS group (Table 4) [32]. Shehata N et al. [28] despite establishing the rate of adherence to transfusion strategies as a primary outcome, demonstrated that patients undergoing preoperative and intraoperative

anemia were at higher risk of suffering adverse events, such as neurological events, dialysis dependent renal failure or increase of more than 50% in creatinine, prolonged low output state, myocardial infarction and death.

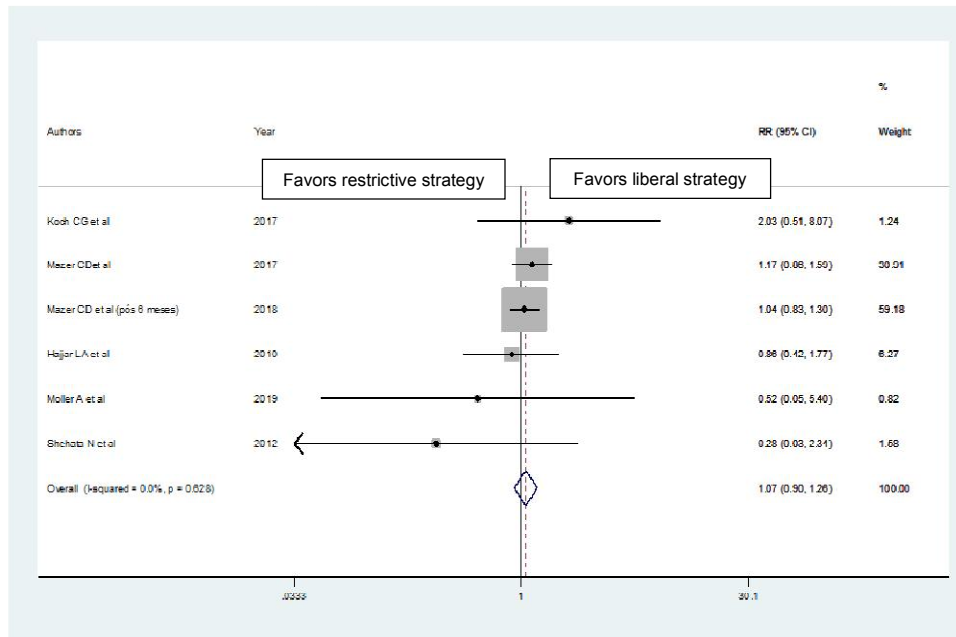


Fig. 2. Meta-analysis of mortality outcome (restrictive X liberal strategy)

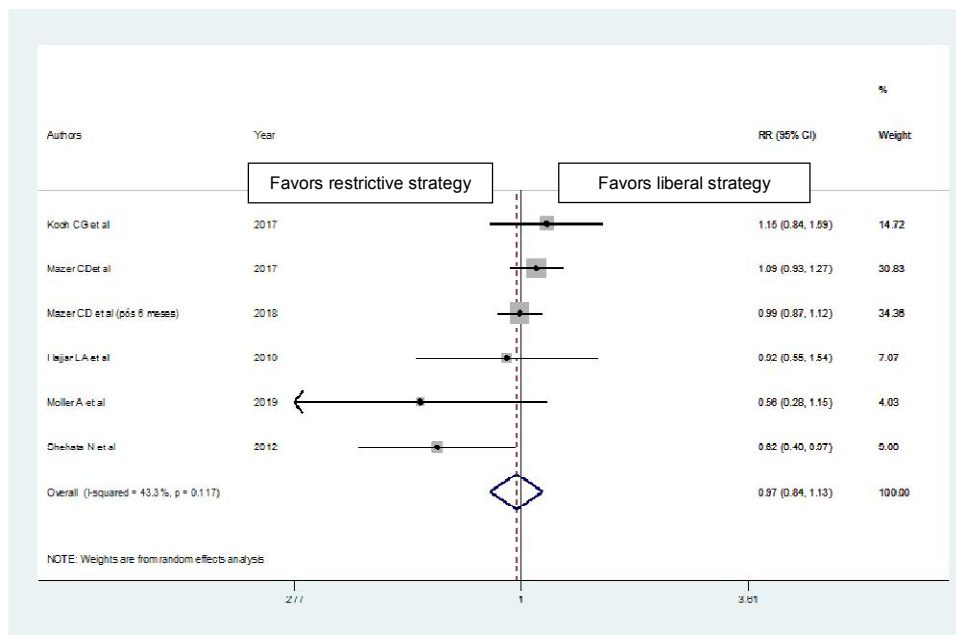


Fig. 3. Meta-analysis of adverse events outcome (restrictive X liberal strategy)

**Table 2. JBI Critical Appraisal Checklist for Randomized Controlled Trials of the studies included in the systematic review and meta-analysis**

	Hajjar LA et al. [11]	Shehata N et al. [28]	Koch CG et al. [29]	Mazer CD et al. [30]	Mazer CD et al. [31]	Møller A et al. [32]
1. Was true randomization used for assignment of participants to treatment groups?	YES	YES	YES	YES	YES	YES
2. Was allocation to treatment groups concealed?	YES	YES	YES	YES	YES	YES
3. Were treatment groups similar at the baseline?	YES	YES	YES	YES	YES	YES
4. Were participants blind to treatment assignment?	YES	UNCLEAR	YES	YES	YES	YES
5. Were those delivering treatment blind to treatment assignment?	NO	NO	UNCLEAR	NO	NO	NO
6. Were outcomes assessors blind to treatment assignment?	YES	UNCLEAR	YES	YES	YES	YES
7. Were treatment groups treated identically other than the intervention of interest?	YES	YES	YES	YES	UNCLEAR	YES
8. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	YES	YES	YES	YES	UNCLEAR	YES
9. Were participants analyzed in the groups to which they were randomized?	YES	YES	YES	YES	YES	YES
10. Were outcomes measured in the same way for treatment groups?	YES	YES	YES	YES	YES	YES
11. Were outcomes measured in a reliable way?	YES	YES	YES	YES	YES	YES
12. Was appropriate statistical analysis used?	YES	YES	YES	YES	YES	YES
13. Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	YES	YES	YES	YES	YES	YES

**Table 3. Characteristics of Studies Included in the Systematic Review and Meta-analysis**

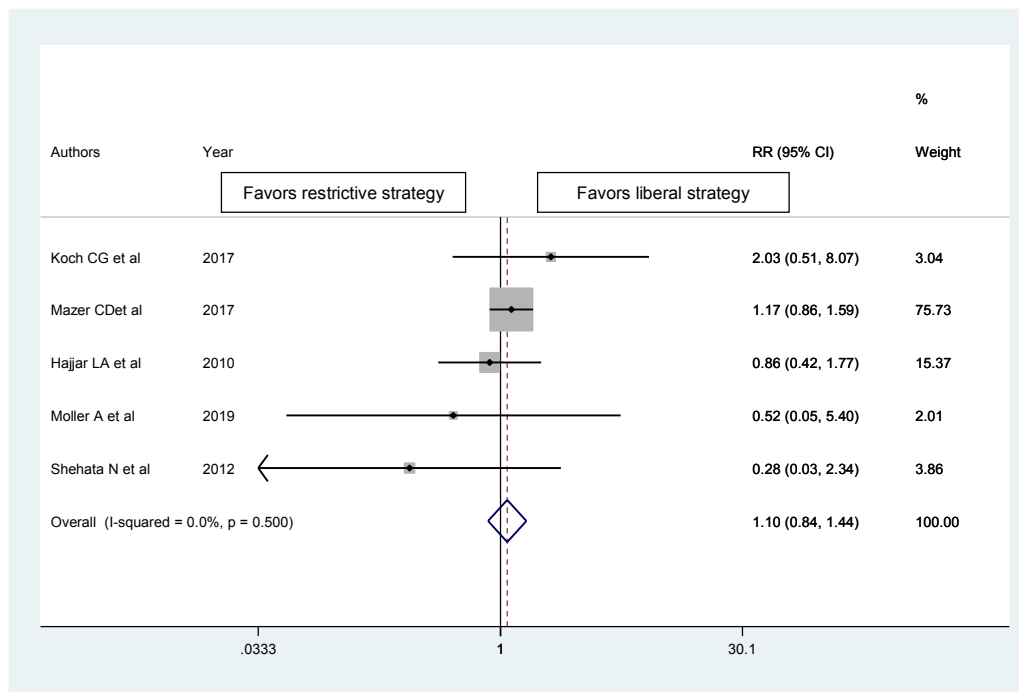
Study - n	Surgery	Age		Transfusion threshold		Average transfused unit		Transfusion rate		Concentration of Hb‡ or Hct§			
		Res*	Lib†	Res	Lib	Res	Lib	Res	Lib	Preoperative		Postoperative	
Hajjar LA et al. [11], 502	Elective myocardial revascularization surgery, repair and valve replacement or combination of the two	58.6	60.7	< 24% Hct	< 30% Hct	0 (0-2)	2 (1-3)	47%	78%	13.4 ± 1.8g/dL; 39.9% ± 5.2	13.1 ± 1.6g/dL; 39.5% ± 4.3	9.1g/dL; 28.4%	10.5g/dL; 31.8%
Shehata N et al. [28], 50	Cardiac surgery with a CARE score of 3 or 4, or age ≥ 80	67.2 ± 11.2	68.8 ± 9.2	≤ 7.0g/dL or ≤7.5g/dL	≤ 9.5g/dL or ≤ 10g/dL	3.8	4.5	52%	88%	14.1g/dL	13.8g/dL	9.1g/dL	10.7g/dL
Koch CG et al. [29], 717	Elective procedures for isolated heart valve, myocardial revascularization surgery with or without valve procedures and ascending aorta replacement performed on CPB <sup>  </sup>	59 ± 15	60 ± 13	< 24% Hct	< 28% Hct	—	—	54%	75%	37% (35-40)	38% (35-40)	22%	24%
Mazer CD et al. [30], 4,860	Elective cardiac surgery with CPB and EUROSCORE ≥ 6	72 ± 10	72 ± 10	< 7.5g/dL	< 9.5g/dL or < 8.5g/dL	2 (1-4)	3 (2-5)	52.3%	72.6%	13.1 ± 1.8g/dL	13.1 ± 1.7g/dL	Concentrations were separated by ± 1g/dL from ICU¶ admission up to 28th day	
Mazer CD et al. [31]. (after 6 months), 4,664/4,860	Elective cardiac surgery with CPB and EUROSCORE ≥ 6	72 ± 10	72 ± 10	< 7.5g/dL	< 9.5g/dL or < 8.5g/dL	2 (1-4)	3 (2-5)	52.3%	72.6%	13.1 ± 1.8g/dL	13.1 ± 1.7g/dL	Concentrations were separated by ± 1g/dL from ICU admission up to 28th day	
Møller A et al. [32], 58	Elective surgery to repair an open infra-renal abdominal aortic aneurysm or CPB	71.3 ± 9.4	73.7 ± 7.3	< 8.0g/dL	< 9.7g/dL	1 (0-2)	3 (2-6)	66%	100%	12.3 ± 1.8g/dL	12.4 ± 2.2g/dL	9.46g/dL	10.33g/dL

\* Restrictive transfusion strategy; † Liberal transfusion strategy; ‡ Hemoglobin; § Hematocrit; || Cardiopulmonar bypass; ¶ Intensive care Unit



**Table 4. Percentages of postoperative complications of the studies included in the systematic review and meta-analysis**

Study	Complications					
	Mortality			Adverse events		
	Restrictive	Liberal	P value	Restrictive	Liberal	P value
Hajjar LA et al. [11]	<b>6%</b> (CI 95%, 3% a 9%)	<b>5%</b> (CI 95%, 2% a 7%)	.93	<b>11%*</b> (CI 95%, 7% a 15%)	<b>10%*</b> (CI 95%, 6% a 13%)	.85
Shehata N et al. [28]	<b>16%</b>	<b>4%</b>	—	<b>38<sup>†</sup></b>	<b>15<sup>†</sup></b>	—
Koch CG et al. [29]	<b>0.8%</b>	<b>1.7%</b>	—	<b>16%</b>	<b>19%</b>	0.71
Mazer CD et al. [30]	<b>3%</b> (CI 95%, -1.54 a 0.47)	<b>3.6%</b> (CI 95%, 0.62 a 1.16)	—	<b>11.4%*</b> (CI 95%, -2.93 a 0.72)	<b>12.5%*</b> (CI 95%, 0.76 a 1.07)	< 0.001
Mazer CD et al. [31]. (after 6 months)	<b>6.2%</b>	<b>6.4%</b>	—	<b>17.4%*</b> (CI 95%, -1.95 a 2.39)	<b>17.1%*</b> (CI 95%, 0.87 a 1.18)	0.006
Møller A et al. [32]	<b>7%</b>	<b>3%</b>	0.426	<b>62%</b>	<b>28%</b>	0.007



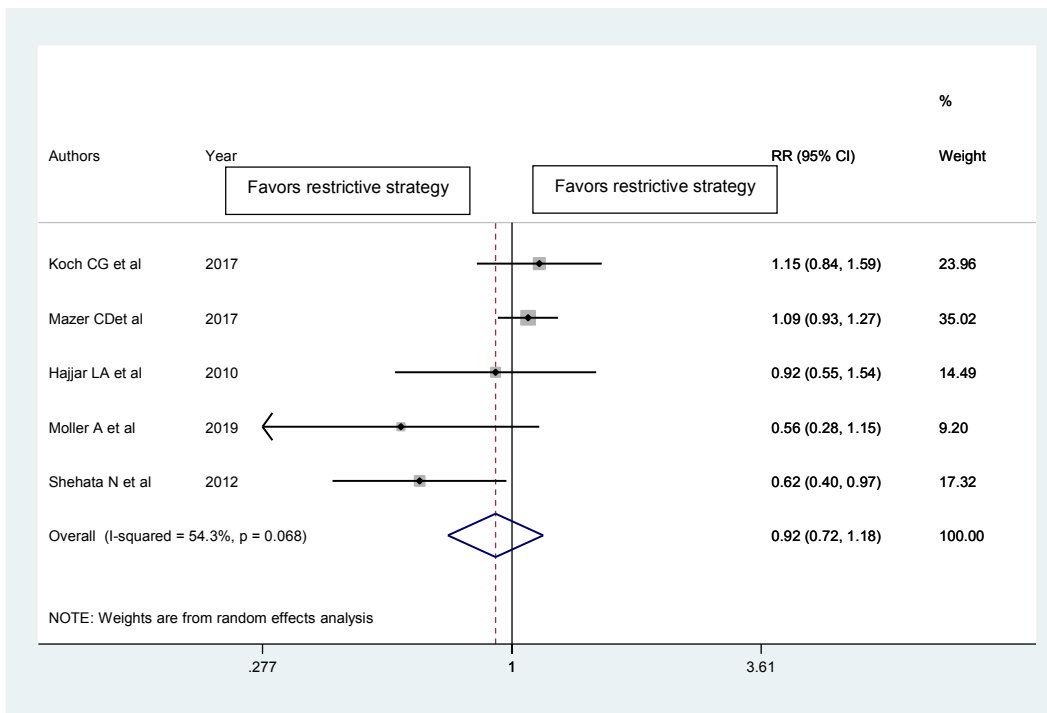
**Fig. 4. Meta-analysis of mortality outcome (restrictive X liberal strategy), without the study by Mazer CD et al. after six months**

The RS in the mortality outcome caused a total of 239 deaths (4.4%) among 5,384 patients allocated to this group [11,28-32]. In comparison, in the LS there were 257 deaths (4.8%) among 5,408 patients [11,28-32]. The meta-analysis demonstrated that the risk of mortality did not differ among the patients assigned to the RS versus the LS (RR = 1.07; 95% CI = 0.90, 1.26)

and the inconsistency test showed homogeneity ( $I^2 = 0.0\%$ ;  $P = 0.628$ ) - (Fig. 2).

In the outcome of adverse events, out of 5,386 allocated to the RS, 782 patients (14.5%) had some complications in the postoperative period, while in the LS there were 806 patients (14.9%) out of 5,412 [11,29-32]. Moreover, Shehata N et al. [28] in this outcome brought the total number

of adverse events, being 38 in the RS versus 15 in the LS. The meta-analysis showed that the risk of adverse events also did not differ between the transfusion strategy groups



**Fig. 5. Meta-analysis of adverse events outcome (restrictive X liberal strategy), without the study by Mazer CD et al. after six months**

(RR = 0.97; 95% CI = 0.84, 1.13) and the heterogeneity was low ( $I^2 = 43.3\%$ ;  $P = 0.117$ ) - (Fig. 3).

In order to exclude any possibility of bias, another meta-analysis was carried out not including the study by Mazer CD et al. [31], and the results found remained the same: the risk of mortality did not differ among the patients assigned to the RS versus the LS (RR = 1.10; 95% CI = 0.84, 1.44) and the inconsistency test showed homogeneity ( $I^2 = 0.0\%$ ;  $P = 0.500$ ) - (Fig. 4); the risk of adverse events also did not differ between the transfusion strategy groups (RR = 0.92; 95% CI = 0.72, 1.18) and the heterogeneity was low ( $I^2 = 54.3\%$ ;  $P = 0.068$ ) - (Fig. 5).

### 3.3 Secondary Outcomes

Patients allocated to the RS group were less transfused compared to LS patients [11,28-32]. Transfusion rates reported in the six studies ranged from 47% to 100% [11,28-32], and the mean number blood components and derivative

units transfused per patient ranged from zero to four and a half (0 - 4.5) in five studies [11,28,30-32]. One study did not report red blood cell transfusion units [29].

In addition, the study by Hajjar LA et al. [11] also concluded that the number of transfused red blood cell units was an independent risk factor for the occurrence of several clinical complications. For each unit transfused the risk of occurrence increased for respiratory, cardiac and renal complications, and the transfusion of 5 or more units was associated with higher mortality [11].

### 4. DISCUSSION

This meta-analysis demonstrated that an RS is not inferior to a LS in relation to the complications resulting from CVS in adult patient. In this context however, as well as other medical interventions, blood transfusion is not risk-free. On the other hand, anemia is also associated with several unfavorable results.

Based on the premise that blood transfusion is an independent predictor for morbidity (infections, ischemic outcomes, nosocomial pneumonia, renal failure, stroke) and mortality, both in the short and long term [13,16,33], the damage caused by it is probably more common and more severe than is generally evaluated and documented in the literature. Furthermore, due to the lack of well-established criteria many patients are still imprudently transfused. It is also important to emphasize that transfusion prolongs the length of stay in the intensive care unit and the postoperative length stay [13,33], leading to a greater use of resources and consequently, additional costs.

On the other hand, studies also show that anemia can cause higher mortality and increase the risk of fractures, kidney disease, heart failure, cardiovascular events, readmissions, worse graft outcome, worse functional status and lower quality of life [34]. However, the study *"The Transfusion Requirements in Critical Care"* (TRICC) demonstrated that even in critically ill anemic patients, an RS is as effective as a LS [21].

The meta-analysis of the studies in patients undergoing heart surgery, by Hajjar LA et al. [11], Koch CG et al. [29] and Mazer CD et al. [30] showed that there was no difference between the strategies in relation to mortality outcomes and adverse events, including long-term (six months after the procedure) [31]. Furthermore, in agreement with the literature and the study by Ergoren MC et al. [16], the Hajjar LA et al. [11] (TRACS) clinical trial demonstrated that the number of red blood cell unit transfused is an independent risk factor for worse outcomes.

In addition, it was possible to notice a reduced tendency of transfusion adherence in the LS group, suggesting a bias with great potential to influence the practice and results of the studies. Thus, although Shehata N et al. [28], in cardiac surgery, and Moller A et al. [32], in vascular surgery, showed a higher mortality rate and adverse events in the RS group, this divergence of results compared to the other articles is most likely due to greater exposure from the RS group to the transfusion practice, and consequently to postoperative complications. However, the meta-analysis of these studies also confirmed that there was no difference between the transfusion strategies in the analyzed outcomes.

In these conditions, knowing that in the LS group more patients receive a red blood cell's transfusion and more units of red blood cells [11,28-32], the RS group gains strength in a scenario where blood bags are scarce.

This systematic review with randomized clinical trial meta-analysis has some limitations. First of all, the number of people in the study samples were divergent and the adherence to the strategies was not uniform, which may be responsible for the controversies in the literature. Moreover, transfusion thresholds, both in the RS and LS groups, varied between trials and surgery types, and the adverse events listed differed in each study included, making it impossible to standardize the results. Another limitation of the study was the search restrictions in relation to the year and the language of the articles for selection.

## 5. CONCLUSION

In CVS, an RS is not inferior to a LS in the decision-making regarding blood transfusion in adult patients. However, an individual analysis of each patient's profile is important and essential in order to choose the strategy that provides the best results in the field of morbidity and mortality. In addition, further randomized clinical trials are necessary to better define the minimum value allowed for the RS in CVS.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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## APPENDIX

Search Strategy for PubMed, for example:

#1	(((((blood transfusion) OR (red cell transfusion)) OR (platelets transfusion)) OR (plasma transfusion)) OR (cryoprecipitate transfusion))
#2	(Liberal strategy) OR (restrictive strategy)
#3	complications
#4	((cardiovascular surgery) OR (cardiac surgery)) OR (vascular surgery)
#5	adults patients
#6	(((((#1) AND (#2)) AND (#3)) AND (#4)) AND (#5))
#6	("blood transfusion"[MeSH Terms]. OR ("blood"[All Fields]. AND "transfusion"[All Fields]) OR "blood transfusion"[All Fields]. OR (("erythrocytes"[MeSH Terms]. OR "erythrocytes"[All Fields]. OR ("red"[All Fields]. AND "cell"[All Fields]) OR "red cell"[All Fields]) AND ("blood transfusion"[MeSH Terms]. OR ("blood"[All Fields]. AND "transfusion"[All Fields]) OR "blood transfusion"[All Fields]. OR "transfusion"[All Fields]. OR "transfusions"[All Fields]. OR "transfusable"[All Fields]. OR "transfusate"[All Fields]. OR "transfuse"[All Fields]. OR "transfused"[All Fields]. OR "transfuses"[All Fields]. OR "transfusing"[All Fields]. OR "transfusion s"[All Fields])) OR ("platelet transfusion"[MeSH Terms]. OR ("platelet"[All Fields]. AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields]. OR ("platelets"[All Fields]. AND "transfusion"[All Fields]) OR "platelets transfusion"[All Fields]) OR (("plasma"[MeSH Terms]. OR "plasma"[All Fields]. OR "plasmas"[All Fields]. OR "plasma s"[All Fields]) AND ("blood transfusion"[MeSH Terms]. OR ("blood"[All Fields]. AND "transfusion"[All Fields]) OR "blood transfusion"[All Fields]. OR "transfusion"[All Fields]. OR "transfusions"[All Fields]. OR "transfusable"[All Fields]. OR "transfusate"[All Fields]. OR "transfuse"[All Fields]. OR "transfused"[All Fields]. OR "transfuses"[All Fields]. OR "transfusing"[All Fields]. OR "transfusion s"[All Fields])) OR (("cryoprecipitability"[All Fields]. OR "cryoprecipitable"[All Fields]. OR "cryoprecipitate"[All Fields]. OR "cryoprecipitated"[All Fields]. OR "cryoprecipitates"[All Fields]. OR "cryoprecipitating"[All Fields]. OR "cryoprecipitation"[All Fields]) AND ("blood transfusion"[MeSH Terms]. OR ("blood"[All Fields]. AND "transfusion"[All Fields]) OR "blood transfusion"[All Fields]. OR "transfusion"[All Fields]. OR "transfusions"[All Fields]. OR "transfusable"[All Fields]. OR "transfusate"[All Fields]. OR "transfuse"[All Fields]. OR "transfused"[All Fields]. OR "transfuses"[All Fields]. OR "transfusing"[All Fields]. OR "transfusion s"[All Fields])))) AND (((("liberal"[All Fields]. OR "liberalization"[All Fields]. OR "liberalize"[All Fields]. OR "liberalized"[All Fields]. OR "liberalizing"[All Fields]. OR "liberally"[All Fields]. OR "liberals"[All Fields]. OR "politics"[MeSH Terms]. OR "politics"[All Fields]. OR "liberalism"[All Fields]) AND ("strategie"[All Fields]. OR "strategies"[All Fields]. OR "strategy"[All Fields]. OR "strategy s"[All Fields])) OR (("restrict"[All Fields]. OR "restricted"[All Fields]. OR "restricting"[All Fields]. OR "restriction"[All Fields]. OR "restrictions"[All Fields]. OR "restrictive"[All Fields]. OR "restrictiveness"[All Fields]. OR "restricts"[All Fields]) AND

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("strategie"[All Fields]. OR "strategies"[All Fields]. OR "strategy"[All Fields]. OR "strategies"[All Fields])) AND ("complicances"[All Fields]. OR "complicate"[All Fields]. OR "complicated"[All Fields]. OR "complicates"[All Fields]. OR "complicating"[All Fields]. OR "complication"[All Fields]. OR "complications"[All Fields]. OR "complications"[MeSH Subheading]. OR "complications"[All Fields]) AND ("cardiovascular surgical procedures"[MeSH Terms]. OR ("cardiovascular"[All Fields]. AND "surgical"[All Fields]. AND "procedures"[All Fields]) OR "cardiovascular surgical procedures"[All Fields]. OR ("cardiovascular"[All Fields]. AND "surgery"[All Fields]) OR "cardiovascular surgery"[All Fields]. OR ("thoracic surgery"[MeSH Terms]. OR ("thoracic"[All Fields]. AND "surgery"[All Fields]) OR "thoracic surgery"[All Fields]. OR ("cardiac"[All Fields]. AND "surgery"[All Fields]) OR "cardiac surgery"[All Fields]. OR "cardiac surgical procedures"[MeSH Terms]. OR ("cardiac"[All Fields]. AND "surgical"[All Fields]. AND "procedures"[All Fields]) OR "cardiac surgical procedures"[All Fields]. OR ("cardiac"[All Fields]. AND "surgery"[All Fields])) OR ("vascular surgical procedures"[MeSH Terms]. OR ("vascular"[All Fields]. AND "surgical"[All Fields]. AND "procedures"[All Fields]) OR "vascular surgical procedures"[All Fields]. OR ("vascular"[All Fields]. AND "surgery"[All Fields]) OR "vascular surgery"[All Fields])) AND (("adult"[MeSH Terms]. OR "adult"[All Fields]. OR "adults"[All Fields]. OR "adult s"[All Fields]) AND ("patient s"[All Fields]. OR "patients"[MeSH Terms]. OR "patients"[All Fields]. OR "patient"[All Fields]. OR "patients s"[All Fields]))

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