

Restrictive vs liberal blood transfusion strategy for patients with burn trauma: a systematic review and meta-analysis

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Introduction

Anaemia is a frequent occurrence in patients with burn trauma, and is associated with surgical procedures including staged wound excision, phlebotomy for laboratory studies, increased erythrocyte destruction and reduced erythrocyte production as a result of abnormal bone marrow responses (Kwan et al, 2006; Palmieri et al, 2017, 2019). To prevent its detrimental effects, including decreased tissue perfusion and increased cardiac work, the intervention of choice is red blood cell transfusion (Jeschke et al, 2007). However, liberal transfusion may have adverse consequences, including transfusion transmissible infections, sepsis, acute reactions and volume overload (Salehi et al, 2021). Moreover, safe blood supplies are not always available and accessible, especially in low- and middle-income countries (Zhang et al, 2021).

The threshold for blood transfusion has been challenged. The haemoglobin threshold for traditional liberal transfusion is 10 g/dl, while restrictive blood transfusion administers blood more sparingly at 7–8 g/dl (Jeschke et al, 2007; Palmieri et al, 2019). Several trials have been conducted to observe the clinical outcomes of restrictive transfusion, but the risks and benefits for patients with burn trauma remain unclear.

Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (Moher et al, 2009) (Figure 1). Databases including PubMed, Cochrane, Google Scholar, MEDLINE, ProQuest and Scopus were searched for eligible clinical studies assessing restrictive blood transfusion for burn

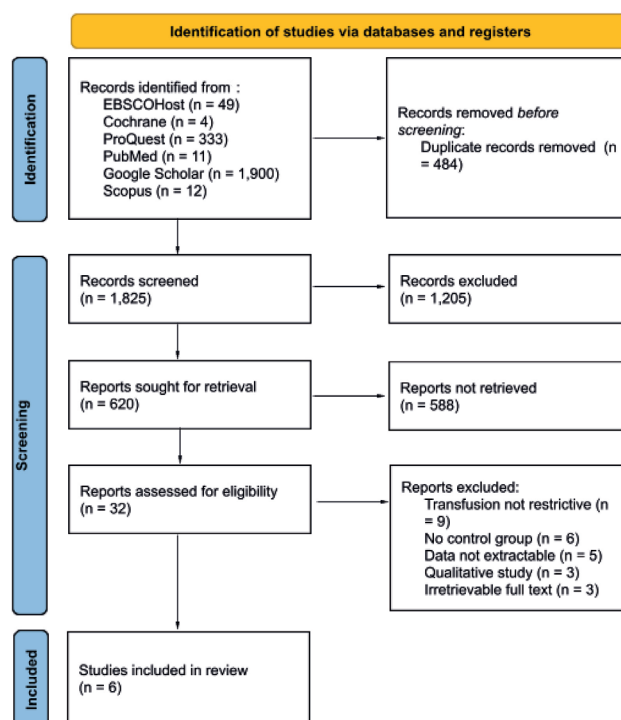


Figure 1. PRISMA diagram.

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trauma patients from inception up to October 2022. The following inclusion criteria were pre-specified for the literature search: clinical studies, assesses restricted transfusion as intervention for burn trauma patients, clinical outcomes reported. Studies with the following criteria were excluded: language other than English, studies with irretrievable full-text, outcomes reported in qualitative, unquantifiable measures.

Critical appraisal was performed using the Cochrane Risk of Bias tool 2.0 (Sterne et al, 2019) for randomised trials or the Newcastle–Ottawa Scale for cohort studies and converted to Agency for Healthcare Research and Quality standards (Wells et al, 2000; Viswanathan et al, 2012).

Statistical analysis was performed in Review Manager 5.4 (Cochrane Reviews) to obtain pooled odds ratios (OR) and mean differences (MD), as well as their respective 95% confidence intervals (95% CI). Inverse variance, random effects model was used for quantitative synthesis to account for expected heterogeneity (Riley et al, 2019). Heterogeneity was assessed using I² statistics, in which 0%, 25%, 50% and 75% were categorised as negligible, low, moderate, and high, respectively (Higgins et al, 2003). Subsequent subgroup and sensitivity analyses were performed where appropriate.

Results

Six studies were included with a total of 1888 patients – three were randomised trials and three were non-randomised studies. Two studies reported massive burns (>60% total body surface area), while the rest reported burns affecting a smaller area. Two studies were conducted in Canada, one in Iran, one in the United States of America, and two were multicentre studies. Outcomes reported from the studies included mortality (Figure 2), sepsis (Figure 3), ventilator days (Figure 4) and length of stay (Figure 5).

Risk of bias assessment by the Cochrane Risk of Bias 2.0 revealed that one study was good quality, although there were some concerns in two other studies because there was no blinding (Figure 6). Meanwhile, for non-randomised studies analysed with the Newcastle–Ottawa Scale, overall good quality was found for two of the studies, while one had poor quality as a result of baseline between-group differences (Figure 7).

Discussion

Burn trauma and transfusion

Patients with traumatic burns tend to present with loss of skin (the major barrier to infection) and inhalation injury (Gomez et al, 2008). Blood loss is common and transfusion remains the main treatment. Aside from its requirement during surgery, blood transfusion

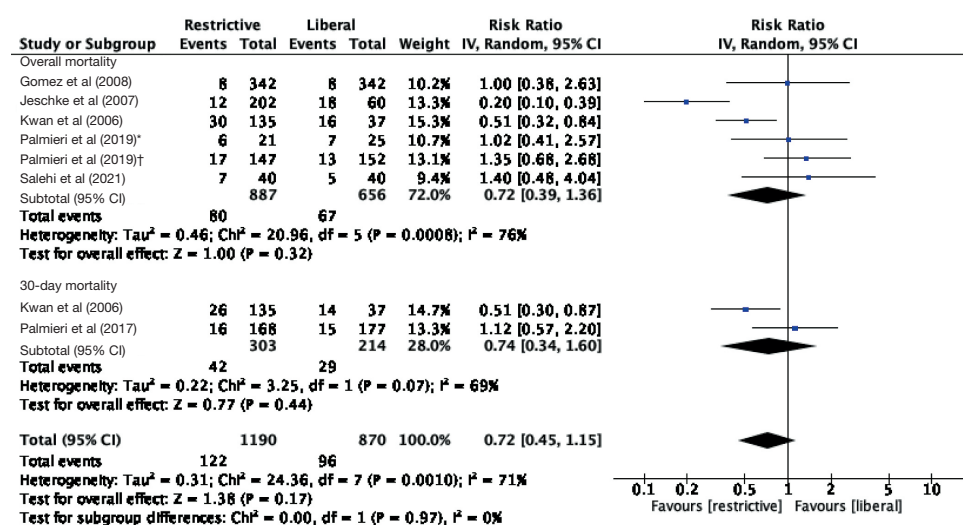


Figure 2. Subgroup analysis for mortality. CI = confidence interval; IV = inverse variance. * = patients with ≥60% total body surface area burns; † = patients with 20–59% total body surface area burns.

allows increased oxygen delivery and therefore may help with wound healing (Jeschke et al, 2007; Palmieri et al, 2017). Patients with severe thermal burns are at higher risk of anaemia as a result of grafting procedures, multiple excision and frequent blood sampling, so a rational transfusion strategy that provides more benefits than complications must be selected (Jeschke et al, 2007).

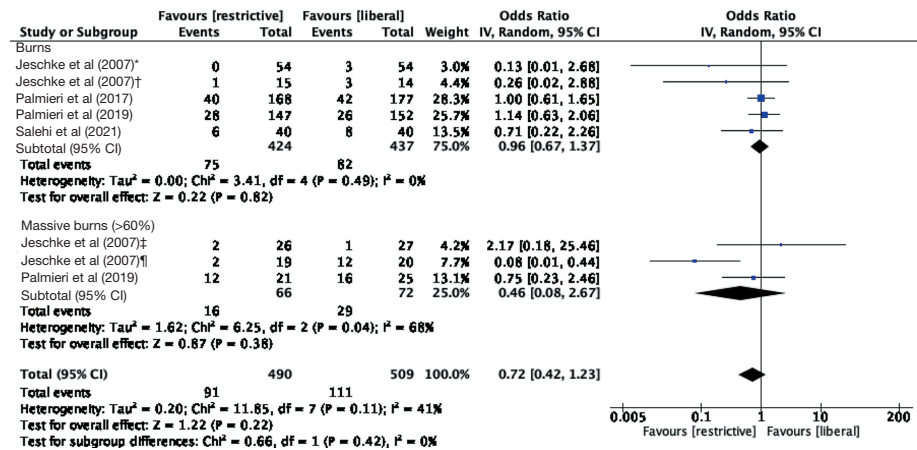


Figure 3. Subgroup analysis for sepsis. CI = confidence interval; IV = inverse variance. * = patients with 40–60% total body surface area burns without inhalation injury; † = patients with 40–60% total body surface area burns with inhalation injury; ‡ = patients with >60% total body surface area burns without inhalation injury; ¶ = patients with >60% total body surface area burns with inhalation injury.

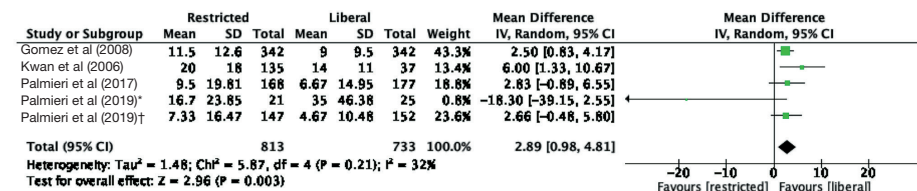


Figure 4. Forest plot for ventilator days. CI = confidence interval; IV = inverse variance; SD = standard deviation. * = patients with ≥60% total body surface area burns; † = patients with 20–59% total body surface area burns.

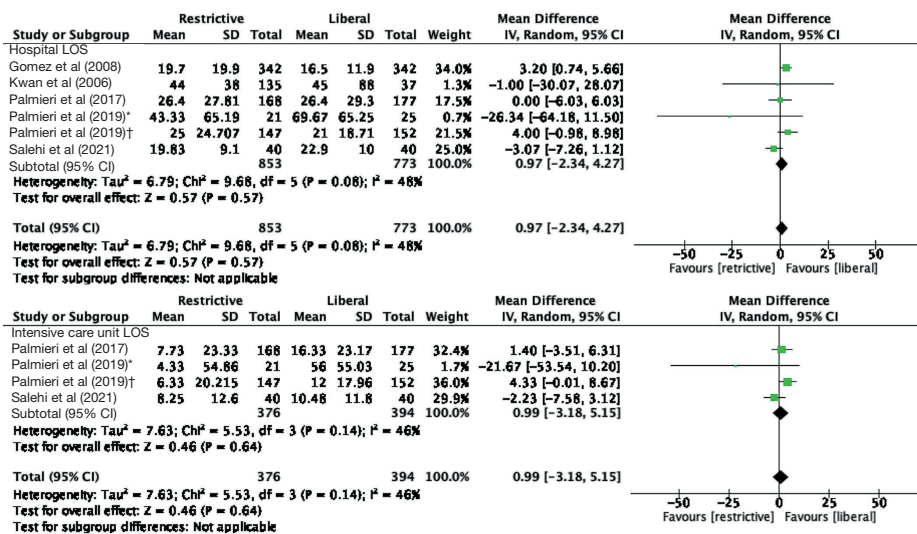


Figure 5. Forest plots for length of stay (LOS). a. Hospital LOS. b. Intensive care unit LOS. CI = confidence interval; IV = inverse variance; SD = standard deviation. * = patients with ≥60% total body surface area burns; † = patients with 20–59% total body surface area burns.

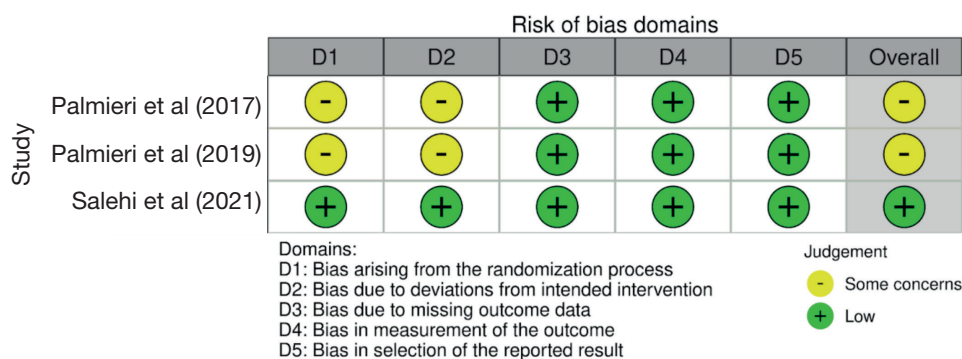


Figure 6. Risk of bias summary using Cochrane Risk of Bias 2.0.

Cohort studies (using Newcastle-Ottawa Scale)					
Categories	Item No.	Quality assessment criteria	Gomez et al, 2008	Jeshcke et al, 2007	Kwan et al, 2006
Selection (4)	1	Representativeness of the exposed cohort	*	*	*
	2	Selection of the non-exposed cohort	*	*	*
	3	Ascertainment of exposure	*	*	*
	4	Demonstration that outcome of interest was not present at start of study	*	*	*
Comparability (2)	5	Study controls for age and TBSA	*	-	*
	6	Study controls for other factors	-	-	-
Outcome (3)	7	Assessment of outcome	*	*	*
	8	Was follow-up long enough for outcomes to occur	*	*	*
	9	Adequacy of follow-up of cohorts	*	*	*
AHRQ Standard - Quality			Good	Poor	Good

Figure 7. Risk of bias summary using the Newcastle-Ottawa Scale. AHRQ = Agency for Healthcare Research and Quality; TBSA = total body surface area.

Mortality

The lower transfusion threshold in the restrictive strategy might reduce exposure to triggers for adverse transfusion reactions, while still maintaining the blood requirement for survival. In this analysis, mortality tended towards lower odds with restrictive transfusion (pooled OR=0.72; 95% CI=0.45–1.15; not significant at $P=0.17$). Although the between-group difference was not statistically significant ($P=0.97$), the odds were further reduced for the overall (pooled OR=0.72; 95% CI=0.39–1.36; $P=0.32$) than the 30-day mortality subgroup (pooled OR=0.74; 95% CI=0.34–1.60; $P=0.07$), signifying that restricted transfusion maintained long-term outcomes. Considerable heterogeneity was found ($I^2=71%$), with Jeshcke et al’s (2007) study being an outlier, possibly because it used a different approach, dividing the intervention based on burn size and units given.

Sepsis

Blood transfusions increase the risk of infections, leading to an escalated inflammatory response, and can cause hypermetabolism, contributing to multiple organ dysfunction and mortality. In patients with burn trauma, sepsis can lead to immediate fatal outcomes. The combined odds ratio (pooled OR=0.72; 95% CI=0.42–1.23; $P=0.22$; $I^2=41%$) showed that the rate of infections was slightly lower when using restrictive strategies. Furthermore, the effect was more profound in patients with massive burns (pooled OR=0.46; 95% CI=0.08–2.67; $P=0.38$) compared to burns affecting smaller area (pooled OR=0.96; 95% CI=0.67–1.37; $P=0.82$).

Ventilation days

Ventilation days are the period where the patient is intubated and the following consecutive 48 hours without support. With restricted transfusion, pooled MD for ventilation days was 2.89 days longer than with liberal transfusion (95% CI= 0.98–4.81; $P=0.003$). Ventilators are needed to treat respiratory dysfunction, thus longer days might indicate more inhalation

trauma independent of the burns. Moderate heterogeneity was found ($I^2=32\%$), identifying Palmieri et al's (2019) study (which assessed more massive burns) as an outlier, resulting in fewer ventilation days.

Length of stay

In terms of length of stay, liberal transfusion was slightly favoured over restrictive transfusion, although restrictive transfusion resulted in prolongation of both hospital (pooled MD=0.97; 95% CI= -2.34–4.27; $P=0.57$; $I^2=48\%$) and intensive care unit (pooled MD = 0.99; 95% CI= -3.18–5.15; $P=0.64$; $I^2=46\%$) length of stay. The findings of the current meta-analysis are similar to those of Docherty et al (2016), showing slightly longer stay for restrictive transfusion in cardiovascular patients. However, outcomes in terms of reducing mortality are more important than those relating to length of stay.

Strengths and limitations

According to the literature, this study is the first to examine the effectiveness of restrictive transfusion approaches in patients with burn trauma using a systematic approach. The primary limitations are the heterogeneity of data, which might be a result of clinical differences between patients, and some concerns about bias.

Conclusions

Restrictive transfusion is non-inferior to liberal transfusion in terms of reducing mortality and sepsis in patients with burn trauma. Further studies are recommended to strengthen the evidence.

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References

- Docherty AB, O'Donnell R, Brunskill S et al. Effect of restrictive versus liberal transfusion strategies on outcomes in patients with cardiovascular disease in a non-cardiac surgery setting: systematic review and meta-analysis. *BMJ*. 2016;352:i1351. <https://doi.org/10.1136/bmj.i1351>
- Gomez M, Cartotto R, Knighton J, Smith K, Fish JS. Improved survival following thermal injury in adult patients treated at a regional burn center. *J Burn Care Res*. 2008;29(1):130–137
- Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557–60. <https://doi.org/10.1136/bmj.327.7414.557>
- Jeschke MG, Chinkes DL, Finnerty CC, Przkora R, Pereira CT, Herndon DN. Blood transfusions are associated with increased risk for development of sepsis in severely burned pediatric patients. *Crit Care Med*. 2007;35(2):579–583. <https://doi.org/10.1097/01.CCM.0000253812.09236.98>
- Kwan P, Gomez M, Cartotto R. Safe and successful restriction of transfusion in burn patients. *J Burn Care Res*. 2006;27(6):826–834. <https://doi.org/10.1097/01.BCR.0000245494.45125.3E>
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097. <https://doi.org/10.1371/journal.pmed.1000097>
- Palmieri TL, Holmes JH 4th, Arnoldo B et al. Transfusion Requirement in Burn Care Evaluation (TRIBE): a multicenter randomized prospective trial of blood transfusion in major burn injury. *Ann Surg*. 2017;266(4):595–602. <https://doi.org/10.1097/SLA.0000000000002408>
- Palmieri TL, Holmes JH, Arnoldo B et al. Restrictive transfusion strategy is more effective in massive burns: results of the TRIBE multicenter prospective randomized trial. *Mil Med*. 2019;184(Suppl 1):11–15. <https://doi.org/10.1093/milmed/usy279>
- Riley RD, Moons KGM, Snell KIE et al. A guide to systematic review and meta-analysis of prognostic factor studies. *BMJ*. 2019;364:k4597. <https://doi.org/10.1136/bmj.k4597>
- Salehi SH, Daniali M, Motaghi P, Momeni M. The best strategy for red blood cell transfusion in severe burn patients, restrictive or liberal: A randomized controlled trial. *Burns*. 2021;47(5):1038–1044. <https://doi.org/10.1016/j.burns.2020.06.038>

- Sterne JAC, Savović J, Page MJ et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:14898. <https://doi.org/10.1136/bmj.14898>
- Viswanathan M, Ansari MT, Berkman ND et al. Assessing the risk of bias of individual studies in systematic reviews of health care interventions. 2012. <https://www.ncbi.nlm.nih.gov/books/NBK91433/> (accessed 18 April 2023)
- Wells GA, Shea B, O'Connell D et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2000. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed 18 April 2023)
- Zhang Y, Xu Z, Huang Y et al. Restrictive vs. Liberal red blood cell transfusion strategy in patients with acute myocardial infarction and anemia: a systematic review and meta-analysis. *Front Cardiovasc Med*. 2021;8:736163. <https://doi.org/10.3389/fcvm.2021.736163>