Critical Review Form
Therapy

PGY-2

HYPERLINK "http://pmid.us/34269467"Braverman MA, Smith A, Pokorny D, et al. Prehospital whole blood reduces early mortality in patients with hemorrhagic shock. Transfusion. 2021 Jul;61 Suppl 1:S15-S21.

Objectives: **"to determine if prehospital LTOWB transfusion compared to no prehospital LTOWB transfusion improves survival in three distinct groups of trauma patients: in-hospital transfusion only, prehospital cardiac arrest, or patients with development of shock physiology in the field." (p. S16)**

Methods: **This retrospective observational study was conducted using data from the institutional trauma registry at University Hospital in San Antonio, Texas, an academic Level I trauma center. Consecutive patients enrolled in the registry from 2015 to 2019 who underwent transfusion after arrival to the ED were enrolled and stratified based on whether they received low titer type O, Rh+ whole blood (LTOWB) (PHT group) or did not receive LTOWB (NT group). Patients with incomplete or missing prehospital records were excluded.**

Outcomes included mortality in the ED, at 6 hours, at 12 hours, and during hospitalization; need for massive transfusion (> 10 U or product transfused in 24 hours); transfusion of > 3 U in one hour; transfusion volume in the ED; and transfusion volume during hospitalization. A 2:1 propensity-matched group based on injury severity score (ISS), age, male gender, and penetrating mechanism was generated for patients who presented in shock (SBP ≤ 90 mmHg).

A total of 803 patients who underwent transfusion after hospital arrival were identified, of whom 538 remained after exclusions. Of these, 107 (19.8%) received PHT while 431 did not (NT group). There were 214 patients in the propensity-matched cohort, with 58 in the PHT group and 156 in the NT group.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	No. This was a retrospective, observational study at high risk for selection bias. While the authors used propensity matching based on several prognostic factors, such statistical methods are not a replacement for randomization.
2.	Was allocation concealed? In other words, was it possible to subvert the	N/A. This study was not randomized.

	randomization process to ensure that a patient would be "randomized" to a particular group?	
3.	Were patients analyzed in the groups to which they were randomized?	Yes. Patients were not randomized and were analyzed based on whether or not they received prehospital whole blood transfusion.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No. The PHT group had a higher proportion of male patients (84.1% vs. 69.4%) and were more likely to have suffered a penetrating injury (63.6% vs. 27.6%), and lower median ISS scores (17 vs. 22). After propensity matching, patients were similar with respect to age and median ISS, but the PHT group still had a higher percentage of male patients and a higher incidence of penetrating trauma.
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	Likely yes. Patients were not blinded to group allocation and may have been aware that they received blood in the prehospital setting. It is unlikely that performance bias on the part of patients would have impacted outcomes.
2.	Were clinicians aware of group allocation?	Yes. Clinicians were not blinded to group allocation and would have been aware if whole blood was administered in the prehospital setting. It is possible that performance bias on the part of clinicians would have impacted outcomes.
3.	Were outcome assessors aware of group allocation?	Yes. The authors make no mention of blinding of outcome assessors (observer bias).
4.	Was follow-up complete?	Yes. Outcome data was available for all 538 patients in the final analysis.
II.	**What are the results ?**	
1.	How large was the treatment effect?	● There was no statistically significant difference in mortality at any time point between the PHT and NT groups: ○ 10.3% vs 13.2% in the ED (p = 0.41) ○ 16.8% vs. 19.3% at 8 hours (p = 0.56) ○ 22.4% vs. 24.9% at 24 hours (p = 0.60) ○ 29% vs. 34.8% in hospital (p = 0.25) ● While there was no difference in need for massive transfusion between the groups, patients in the PHT group were less likely to

		require massive transfusion in the first 24 hours (30.8% vs. 42.2%, p = 0.03). ● Patients in the PHT group required less blood product in the ED (median 1000 mL vs 1400 mL, p < 0.03), but required a similar volume over the course of their hospital stay. <u>Propensity Matched Cohort</u> ● Following propensity matching, patients in the PHT group had significantly lower mortality in the ED (0% vs. 7.1%, p = 0.04). o While there was a trend toward lower mortality in the PHT group at 6 hours (5.3% vs. 14.1%), 24 hours (17.2% vs. 23.1%), and during hospitalization (13.8% vs. 25%), none of these differences achieved statistical significance. ● There was no statistically significant difference in the incidence of massive transfusion (61.5% vs. 41.7%, p = 0.23) or transfusion of > 3 units in one hour (53.4% vs. 60.3%, p = 0.37)
2.	How precise was the estimate of the treatment effect?	See above. Confidence intervals were not provided for any outcome.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	Yes. This study was conducted at a large, level I, urban, academic trauma center in the US. Patients, injuries, and standards of care would likely be similar to those seen in our institution.
2.	Were all clinically important outcomes considered?	Mostly yes. The authors considered mortality at various time points, need for transfusion, and transfusion volume. They did not assess transfusion reactions, acute lung injury, length of stay, or need for surgical intervention.
3.	Are the likely treatment benefits worth the potential harm and costs?	No. Based on this retrospective study alone, PHT was mot associated with improved mortality at any time point, and following propensity matching was only associated with improved mortality in the ED with a non-statistically significant trend toward improved mortality at other time points. Further research with randomized controlled trials will be needed to clarify the effect of prehospital whole blood transfusions on mortality.

Limitations:

1. **This was a retrospective, observational study at high risk for selection bias. While the authors used propensity matching based on several prognostic factors, such statistical methods are not a replacement for randomization.**

2. **No primary outcome was identified.**

3. **The authors did not provide measures of effect size of 95% confidence intervals for any of their outcomes.**

4. **A significant proportion of eligible patients (33%) had incomplete prehospital data and were excluded.**

5. **The study was underpowered to detect potentially clinically significant differences in several outcome with statistical significance (i.e. a 9.2% reduction in in-hospital mortality).**

Bottom Line:

This single-center, retrospective, observational trial conducted at a large level 1 trauma center in San Antonio, TX found that prehospital administration of whole blood in trauma was not associated with improvements in mortality at multiple time points, but was associated with a decreased need for massive transfusion in the first 24 hours (30.8% vs. 42.2%). Following propensity matching, there was a reduction in ED mortality, but no difference in mortality at 6, 12, or 24 hours or during hospitaliszation. There was also no significant difference in need for massive transfusion or transfusion more than units of blood in a one-hour period.