Critical Review Form
Therapy

Effect of Plasma and Red Blood Cell Transfusions on Survival in Patients with Combat Related Traumatic Injuries, *J Trauma* 2008; 64: 569-578

Objective: **"To determine the effect of fresh frozen plasma (FFP) and RBC transfusion on in-hospital survival for patients with combat-related injuries who required any blood product administration." (p. 570)**

Methods: **Retrospective analysis of the Joint Theater Trauma Registry of trauma patients admitted to one combat support hospital in Iraq between November 2003 and December 2004. Eligible patients received one or more units of any blood product. The following variables were abstracted: age, admission vital signs, base deficit, pH, hematocrit, INR, GCS, injury severity score (ISS), recombinant Factor VII a used, 24 hour use of red blood cells (RBC), fresh frozen plasma (FFP), or fresh whole blood (used in lieu of apheresis platelets), and when applicable cause of death ascertained by one investigator's review of the chart.**

Multivariate logistic regression analysis was performed using univariate p<0.02 as entry inclusion criteria. A pre-planned subset analysis of those without massive (<10 units RBC's) was performed.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	No. Retrospective review not a RCT.
2.	Was randomization concealed (blinded)?	No blinding, not a RCT.
3.	Were patients analyzed in the groups to which they were randomized?	Not randomized, no allocation so intention-to-treat irrelevant.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Not a RCT so no treatment or control groups. There were no significant differences noted between all patients transfused and patients without massive transfusion in gender, GCS score, SBP, hematocrit, pH, INR or ISS (Table 1, p. 570)

B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	Yes, no randomization or blinding was possible in this retrospective review.
2.	Were clinicians aware of group allocation?	Yes.
3.	Were outcome assessors aware of group allocation?	Yes.
4.	Was follow-up complete?	No lost to follow-up is reported.
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	• 3287 patients were admitted with a median ISS of 6 and in-hospital mortality of 4.4%; 708 (22%) were transfused a blood product and were eligible for this retrospective analysis including 567 (80%) who did not have a massive transfusion. • The predominant site of injury was the head/neck (31%) or abdomen (39%) and hemorrhage was the leading cause of death (43%). • Only 560/708 (79%) had either a pH or base deficit recorded and 356/560 (64%) had shock (base deficit ≥4 or pH ≤ 7.2). • 647/708 (91%) had surgery (celiotomy 31%, craniotomy 16%, vascular repair 13%, and skeletal fixation 11%). • Mean age of transfused RBC's was 33-days. • The following variables were significantly different between survivors (n=621) and non-survivors (n=87)

		<table><tr><th>Variable</th><th>Lived</th><th>Died</th><th>p-value</th></tr><tr><td>GCS</td><td>15</td><td>3</td><td><0.001</td></tr><tr><td>HR</td><td>115</td><td>105</td><td>0.001</td></tr><tr><td>SBP</td><td>115</td><td>102</td><td>0.001</td></tr><tr><td>Temp</td><td>97</td><td>96</td><td>0.02</td></tr><tr><td>Hct</td><td>33.1</td><td>27.9</td><td><0.001</td></tr><tr><td>pH</td><td>7.29</td><td>7.16</td><td><0.001</td></tr><tr><td>Base deficit</td><td>5</td><td>13</td><td><0.001</td></tr><tr><td>INR</td><td>1.4</td><td>2.06</td><td><0.001</td></tr><tr><td>Massive transfusion</td><td>83%</td><td>56%</td><td><0.001</td></tr><tr><td>ISS</td><td>14</td><td>21</td><td><0.001</td></tr></table> • On logistic regression analysis FFP transfusion was associated with increased survival while RBC transfusion was associated with decreased survival. • Each unit of FFP transfused improved in-hospital survival (OR 1.16, 95% CI 1.05-1.28, p=0.003). • Each unit of RBC transfused decreased survival (OR 0.84, 95% CI 0.79-0.9, p=0.001). • Massive transfusion was associated with decreased survival (OR 0.3, 95% CI 0.16-0.84, p=0.02). • These regression analysis conclusions were not changed when the analysis was restricted to non-massive transfusion subset.
2.	How precise was the estimate of the treatment effect?	See 95% CI above.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	No! These are (generally young, healthy) military personnel in Iraq facing ballistic weapons and managed in an Army hospital unit. Some of the patients were Iraqi nationals with subsequent care received in Iraqi hospitals. The external validity of these results in US hospitals is questionable.
2.	Were all clinically important outcomes considered?	No patient-centric or cost outcomes were evaluated or hypothesized.

Limitations

1) **No chart review methods.**

2) **Insufficient detail on patient demographics (Iraqi vs. US, co-morbidities), mechanism of injury, or management which leaves the reader uncertain whether (unrecognized/unmeasured) intrinsic prognostic differences or post-transfusion management resources between patients receiving different transfusion protocols affected the observed results.**

3) **No sensitivity analysis for missing variables.**

4) **Use of whole blood in lieu of platelets may skew results since whole blood contains plasma and RBC's, too.**

5) **Foreign setting, mechanism of injury, and overall fit/healthy patient population all limit the external validity of these results for stateside trauma teams.**

Bottom Line

In warzone trauma victims who receive any blood products, transfusion of plasma was independently associated with improved survival whereas RBC transfusions alone decrease survival. Prospective trials controlling for multiple confounding variables are still needed to confirm these findings.