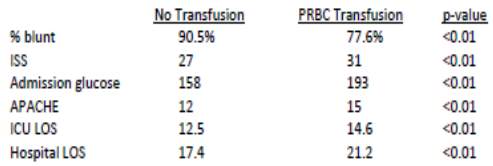
Critical Review Form
Therapy

Early Aggressive Use of Fresh Frozen Plasma Does Not Improve Outcome in Critically Injured Trauma Patients, *Ann Surg* 2008; 248: 578-584

Objective: **"To evaluate the impact of early aggressive FFP transfusion on outcome in critically injured trauma patients who are admitted to the intensive care unit (ICU)." (p. 578)**

Methods: **Prospective cohort at Maryland Shock Trauma enrolled from July 2004 to November 2006 if they presented within 24 hours of injury and required ICU admission. Exclusion criteria were admission for a non-trauma condition or transfers. Data collected prospectively included demographics, blood products transfused, APACHE score, injury severity score (ISS) and GCS. For patients who received both fresh frozen plasma (FFP) and packed red blood cells (PRBC), the ratio of PRBC to FFP was calculated. Bivariate and logistic regression analyses were performed with P<0.20 included in the initial model, p=0.10 required for entry and p=0.15 for removal. Age and ISS were forced to be retained in all models. No details are provided in the methods section on the primary outcome, data collection instruments, chart review personnel or training, or power calculations to gauge sample size and risk of Type I or II error.**

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. This is not an RCT, it is an observational cohort.
2.	Was randomization concealed (blinded)?	No. There was no randomization to conceal.
3.	Were patients analyzed in the groups to which they were randomized?	No. This is not a RCT so intention-to-treat analysis is not relevant.

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 significant differences between the no transfusion (n=441) and PRBC transfusion (n=365) groups (Table 2, p. 580): 
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, not randomized or blinded.
2.	Were clinicians aware of group allocation?	Yes, not randomized or blinded.
3.	Were outcome assessors aware of group allocation?	Yes, not randomized or blinded.
4.	Was follow-up complete?	No lost to follow-up is reported.
II.	**What are the results (answer the questions posed below)?**	

	No Transfusion	PRBC Transfusion	p-value
% blunt	90.5%	77.6%	<0.01
ISS	27	31	<0.01
Admission glucose	158	193	<0.01
APACHE	12	15	<0.01
ICU LOS	12.5	14.6	<0.01
Hospital LOS	17.4	21.2	<0.01

1.	How large was the treatment effect?	• 806 critically injured patients were enrolled, 250 (31%) receiving both FFP and PRBC within 24 hours. • Patients with any PRBC transfused had significantly more PRBC transfused over hospital LOS (median 9 units vs. 2 units, p<0.001) as did those with FFP transfused (median 6 units vs. 0 units, p<0.001). • The mean PRBC to FFP ratio in the dual transfusion group was 1.35 ± 0.90 and 50/250 (20%) received PRBC and FFP in a 1:1 ratio. • The number of units of PRBC transfused in the non 1:1 group was significantly less (6.5 in non 1:1 vs. 9.3 units in 1:1 group, p=0.02). • Higher PRBC to FFP ratios were observed with higher admission glucose, TBI, higher APACHE score, pelvic fractures, or when laparotomy was performed. • Mortality was significantly increased with increased age, increased hospital LOS, increased ICU LOS, or increased APACHE scores among those who received any PRBC within 24 hours. • The ratio of PRBC to FFP was not independently associated with mortality on the logistic regression modeling: Risk Factor / OR / PRBC Transfusion / p-value PRBC: FFP ratio 1.23 0.81-1.87 0.34 Age 1.04 1.02-1.07 <0.01 ISS 1.00 0.97-1.04 0.92 Gender 0.63 0.24-1.66 0.35 APACHE 1.08 1.02-1.15 0.01 Closed Head Injury 2.92 1.13-7.55 0.03 Laparotomy 3.38 1.31-8.72 0.01 ICU (d) 0.90 0.85-0.95 <0.01 • When the logistic regression was performed analyzing only those who received 1:1 as an independent

		variable, the ratio was still not significantly associated with mortality. • Similarly, when performing regression on the 32% who received a massive transfusion (>10 units PRBC) no significant effect was observed for PRBC to FFP ratio (OR 1.49, 95% CI 0.63-3.53, p=0.37) or 1:1 ratio (OR 0.60, 95% CI 0.21-1.75, p=0.35). • The ratio of PRBC to FFP was not predictive of hospital LOS (OR 0.64, 95% CI -1.2 to 2.5, p=0.50) or ICU LOS (OR 0.57, 95% CI -1.07 to 2.2 p=0.49).
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?	Yes. Level I trauma patients admitted to the ICU. These are similar to the sickest of our Level I trauma patients who survive long enough to go to the operating room or SICU.
2.	Were all clinically important outcomes considered?	No patient-centric outcomes were reported except mortality. Future trials will need to assess functional recovery and sequelae of FFP transfusions such as patient-level adverse effects (CHF, renal dysfunction) and systems-level (blood product shortages, time to transfusion).

3.	Are the likely treatment benefits worth the potential harm and costs?	No. Based upon the current evidence the mortality benefits observed with aggressive transfusion of FFP in military settings do not extrapolate to civilian settings. There may be several reasons for these findings. • Differing injury patterns • Differing severity of injury not captured by the ISS • Survival bias whereby sickest civilians do not survive to hospital as do healthy young military personnel • Resources available in US based trauma center (VIR, trauma surgeon, trauma anesthesiologist) not available in the wartime theater.

Limitations

1) **No chart review methods provided on data collection instruments or personnel training.**

2) **No *a priori* or *post hoc* power calculations.**

3) **No bivariate demographic comparison of the 51 with 1:1 ratio versus the 199 with non-1:1 ratio or of those with PRBC + FFP versus those not transfused.**

4) **No details provided on operative or VIR interventions that could impact mortality prognosis.**

5) **No analysis of transfusion timing (<1 hour, <6 hours) or PRBC age.**

6) **No assessment of transfusion related adverse effects.**

7) **Model did not control for baseline PT, temperature or pH or age of PRBC.**

Bottom Line

Advising widespread adoption of one to one PRBC to FFP is not warranted as outcomes will not be improved and blood banks will be strained to meet demands. A subset of trauma patients who will benefit from plasma and FFP in set ratios likely exists, but that population has yet to be defined.