

Emergency Medicine Journal Club

Eastern Virginia Medical School

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P: In patients meeting current "standard of practice" indications for FFP

I: Is the aggressive use of FFP (lower RBC:FFP ratios i.e. 1-1.5RBC to 1FFP)

C: Compared to utilizing a more restrained approach (higher ratios)

O: Associated with significant differences in favorable outcome measures

Title	Authors, Date, Affiliations	Type of Evidence	Inclusion Criteria/ Design	Outcomes	Key Results	Study Limitations
<p>“The effect of plasma transfusion on morbidity and mortality: a systematic review and meta-analysis”</p>	<p>Mohammad Murad, et al.</p> <p>Transfusion</p> <p>June 2010</p> <p>Mayo Clinic and Emory University</p>	<p>Systematic Review and Meta-analysis</p>	<p>RCT or controlled observational studies enrolling adult patients receiving plasma transfusion and comparing them to a control group</p> <p>results were refined to clinical trials, clinical studies, guidelines, and meta-analyses</p>	<p>Death, nonfatal myocardial infarction, stroke (hemorrhagic and ischemic), acute lung injury (ALI), multiorgan failure, blood loss, and RBC transfusion requirements</p>	<p>Patients requiring massive transfusion:</p> <p>In pooled analysis, the transfusion of plasma at plasma:RBC ratios > 1:3 (range 1:2.5-1:1) was associated with a significant reduction in mortality (OR, 0.38; 95% CI, 0.24-0.60; I2 = 85%; p value for Q test = 0.01).</p> <p>Mortality in patients undergoing surgery without massive transfusion</p> <p>Meta-analysis of all surgical studies showed that plasma transfusion was associated with a trend toward increased</p>	<p>quality of evidence was very low because heterogeneity was not explained by sub-group and sensitivity analysis</p> <p>Potential for selection bias</p> <p>Survivor Bias</p> <p>Publishing and reporting biases</p>

risk of death (OR, 1.22; 95% CI, 0.73-2.03, I² = 61%; p value for Q test = 0.02

Mortality in Anticoagulated Patients

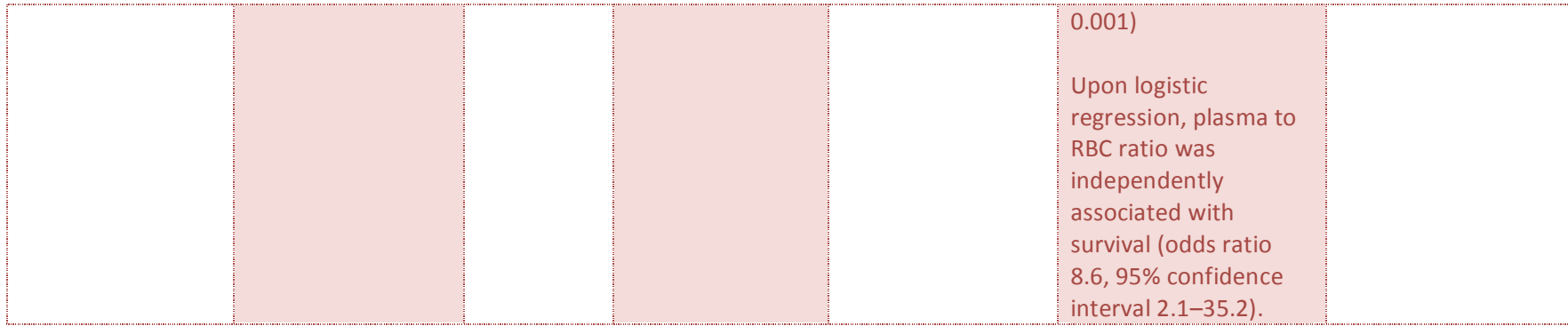
Therapeutic plasma transfusion was associated with a significant reduction in mortality compared to treatments other than plasma (OR, 0.29; 95% CI, 0.09-0.98

<p>“Timing of Fresh Frozen Plasma Administration and Rapid Correction of Coagulopathy in Warfarin-Related Intracerebral Hemorrhage”</p>	<p>Joshua Goldstein, et al. Stroke, 2006 Brigham Women’s Hospital and Massachusetts General Hospital</p>	<p>Retro-spective chart review</p>	<p>Retrospective review of ED management of patients with warfarin-associated ICH diagnosed by CT from January 1998 to June 2004</p> <p>69 patients met inclusion criteria</p>	<p>The primary outcome was INR reversal within 24 hours</p> <p>Any documented follow-up INR <1.4 within 24 hours of arrival in the ED was scored as positive</p>	<p>Of the ED interventions evaluated, only timing of FFP was associated with successful INR reversal</p> <p>Median time to first dose of FFP was 90 (60 to 205) minutes for patients who had an INR <1.4 within 24 hours, and 210 (100 to 375) minutes in those who did not (P<0.02)</p> <p>Early time to treatment and successful INR</p>	<p>Retrospective design</p> <p>No standardization of care across cohort</p>
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Question	Evidence	Design	Population	Intervention	Comparison	Outcomes
<p>“Fresh frozen plasma and platelet transfusions are associated with development of acute lung injury in critically ill medical patients”</p>	<p>Khan, et al. <i>Chest</i>, March 2007 Mayo Clinic College of Medicine. Funded by National heart, lung and blood institute grant</p>	<p>Retro-spective cohort study</p>	<p>841 consecutive critically ill patients were studied for the development of ALI/ARDS.</p> <p>The 298 Patients who received blood product transfusions were compared with those who did not</p> <p>Among the transfused patients, 88% received RBCs, 41% received FFP, and 14% received platelets</p> <p>17 patients received massive transfusion, 13 of them also got FFP and 11 also received platelets</p>	<p>Development of ALI/ARDS during the at risk period after transfusion (defined as 48h before development of pulmonary edema in the study group)</p>	<p>reversal did not improve outcomes.</p> <p>ALI/ARDS developed more commonly (25% vs 18%; p_ 0.025) in patients exposed to transfusion</p> <p>When adjusted for the probability of transfusion and other ALI/ARDS risk factors, any transfusion was associated with the development of ALI/ARDS (odds ratio [OR], 2.14; 95% confidence interval [CI], 1.24 to 3.75).</p> <p>ALI/ARDS was more likely to develop in patients who received FFP transfusions (OR, 2.48; 95% CI, 1.29 to 4.74) and platelet transfusions (OR, 3.89; 95% CI, 1.36 to 11.52) than in those who received only RBC transfusions (OR, 1.39; 95% CI, 0.79 to 2.43).</p> <p>Hospital mortality rate was found to be significantly higher in the transfused group</p>	<p>Observational design</p> <p>some unknown risk factors likely were missed and were actually responsible for the observed differences.</p> <p>Single center trial</p> <p>Some patients who developed ALI/ARDS may have been developing it due to the underlying condition that required ICU admission</p>

					(17% vs 11%, respectively; p = 0.022)	
<p>“Transfusion of fresh frozen plasma in critically ill surgical patients is associated with an increased risk of infection”</p>	<p>Sarani, et al. Critical Care Medicine, 2008 Dept of Trauma and Critical Care, University of Pennsylvania School of medicine</p>	<p>Retro-spective review</p>	<p>380 non-trauma patients who received FFP from 2004-05 compared with 2058 non-trauma patients who did not receive FFP</p>	<p>Relative risk of infectious complication</p>	<p>The overall relative risk of infectious Complication is 2.99 (confidence interval 2.28 –3.93) in those who received FFP vs. those who did not</p> <p>Multivariate regression analysis revealed a significant association between infectious complications and FFP when controlling for age, PRBCs, and APACHE II</p> <p>odds ratio of infection for each unit of FFP transfused is 1.039 (confidence interval 1.013–1.067)</p>	<p>Duration of mechanical ventilation is a risk factor for nosocomial pneumonia-was not controlled for b/c it is colinear with APACHE II score</p> <p>small sample size, lack of power</p>
<p>“Early Aggressive Use of Fresh Frozen Plasma Does Not Improve Outcome in Critically Injured Trauma Patients.”</p>	<p>Scalea, et al. Annals of Surgery October 2008 University of Maryland</p>	<p>Prospective cohort Study</p>	<p>806 consecutive trauma patients admitted to the ICU over 2 years</p> <p>In 250/ 365 Patients who were transfused in the first 24 hours received both PRBC’s and FFP and were stratified by FFP: PRBC transfusion ratio</p>	<p>Intensive care unit days, hospital days, and mortality in patients receiving FFP transfusion compared to those receiving a high ratio of FFP:RBC’s and those who were not transfused</p>	<p>Mean number of PRBCs and FFP transfused were 7.7 ± 12 U, 6 U, and 5 ± 12 U, respectively. 365 (45%) patients were transfused in the first 24 hours.</p> <p>Analyzing these patients by stepwise regression controlling for all significant variables, the PRBC:FFP ratio did not predict intensive care</p>	<p>No specific transfusion protocol</p> <p>Publishing and reporting bias: patients who would have benefited from a one to one RBC FFP resuscitation scheme simply did not survive to be entered into our study</p>

					<p>unit days, hospital days, or mortality.</p> <p>There was no significant difference in outcome when comparing patients who had a 1:1 PRBC:FFP ratio with those who did not receive any FFP.</p>	
<p>“The Ratio of Blood Products Transfused Affects Mortality in Patients Receiving Massive Transfusions at a Combat Support Hospital”</p>	<p>Borgman, et al. Journal of Trauma October 2007 Brooke Army Medical Center</p>	<p>Retro-spective chart review</p>	<p>246 patients at a US Army combat support hospital, each of who received a massive transfusion (≥ 10 units of RBCs in 24 hours)</p>	<p>Mortality rates and the cause of death</p>	<p>For the low ratio group the plasma to RBC median ratio was 1:8 (interquartile range, 0:12–1:5) For the medium ratio group, 1:2.5 (interquartile range, 1:3.0–1:2.3 For the high ratio group, 1:1.4 (interquartile range, 1:1.7–1:1.2) ($p < 0.001$)</p> <p>For low, medium, and high plasma to RBC ratios, overall mortality rates were 65%, 34%, and 19%, ($p < 0.001$); and hemorrhage mortality rates were 92.5%, 78%, and 37%, respectively, ($p <$</p>	<p>incomplete data collection</p> <p>lack of standard timing for measuring variables</p> <p>lack of a massive transfusion protocol that was consistently applied to patients.</p>



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