Trauma Blood Management: Avoiding the Collateral Damage of Trauma Resuscitation Protocols

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The use of high ratios of red blood cells to platelets and plasma in trauma resuscitation protocols is quickly gaining favor in civilian trauma centers. The use of higher ratios of coagulation factors to red blood cells has been shown to improve outcomes in both military and civilian centers, but does the evidence support the use of a 1:1:1 ratio, as has been suggested? There is growing evidence that the use of such high ratios may be excessive and potentially harmful, and there has not been enough emphasis on the other components of evidence-based “damage control” resuscitation.

Transfusion therapy has come full cycle in Iraq and Afghanistan as fresh whole blood use has again found a place in the resuscitation of military casualties. The use of equal ratios of packed red blood cells, plasma, and platelets (so called 1:1:1 therapy) to effectively reconstitute whole blood is gaining ground in civilian trauma centers to attempt to replicate the approach of military trauma teams. Although this is an exciting and potential lifesaving therapy, have we considered the “collateral damage” of these trauma resuscitation protocols and does the current evidence support this approach? A cautionary note to begin the discussion was best phrased by Dr. Stephen Cohen: “As mortality rates range from one-third to one-half of these massively transfused individuals, heroic new measures are aggressively sought after and easily embraced.”

Allogeneic blood can be lifesaving, but it is not a benign substance and has a number of adverse effects that can mitigate or even eliminate clinical benefits. Although the most common causes of death for trauma patients within the first 48 hours is either exanguination or massive head injury, after 48 hours the leading causes of death are sepsis, multisystem organ failure, and acute respiratory distress syndrome, all linked to blood transfusions in a dose-dependent manner. Blood products are known to have both inflammatory and immunomodulatory effects, and lung injury is the most frequent type of serious adverse event. Transfusion-related acute lung injury occurs in 1:1000 to 5000 transfusions and is the leading cause of transfusion-related morbidity and mortality, and transfusion-associated circulatory overload occurs in as many as 1:350 transfusions in the intensive care unit. The great paradox of trauma resuscitation protocols is that the physicians who use them are typically trained in critical care medicine, a specialty that helped define modern blood component therapy and coined the phrase “less is more” to describe the clinical benefits of conservative transfusion triggers. Even in trauma patients, transfusions should always be used in a cautious and thoughtful manner, giving no more or no less blood than the patient needs based on the best available evidence.

Althought much has been made of the experience in Iraq demonstrating the efficacy of “high ratio” FFP:RBC (fresh frozen plasma:packed red blood cell) protocols (approaching 1:1), can we extrapolate this data to civilian trauma patients? Beyond the fact that combat injuries are not easily replicated in civilian trauma centers (thankfully), because these patients often have multiple penetrating wounds and massive orthopedic blast injuries, there also has been intermingling of fresh whole blood along with the use of recombinant factor VIIa in military casualties. Furthermore, the most cited military study by Borgman retrospectively reviewed combat injuries from 2003 to 2005 in Iraq, during which time there were a number of logistic changes to the military trauma system, as well as alterations in the medical management of trauma patients. During this period, the medical management of trauma patients was also undergoing change. So, beyond the military data, there are precautions in interpreting the growing number of papers citing the civilian trauma experience. All civilian studies to date are either retrospective studies or prospective cohorts using retrospective “controls,” again raising the issue of changes in patient care beyond these resuscitation protocols over time. Trauma patients are a tremendously heterogeneous group (as opposed to say hip replacement patients), making comparisons across patient groups, and challenging at best. This particular issue has likely contributed to the undoing of blood substitute studies in trauma thus far. Other issues include a subjective and after-the-fact segmenting of trauma patients into “buckets” of ratio groupings, introducing the possibility of bias, particularly because there at times seems to be an overt push to validate reconstituted whole blood (1:1:1 therapy). This was best illustrated in the Borgman article where they used a “bootstrapping” technique to reduce the initial six groups of ratio patients down to three after their data analysis appeared to show a grouping of mortality rates. Survivor bias is another important confounding factor that has often been overlooked. Trauma patients who survive long enough will receive additional plasma therapy; however, trauma patients who do not survive are assigned to lower plasma ratio groups and as treatment failures. Best described by Snyder et al, “Therefore, it could be concluded that the nonsurvivors in our study population did not die because they got a lower FFP:PRBC ratio; they got a lower ratio because they died.”

The final issue is recently published data from civilian trauma centers that is somewhat at odds with the military data. A review of FFP:RBC ratios and outcomes at two trauma centers (Los Angeles County/University of Southern California and Grady Memorial) showed no further survival benefit in patients given ratios of FFP:RBC beyond 1:3, suggesting that plasma use in higher ratio protocols might be excessive and wasteful. The most concerning data comes out of Denver Health, where an analysis of their data demonstrated a “U”-shaped curve, with a decline in mortality as FFP:RBC ratios increased to 1:3; but, as the ratio climbed further to 1:1, mortality rates also increased. As the authors discussed, once
the therapeutic effect of the plasma has peaked, the adverse effects (eg, transfusion-related lung injury and multisystem organ failure) may predominate. Evidence such as this suggests that blood has a very narrow therapeutic window, so the optimal ratio of FFP:RBC in these trauma protocols is a critically important question.

To minimize the collateral damage of trauma resuscitation, hospitals need to use the best available evidence to develop massive transfusion protocols and continually evaluate their appropriate use and effectiveness. The protocol itself may convey some benefit, independent of blood product ratios, by increasing communication among team members and by allowing quicker access to blood products.15 Beyond the protocol, point-of-care/near patient testing should be used to convert the treatment approach from empiric to goal-directed therapy at the earliest possible time. Finally, blood product therapy should be used as a supplement to other evidence-based “damage control” measures, such as low-volume resuscitation and permissive hypotension until surgical hemostasis is achieved, as well as the prevention or correction of acidosis and hypothermia.16 One of the more promising developments has been the safe and effective use of the antifibrinolytic drug tranexamic acid in trauma patients to reduce transfusion requirements and improve survival in a recent prospective randomized trial.17

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Off-label drug use: Recombinant factor VIIa in trauma patients is discussed.

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