



Prehospital balanced resuscitation may mitigate hypofibrinogenemia in traumatic hemorrhagic shock

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The article ‘Does an early, balanced resuscitation strategy reduce the incidence of hypofibrinogenemia in hemorrhagic shock?’¹ by Lubkin explores the incidence of hypofibrinogenemia (defined by admission fibrinogen <150 mg/dL or rapid thromboelastography (TEG) alpha angle <60°) and the impact of early cryoprecipitate administration on survival in a population of over 30 000 severely injured patients, nearly 2000 of which received balanced resuscitation in the prehospital setting or immediately after arrival. The cohort they studied had a 7% prevalence of hypofibrinogenemia, primarily diagnosed by TEG rather than conventional fibrinogen levels. Importantly, this is a dramatically lower incidence of hypofibrinogenemia compared with other centers that have reported 15% to 60% incidence for similarly injured patients.² The reasons for this are presumed to be multiple. First, this cohort of patients was treated by highly trained prehospital care providers who perform early diagnostics for hemorrhagic shock and initiate hemostatic resuscitation. Furthermore, over half of the patients transfused received whole blood, and those patients had lower odds of hypofibrinogenemia, suggesting that early hemostatic resuscitation may pre-empt the development of severe coagulopathies including hypofibrinogenemia if initiated early enough.

Interestingly, although prehospital whole blood administration was associated with much lower odds of hypofibrinogenemia, there was no overall survival benefit identified. Further, early administration of cryoprecipitate did not seem to affect survival in the patients who had hypofibrinogenemia at admission, although the sample size for this subset of patients was small. Overall, these findings mirror findings of the E-FIT¹³ and CRYOSTAT-2⁴ trials, both of which did not demonstrate survival benefit with early administration of cryoprecipitate for hemorrhagic shock; however, rates of hypofibrinogenemia are not explicitly stated in either of these studies. The authors do attribute the relative low rates of hypofibrinogenemia in their cohort to the initiation of early prehospital balanced resuscitation with blood products or whole blood, which is supported by the PAMPer trial⁵ and others.⁶

Overall, this study is an important contribution to the literature and describes a possible strategy to mitigate a hypofibrinogenemic phenotype of trauma-induced coagulopathy with early prehospital transfusion capabilities. The authors should be applauded for systematically studying a very large population of injured patients with functional coagulation, transfusion, and extensive clinical outcome data to answer increasingly nuanced questions in

the field of early hemostatic resuscitation. It remains unknown what the ‘right’ amount of fibrinogen is in a hemorrhaging patient, and whether hypofibrinogenemia should be defined by the same cut-off for all injured patients. Is it really the amount of fibrinogen on arrival that is relevant to outcomes and to triggering therapeutics? Or, is it the consumption of fibrinogen and the change from the native baseline that is more relevant? As the authors continue to explore this, accounting for detailed transport, transfusion, and therapeutic timing, and obtaining pre-transfusion/pre-therapeutic baseline laboratory measures for comparison will further advance our understanding toward more personalized prevention and correction strategies for trauma-induced coagulopathies including hypofibrinogenemia.

Contributors NS was responsible for drafting the work, the conception and design of the work, final approval of the version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. LK was responsible for revising the work critically for important intellectual content, the conception and design of the work, final approval of the version to be published, and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Competing interests LK—consulting for University of Maryland/ BARDA, Scientific Advisory Board of Cerus, Consulting for Gamma Diagnostics, Consulting for Coagulant Therapeutics, Consulting for Haemonetics and husband is founder of CaptureDx.

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