ANESTHESIOLOGY

Openventio PUBLISHERS

ISSN 2474-8919 Open Journal http://dx.doi.org/10.17140/AOJ-1-e001

Editorial

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Volume 1 : Issue 1
Article Ref. #: 1000AOJ1e001

Article History
Received: January 20th, 2016
Accepted: January 21st, 2016
Published: January 21st, 2016

Citation
Mazzeffi M, Tanaka K. Hemostasis management during adult extracorporeal membrane oxygenation: a shot in the dark? *Anesthesiol Open J*. 2016; 1(1): e1-e3. doi: 10.17140/AOJ-1-e001

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Hemostasis Management during Adult Extracorporeal Membrane Oxygenation: A Shot in the Dark?

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KEYWORDS: Bleeding; Coagulation; Extracorporeal membrane oxygenation (ECMO).

Extracorporeal membrane oxygenation (ECMO) has been used increasingly in adult patients with cardiopulmonary failure.[1] According to the Extracorporeal Life Support Organization's (ELSO's) 2012 report over 51,000 patients have received ECMO. Most cases are for neonates; however, an increasing proportion is for adults.[2] ECMO is a unique life saving therapy, but many patients experience complications including: hemolysis, systemic thromboembolism, neurologic complications, and bleeding.[3] We previously reported that up to 56% of patients experience at least one significant bleeding event during ECMO and the rate of serious bleeding events is approximately 10 per 100 ECMO days.[4] Our data also suggest that bleeding events and the amount of transfusion on ECMO are associated with decreased survival.

Why do ECMO patients bleed and what hemostatic therapies are most effective for treatment? Unfortunately, there are limited data to help answer these questions. To our knowledge there are no studies comparing bleeding rates with different anticoagulation regiments. Our own work showed that over-anticoagulation with unfractionated heparin contributes to bleeding complications during ECMO, as patients with bleeding were more often above their target activated Partial Thromboplastin Time (aPTT).[4] Data from one small observational study suggest that low dose unfractionated heparin with a target Activated Clotting Time ACT of 180-220 seconds is associated with significantly less bleeding than high dose heparin with a target ACT of 180-220 seconds.[5] In this study low dose heparin was not associated with a higher rate of thrombosis or oxygenator changes.

In addition to these anticoagulation issues, ECMO patients experience a complex coagulopathy. Although, no evidence-based treatments can be recommended at the present time, various pathophysiologic mechanisms have been suggested. Similar to ventricular assist devices, ECMO appears to increase cleavage of large von Willebrand factor multimers by the A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS13) enzyme.[6,7] Qualitative platelet dysfunction also develops within 90 minutes of ECMO initiation and enhanced fibrinolysis occurs presumably due to contact pathway activation which facilitates conversion of plasminogen to plasmin.[8,9]

Monitoring patients who are at risk for bleeding during ECMO also remains a significant challenge. Viscoelastic Coagulation Tests (VCT) such as Thromboelastography (TEG) and Rotational thromboelastometry (ROTEM), which have proven useful in other settings have not been shown to predict bleeding events in ECMO patients.[10,11] Our own experience is that patients who are on ECMO typically have elevated fibrinogen levels and have a normal Maximum Amplitude (MA) on heparinase TEG or normal Maximal Clot Formation (MCF) on ROTEM EXTEM or FIBTEM. This is presumably related to elevated fibrinogen levels during ECMO. These tests are also not sensitive for detecting fibrinolysis, unless it is a systemic phenomenon.[12] Likewise, standard plasma based coagulation tests such as the International

ISSN 2474-8919 Open Journal http://dx.doi.org/10.17140/AOJ-1-e001

Normalized Ratio (INR) cannot rule out fibrinolysis or qualitative platelet dysfunction and are also unlikely to be sensitive tests for identifying ECMO patients with high bleeding risk. Taken together, the ECMO care team is often left with difficult decisions to ascertain the adequacy of their anticoagulation, and select optimal hemostatic interventions when patients bleed.

Few studies have examined hemostatic therapies in adult ECMO patients with severe refractory bleeding. One small observational study of 15 patients suggested that treatment with activated recombinant Factor VII is safe and effective for treating intractable bleeding during ECMO.[13] However, there is also a case report of a fatal thrombosis in an ECMO patient who received activated recombinant factor VII and activated prothrombin complex.[14]

In summary, bleeding during ECMO remains a serious problem, which impacts patient survival. Clinical trials comparing alternative anticoagulation regiments are badly needed as are mechanistic studies and studies of hemostatic therapies in patients who experience significant bleeding. Unfortunately, until such evidence is available the ECMO care team is left with few evidence-based interventions to prevent and treat serious bleeding.

ACKNOWLEDGEMENTS: None.

CONFLICTS OF INTEREST: None.

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