

EDITORIAL

Anticoagulation therapy during ECMO: Scylla and Charybdis

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Extracorporeal membrane oxygenation (ECMO) has been widely accepted for life-threatening cardiac or pulmonary failure, even when occurring due to a cardiac arrest. Managing anticoagulation during ECMO is still challenging. The Extracorporeal Support Organisation (ELSO) database contains almost 90,000 ECMO runs, including almost 30,000 adults.^[1] Of these ECMO runs, 16% are associated with thrombotic complications (pump malfunction, oxygenator clotting, infarction of the central nervous system (CNS) of the patient).^[1] Of the reported ECMO runs, 40% are complicated by haemorrhagic events, such as haemorrhage of the gastrointestinal tract, surgical site bleeding, cannula site bleeding, pulmonary haemorrhage, or CNS haemorrhage.^[1] CNS haemorrhage or CNS ischaemia occurs in approximately 6-10% of the ECMO runs.^[1]

In this issue of the Netherlands Journal of Critical Care, Lancé and co-workers provide an excellent outline of anticoagulation management during ECMO.^[2] This review describes why anticoagulation management differs in ECMO patients compared with other patients on the ICU who need anticoagulation. Also anticoagulation practice and anticoagulation monitoring is extensively described.

As noted by the authors, there is still much debate on the optimal monitoring strategy during ECMO. Unfortunately, no randomised controlled trials have been performed to investigate the best anticoagulation strategy for ECMO patients. A concept for managing anticoagulation during ECMO is provided. The authors propose a safe sailing course between clotting and bleeding, guided by multiple parameters of haemostasis. In ECMO, no single parameter, including the activated partial thromboplastin time (aPTT), predicts clotting risk and/or bleeding risk.^[3,4] Inflammation may shorten aPTT and consumption coagulopathy may prolong aPTT, which may lead to misinterpretation of heparin effects. Internationally, a growing number of centres use a multimodal approach, acknowledging the multifactorial process of anticoagulation,

which is not captured by aPTT alone. This multimodal approach, however, is not based on evidence, but on expert opinion, as discussed in an expert round table conference in Rotterdam in 2016. Lancé et al. describe a multimodal approach to anticoagulation during ECMO that entails daily monitoring of multiple coagulation parameters. These tests include aPTT, aXa, platelet count and thromboelastometry (ROTEM®, including EXTEM, INTEM, FIBTEM and HEPTM tests). In a patient with a normal bleeding and thrombosis risk, aXa levels would usually be maintained between 0.5-0.7 IU/ml, with a difference in clotting time between INTEM and HEPTM of approximately 80 sec. This should correspond with an aPTT of approximately 60 sec. In a practical example, when aXa is 0.3 IU/ml, the clotting time difference between INTEM and HEPTM is 30 sec, aPTT is 70 sec and platelet counts are declining, consumption coagulopathy could be suspected, perhaps due to heparin under-dosing. Then, despite elevated aPTT, increasing the heparin dose could be the appropriate therapeutic intervention. This example illustrates how monitoring of only the aPTT could lead to misinterpreting the coagulation status. As it is unpractical to monitor the whole anticoagulation status every six hours, usually the whole package is monitored once a day. After interpreting all the anticoagulation parameters, a new target aPTT is set and monitored every six hours, for the next 24 hours.

For monitoring of the coagulation status of the ECMO machine, D-dimers, fibrinogen and free haemoglobin concentration are measured. D-dimers >30 g/l for more than two days,^[5] decrease of fibrinogen >50% or <1 g/l or a free haemoglobin concentration greater than 50 µmol/l could be an indication of clotting in the oxygenator or of an imminent blood clot in the pump head.

The level of anticoagulation is dependent on many factors. Patients with high bleeding risk (for example trauma or postoperative patients) are maintained at a lower level of anticoagulation, whereas patients with a high thrombosis risk

(for example pulmonary embolism) are maintained at a higher level of anticoagulation. Ideally, bleeding risk or thrombosis risk is assessed on a daily basis. Anticoagulation should be achieved by the effect of heparin. Prolonged coagulation tests should be due to the effect of heparin, and not to a shortage of coagulation factors or an excess of anticoagulation proteins. The ECMO system also determines the anticoagulation threshold. Low ECMO flow or ECMO system characteristics may warrant adjustment of the targeted anticoagulation level. Of note, cannulas have been shown to cause endothelial trauma, leading to endothelial thrombosis resulting in occlusion of the inferior caval vein.^[6]

Coagulation on ECMO is an evolving area, in which evidence is lacking. Most of the strategies are based on expert opinion. Although the review provided by Lancé and co-workers adds

to the understanding of anticoagulation strategies during ECMO, much more research is needed, contributing to further improvement of outcome of ECMO therapy.

References

- 1) International Summary of the ELSO database July 2017, <https://www.else.org/Registry/Statistics/InternationalSummary.aspx>. Accessed on 21 December 2017.
- 2) Lancé M, Mulder M, Fawzy I. ECMO and anticoagulation: a comprehensive review. *Neth J Crit Care*. 2018;26:6-13.
- 3) Ranucci M, Baryshnikova E, Isgro G, et al. Heparin-like effect in postcardiotomy extracorporeal membrane oxygenation patients. *Crit Care*. 2014;18:504.
- 4) Esper SA, Welsby IJ, Subramaniam K, et al. Adult extracorporeal membrane oxygenation: an international survey of transfusion and anticoagulation techniques. *Vox Sang*. 2017;112:443-52.
- 5) Dornia C, Philipp A, Bauer S, et al. D-dimers Are a Predictor of Clot Volume Inside Membrane Oxygenators During Extracorporeal Membrane Oxygenation. *Artif Organs*. 2015;39:782-7.
- 6) Bein T, Philipp A, Pregler B, Noeva E, Graf BM, Stroszczyński C. Long-segment caval Thrombus after removal of ECMO cannula. *Intensive Care Med*. 2015;41:1967-8.