

Challenges in extracorporeal membrane oxygenation

Citation for published version (APA):

Martucci, G. (2022). *Challenges in extracorporeal membrane oxygenation: Precision management to improve survival*. [Doctoral Thesis, Maastricht University]. Maastricht University. <https://doi.org/10.26481/dis.20220117gm>

Document status and date:

Published: 01/01/2022

DOI:

[10.26481/dis.20220117gm](https://doi.org/10.26481/dis.20220117gm)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Chapter 11

Impact



This thesis deals with several unresolved challenges in the field of ECMO.

In the case of V-V configuration, the principal challenges are the decisions on anticoagulation and transfusion thresholds, which are discussed from different sides. In the field of anticoagulation, a protocol based on heparin administration at a low-dose (and stopped in case of any bleeding), accompanied by daily supplementation of antithrombin has been proposed, as well as a tolerance of thrombocytopenia and case-based decisions regarding platelet transfusion according to the risk of bleeding more than rather the mere number of platelets. In this large series, one of the lower heparin mean doses was reported, despite the fact that the total number of bleedings was not lower than the one reported in the literature, the number of severe and fatal bleedings reported was low. Moreover, strictly linked to this approach the transfusion practice for PRBC was also proposed. This was proposed with a lower trigger, and mainly was considered always in the light of several clinical considerations related to the patient, concomitant comorbidities or clinical conditions (e.g., septic shock), and also taking into account the function of the ECMO circuit, which, it should always be remembered, is a modified cardiopulmonary bypass system that has no reservoir other than the patient. This protocol and these concepts were also a source of inspiration for other centers to define protocolized optimization of blood flow and, as reported in a recent meta-analysis, was able to reach very successful outcomes in terms of survival.

As said, one of the key component of the anticoagulation protocol was antithrombin. This blood-derived component was of interest in sepsis management in the 1990s, but lately has been removed from daily practice and interventional trials because it is an expensive drug and (with methodological biased studies) it was impossible to gather solid evidence in favor of its use. But as we highlighted in our review, ECMO may be the field of concrete application of this blood product. In fact, currently the standard of care in terms of circuit anticoagulation is heparin, which needs antithrombin. In cases of heparin resistance in the cardiopulmonary bypass, the restoration of antithrombin levels is the treatment of choice. In pediatric ECMO there is vast experience in the use of that and, finally, as we largely elucidated, antithrombin is a link between inflammation and anticoagulation also at a genomic level, with many microRNA involved in its synthesis and in the coagulation process. This may contribute to the preservation of the endothelium, which is heavily damaged when the blood flows through an extracorporeal circuit.

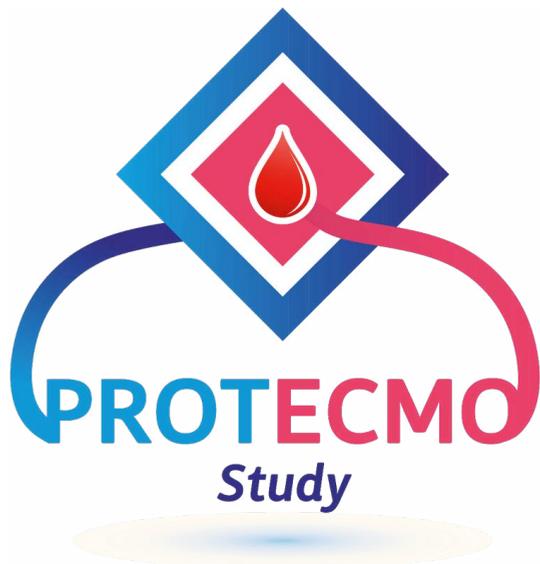
Further investigations regarding the ECMO circuit highlighted the impact of the use of shorter and bioline-coated cannulas on the transfusion of PRBC. This observation stresses the concept of patient-machine fluid interaction in a wide vision. The amount of fluids administered should be linked to the hemoglobin available and to the inflammation and damage of the cellular part of the blood.

The hemoglobin level accepted in ECMO has been explored also by an international survey endorsed by the European Society of Intensive Care Medicine. With all the caution that the use of a survey should be taken with, this survey aimed at covering the knowledge gap about the current use of hemoglobin triggers. In fact, in critically ill patients the comparison between the ABC study and the ICON study at a distance of about ten years has demonstrated that the hemoglobin trigger is lower today compared with the past, and currently ICU patients are transfused (at least in Europe) less frequently, but are also older and sicker. Among the sicker patients there is certainly also the increased number of ECMO patients. Our survey highlighted how, in ECMO, the tolerated hemoglobin is lower than in the past, but currently higher than the last recommendations for general critically ill patients. This was also confirmed in 2020 by the meta-analysis by Abbasciano and collaborators, with a select number of studies.

Strictly related to hemoglobin management there are the episodes of bleeding during ECMO, and among them gastro-intestinal bleeding is one of the major ones. The occurrence of stress ulcer is frequent in critically ill patients due to altered gastrointestinal perfusion, drug administration, and imbalance of the gastric acid production, but when it occurs in ECMO it can become an uncontrolled bleeding, prompting an increase of blood product transfusion, impairing the ability to use adequate anticoagulation and, finally, increasing mortality. The use of advanced endoscopy in our series was able to arrive at a mortality comparable to that of the ECMO population without gastro-intestinal bleeding. The management of complications in proper way is one of the key components for fostering increased survival in higher volume centers.

Finally, in peripheral V-A ECMO, one of the unsolved questions is the occurrence of limb ischemia in the leg, where the arterial cannula is placed. In our thorough review of the literature, the risk factors as well as the need for adequate planning and prevention are highlighted, and an operative algorithm is proposed.

All these considerations taken together may contribute to a more precise ECMO management, and contribute to better outcomes in this resource-demanding procedure. All the explored topics will need further data gathered worldwide to build the current practice of ECMOlogy. All the studies collected in this thesis were fundamental pieces in creating a prospective multicenter observational study, the PROTECMO study, which is focused on transfusions, anticoagulation management, and type and severity of bleeding, and that will arrive at its first results in the near future.



PROTECMO

Study