

Bleeding-related conditions and complications in extracorporeal life support

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In this dissertation, the amount of bleeding complications in extracorporeal life support (ECLS) and the balance of hemostasis and risk factors were investigated. Furthermore, the possibilities and challenges of application of ECLS in high-risk trauma patients were reviewed and discussed.

The dissertation presents substantial knowledge of bleeding-related complications in the use of ECLS based on the extracorporeal life support organization (ELSO) registry data and available literature. The trend of bleeding complications was thought to be decreasing, however the absolute decrease analysis was previously not performed due to the heterogenous characteristics between studies and lack of uniform complication definitions. This manuscript presents the first study with trend calculations on bleeding complications over a twenty-year period including international data with more than 50 000 patients.

Furthermore, this thesis presents the development of the prediction models for bleeding complications in veno-venous (V-V) and veno-arterial (V-A) ECLS based on the multi-international ELSO database including a high number of patients and using a standardized definition of bleeding complications. Prior to these studies, only one prediction model for bleeding ocmplications during ECLS was available. However, this model did not separate V-V and V-A ECLS, so underlying differences of pathophysiology were not considered in these analyses. Additionally, the development of the presented models is based on high number of patients and the analytical methods ensured a robust model development.

Researchers could benefit from models and the presented odds ratios. The odds ratios for all variables provide insight of the risk factors contributing to bleeding complications. The prediction models presented can be used in research settings to differentiate low and high-risk patients for bleeding complications. This can be implemented in studies assessing different types of anticoagulation managements such as low-dose anticoagulation or an anticoagulation-free period during ECLS. Prevention of bleeding complications in the future seems increasingly realistic and subsequently can contribute in anticipating on bleeding complications with altered anticoagulation methods.

In the future, improving the prediction models with additional factors such as anticoagulation use and laboraty findings, will have major impact on working towards personalized medicine.

Also, we present a great overview of improvement of the circuit and anticoagulation management during ECLS, where the collaboration between clinical and basic scientists is clarified to be essential to enable research from bench to bedside.

In addition, the dissertation focusses on high-risk trauma patients supported on ECLS.

In the presented analysis, almost 280 trauma patients were included, one of the largest cohorts presented in ECLS investigation focussed on trauma patients. In this analysis, a decrease of complications was found with the increase of use of ECLS in trauma patients, emphasizing the need for further investigation in this subgroup of patients. Moreover, in the following review we provided a great synopsis of the applications of ECLS in different types of trauma.

With the outcomes presented in this dissertation the ECLS society, including intensivist, surgeons, cardiologists, pulmonologists, perfusionists and other clinicians working with ECLS, should be encouraged to continue the use of ECLS in challenging cases with bleeding risks and contribute research in ECLS settings. The increase of ECLS use with decreasing mortality and bleeding complications should strengthen the believe in effectiveness of ECLS. Furthermore, the ECLS society should be inspired to improve the ELSO database by including a trauma addendum and possibly anticoagulation and laboratory data in the future to improve research in the future.