EuroELSO working group on coagulation, antithrombotic and patient blood management

The following populations and topics will be covered within the scope of this working group:

- Adults (age > 18 years) and Pediatrics (age < 18 years)
- Devices: V-V ECMO, V-A ECMO
- Topics: Bleeding/Thrombosis, anticoagulation, antiplatelets, patient blood management/transfusions, bleeding scores, haemolysis in relation to mechanical devices, hematological aspects

Creation of a working group within EuroELSO- Why is this topic so important?

1) The strong rational, why ECMO impacts coagulation and frequently requires transfusions

Extracorporeal life support majorly impacts the human coagulation system. Extracorporeal surfaces provide artificial surfaces activating the contact system and may trigger subsequent clot formation with consumptive coagulopathy, high flow rates and shear stress promote platelet dysfunction, and underlying pathologies including sepsis/sepsis-like conditions (such as after cardiac arrest) or post-surgical admissions further promote coagulopathy.
Not only severe bleeding, which can be closely linked to coagulopathy, but several other factors contribute to the high demand of blood products during ECLS. These factors include eg. hemodilution, hemolysis, iatrogenic blood loss from phlebotomy and others for packed red blood cell transfusion and thrombocytopenia, arising from eg. consumptive coagulopathy, platelet sequestration, bone marrow suppression, which is why platelet transfusions are often performed.
As an example, the most recent randomized controlled trial in cardiogenic shock have shown a significant rate of major bleeding contributing to the high mortality rate, in the absence of guidance in management of antithrombotics (ECLS Shock trial, DOI: 10.1056/NEJMoa2307227). Similarly, data in V-V ECMO have shown the contribution of clinically relevant bleeding to excess mortality (PROTECMO study, DOI: 10.1164/rccm.202305-0896OC).

2) Heterogeneity across reporting of bleeding and thromboembolic events

Complications arising from coagulopathy, including bleeding and thromboembolism, are frequent among ECLS patients and affect mortality. However, reporting of clinically relevant bleeding and thromboembolic events displays large heterogeneity, which makes a direct comparison of data often difficult.

3) Heterogeneity across anticoagulation regimes

The majority of ECLS patients require anticoagulation to avoid clotting of the circuit and its components. Prospective data on intensity and choice of anticoagulants are scarce, which

largely limits the evidence for scientific guidelines with strong recommendations. Therefore, the majority of centers use in-house protocols (DOI: 10.1093/ehjacc/zuae040), which further promotes the heterogeneity of complications reported across centers.

4) **Heterogeneity across transfusion thresholds**

Recent studies and surveys have shown that clinical practice and transfusion thresholds largely vary between centers (PROTECMO study, DOI: 10.1016/S2213-2600(22)00353-8; DOI: 10.1111/trf.17505). However, it remains to be elucidated, which transfusion cut-off counterbalances the benefits of transfusions best with the potential of infectious and immunological adverse events. Additionally, for a significant amount of patients, ECMO serves as a bridge-to-transplant option, where alloimmunization needs to be considered. Furthermore, shortage of blood products needs to be considered and alternatives to transfusions currently remain scarcely investigated in the ECLS population.

Why should this working group be established within EuroELSO?

This group will comprise a panel of experts to (i) identify clinically important knowledge gaps answering the even most basic questions in antithrombotic management of ECMO patients, (ii) create evidence through multinational studies of all kind, (iii) provide guidance through establishing guidelines and (iv) provide content for educational purpose.

Antithrombotic and patient blood management in ECMO has thus far - to the best of our knowledge - not been specifically addressed in any working group activities of EuroELSO.

Main objectives

1) Assess current knowledge gaps regarding antithrombotic and patient blood management and provide expert consensus on research priorities;
2) Understand the mechanism of coagulopathy during ECMO and its clinical impact;
3) Understand the difficulties of patient blood management during ECMO;
4) Characterize and optimize reporting of bleeding and thromboembolic events.
5) Characterize and optimize management of Haemolysis during ECMO support

Specific objectives

Specific objectives will be defined during the first meetings of the working group. A survey will be sent out to all members to provide an overview on research interests and practice standards. Preliminary objectives will span across:

1) **Evaluation of knowledge gaps**
   i) Systematic review, evidence mapping and evidence gap analysis on a) coagulation and b) patient blood management on particular subgroups of ECMO, including postsurgical V-A ECMO, V-A ECMO in cardiogenic shock, eCPR, and VV ECMO.

ii) Expert consensus on research priorities for a) coagulation and b) patient blood management in the respective fields.

2) **Mechanism of coagulopathy & Difficulties of patient blood management**
   i) Create a prospective/retrospective multinational registry including coagulation and transfusion parameters
3) **Reporting of bleeding and thromboembolic events**
   i) Systematic review on different reporting of bleeding and thromboembolic events across the literature
   ii) Prospective observational study using different classifications to find the optimal classification (=discriminating best for clinical relevance)
   iii) Consensus on reporting of bleeding and thromboembolic events & recommendation for minimum reporting in ECLS studies
4) **Reporting of Haemolysis events in relation to ECLS**

Members

- Chairs:
  - Nina Buchtele (Austria) & Christophe Vandenbriele (Belgium/UK)
- Member of steering committee
  - Annemieke Oude Lansink-Hartgring (Netherlands)
- Member of scientific committee
  - Jan Bělohlávek (Czech Republic)

General activities (to be discussed):

- Coordinate/lead/support research activities → research proposals are welcomed from all working group members
- Keep guidelines updated
- Participate in Annual congress
- Educational activities: webinar, podcasts, workshops, lectures, sessions, simulation-based courses, journal clubs
- Promote multidisciplinary collaborations
- Links with other scientific/medical societies related with the topic

General structure

We propose two chairs who will share the responsibilities listed in the *EuroELSO working group requirements* for this working group for the following reasons:

The idea to have two chairs will be

(i) to broadly cover the wide aspects of coagulation in ECMO. The two proposed chairs, one who is experienced in research and management regarding acute cardiovascular care with a focus on V-A ECMO and mechanical assist devices (Christophe Vandenbriele) and one who is experienced in research and management regarding V-V ECMO especially in infectious diseases/haemonc

critical care and haemostaseology in ECMO (Nina Buchtele). These joint forces will help to cover the broad range of various aspects of coagulation among ECMO patients and optimize the definition of research priorities within the group.

(ii) To create a fair balance regarding gender and career stages (Christophe as an established researcher and board member of the ESC ACVC, Nina as an earlier career researcher), which will aid in communication with different audiences in educational activities, communication with the industry and provide advantages for obtaining successful funding from research grants.

(iii) To ensure (organizational) success of the working group by shared responsibilities of the two chairs to limit the individual work load and increase the visibility of the working group among societies with in-person visits to relevant annual meetings of other societies interested in cooperation.