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Variability in anticoagulation management of patients on extracorporeal membrane oxygenation: an international survey

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Abstract

Objective—The objective of this study was to determine current practices of anticoagulation in patients on extracorporeal membrane oxygenation (ECMO).

Design—Internet-based cross-sectional survey distributed between November 2010 – May 2011.

Setting—Extracorporeal Life Support Organization (ELSO)-registered ECMO centers internationally.

Participants—ECMO medical directors and coordinators.

Interventions—None.

Measurements and Main Results—There were 121 responses from ECMO medical directors and coordinators at 187 ELSO centers with access to the survey. Eight-four of 117 (72%) respondents reported having a written institutional ECMO protocol for both anticoagulation and blood product management at their institution. Sixty-nine of 117 (59%) respondents reported use of tip-to-tip or partially heparin-bonded circuits. Unfractionated heparin was used at all centers; only 8% of respondents indicated use of alternative anticoagulation medications in the 6 months prior to the survey. The preferred method of anticoagulation monitoring was the serial measurement of activated clotting time (ACT), as reported by 97% of respondents. In this survey, 82% of respondents reported antithrombin III (ATIII) testing, 65% reported anti-factor Xa testing, and 43% reported use of thromboelastography during ECMO. Goal ranges for these three tests and interventions triggered by out-of-range values were found to be variable.

Conclusions—ECMO anticoagulation management policies vary widely by center. The majority of ECMO programs employ ACT as the preferred anticoagulation monitoring tool. The coagulation system is also monitored using more specific markers such as ATIII, anti-factor Xa and thromboelastography by a large number of centers. Future research is needed to elucidate optimal anticoagulation management and improve outcomes.

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The authors have no conflicts of interest relevant to this article.

Keywords

ECMO; extracorporeal membrane oxygenation; antithrombin; anti-factor Xa; thromboelastography; anticoagulation

Introduction

Management of anticoagulation and blood product administration in patients undergoing extracorporeal membrane oxygenation (ECMO) is controversial despite more than 30-years of ECMO experience.(1, 2) The rate of disorders of coagulation, including life-threatening hemorrhage and thrombosis, remains high, between 10%–33%.(3) At present, there are no established evidence-based guidelines for anticoagulation during ECMO.

The Extracorporeal Life Support Organization (ELSO), an organization composed of international ECMO centers is spearheading an effort to create ECMO anticoagulation and blood product management guidelines for newborns, children and adults. As a starting point for this endeavor, we launched a survey with the overall goal of characterizing anticoagulation practices among ECMO centers in the U.S. and throughout the world.

We hypothesized that anticoagulation and blood product management practices vary widely among ECMO centers and that more specific methods to monitor the status of the coagulation system, such as anti-factor Xa, antithrombin III (ATIII) and thromboelastograms (TEG) are starting to be used broadly compared to traditional monitoring methods such as activated clotting time (ACT), prothrombin time (PT) and activated partial thromboplastin time (aPTT).

Methods

We conducted an anonymous, single cross-sectional survey of ECMO medical directors and ECMO program coordinators from all ELSO-reporting centers. The survey was piloted by four ECMO medical directors and program coordinators for clarity of the questions. The sampling frame consisted of the publicly available list of ELSO-registered ECMO centers (<http://www.elso.med.umich.edu/Member.asp>) at the time the survey was launched in November 2010. The survey was then disseminated through the monthly ELSO newsletter (four postings) and on an internet page dedicated to ECMO professionals with ELSO affiliation (<http://www.ecls-net.net/>) (one posting). The survey was distributed using a commercial web-based instrument (SurveyMonkey.com®), and was open from November 2010 to May 2011.

The survey was organized around the following four domains: 1) ECMO program characteristics, 2) patient population characteristics, 3) institution-specific anticoagulation protocols and blood product transfusion protocols and 4) methods for anticoagulation monitoring. Due to anonymity requirements by the Johns Hopkins Institutional Review Board (IRB), only the continent of origin was recorded. Only one response per institution was requested. A duplicate check was conducted for all variables, as well as for sets of variables within the four domains of the survey, for all respondents, and by continent. When two respondents were found to have more than two identical responses within one domain, a secondary check for duplicate answers was done focused on those respondents for the remainder of variables in the same domain as well as the other three domains. We found no evidence for answers originating from the same ECMO program. After the survey was closed, we performed exploratory data analysis and reported means, standard deviations and proportions of respondents, as appropriate. Respondents were divided by location, size of intensive care unit, ECMO capacity and primary patient population (i.e., neonatal, pediatric,

adult or mixed). Differences between groups were analyzed using Wilcoxon rank sum test for non-normally distributed continuous variables, Student's *t* test for normally distributed continuous variables or χ^2 test for binary variables. A *p*-value of 0.05 was considered significant. Statistical analysis was conducted using STATA 11.0 (StataCorp, College Station, TX, 2009).

Results

At the time the survey was open in November 2010, there were 187 ELSO-registered ECMO centers from 22 countries on five continents (132 in the USA, 7 in Canada, 31 in Europe, 9 in Australia and New Zealand, 5 in Asia and 3 in South America). The ELSO newsletter is only available to ELSO-registered ECMO medical director(s) and ECMO coordinator(s). There were 121 respondents who replied to at least one question of the survey, yielding an overall 65% response rate assuming no duplicates. There were 103 responses from North America, 12 responses from Europe and 6 responses from Australia and New Zealand. Twenty-four of 121 (20%) respondents were from ECMO programs that served a single intensive care unit (ICU) and 97 (80%) served more than one ICU. The programs were pediatric-only (neonatal ICU, pediatric ICU and/or pediatric cardiac ICU), 81 (67%), adult-only (adult cardiac ICU, adult surgical ICU and/or adult medical ICU), 4 (3%) or mixed pediatric and adult, 36 (30%). The size of the ICUs served was 10 beds, 5 (4%), 11–30 beds, 51 (42%), and >30 beds, 65 (54%). The ECMO capacity (i.e., maximum number of simultaneous ECMO runs the program can provide) was 1–4, 93 (77%) or 5–10, 28 (23%). In the six months prior, respondents have used ECMO at their respective centers for cardiac failure, 102/120 (85%), respiratory failure, 115/120 (96%), sepsis, 71/120 (59%), and extracorporeal cardiopulmonary resuscitation (ECPR), 65/120 (54%).

Institutional protocols and circuit characteristics

Most respondents reported having a written institutional ECMO protocol for both anticoagulation and blood product management at their institution, 84/117 (72%). Others had a written protocol for ECMO anticoagulation only, 15/117 (13%), for ECMO blood product management only, 7/117 (6%), or neither, 11/117 (9%). Presence or absence of an institutional protocol was not associated with the size of the ICU(s) served nor with the maximum ECMO capacity or the population served ($p>0.05$). Anticoagulation was managed mainly by the ICU staff on service making day-to-day decisions, 81/118 (69%) respondents. Forty-three respondents indicated that “Dedicated “expert” ICU staff makes/helps with decisions”. With regards to the involvement of a Hematology/Thrombosis consulting service: the “Hematology/Thrombosis team is only consulted when the ICU team has difficulties” (32/118 respondents), “ICU staff and Hematology/Thrombosis team make decisions together” (16/118), “Hematology/Thrombosis team rounds with ICU team daily” (4/118), “Hematology/Thrombosis team is never consulted” (5/118), and “Hematology/Thrombosis team makes all decisions” (1/118).

Equipment

Forty-eight of 117 (41%) ECMO centers did not use heparin-bonded circuits, 38/117 (32%) reported use of tip-to-tip heparin-bonded circuits and 31/117 (27%) reported that certain components of the circuits were heparin bonded. Neonatal and pediatric centers use roller pumps only [43/81 (53%)], and centrifugal pumps or both centrifugal and roller pumps [38/81 (47%)], while the majority of adult ECMO centers use centrifugal pumps [36/40 (90%)].

Circuit priming solutions

The most common solution combination for ECMO circuit priming included packed red blood cells (PRBC), heparin, albumin, calcium chloride or calcium gluconate and sodium bicarbonate. (Table 1) Fresh frozen plasma (FFP) use was reported by 50% of respondents. Age differences were noted for PRBCs, heparin, sodium bicarbonate, which were all significantly more used in pediatric-only vs adult-only and mixed adult and pediatric centers ($p<0.05$). There were significant differences in priming practices by geographic location. Respondents from Australia/New Zealand reported no usage of normal saline and FFP, whereas both are commonly used in North America and Europe. All steroid and tromethamine use in circuit priming was reported from North America and none was reported from Europe and Australia/New Zealand. Use of PlasmaLyte and similar solutions was not reported by respondents from Europe, but was reported by half of the respondents from Australia/New Zealand, 3/6 (50%), and by 17/103 (17%) of North American respondents.

Heparin and other coagulation-related medications

All respondents indicated use of a continuous unfractionated heparin (UFH) infusion, with varying minimum and maximum heparin infusion rates as detailed in Table 1. Use of non-UFH anticoagulation remains rare: 10/117 respondents (8%) reported use of argatroban, lepirudin and/or bivalirudin in the 6 months prior to answering the survey. Fifty-seven of 107 (53%) respondents reported availability of argatroban, lepirudin and/or bivalirudin should an indication such as heparin-induced thrombocytopenia arise. There were no significant differences in usage of non-UFH products by patient population (children vs. adults), size and/or location of ECMO centers ($p>0.05$).

A variety of adjunct medications are used during ECMO to better control anticoagulation and/or hemorrhage or thrombosis, such as hemostatic agents (ϵ -aminocaproic acid, tranexamic acid, recombinant human factor VIIa, aprotinin and other serine protease inhibitors), antiplatelet agents (acetylsalicylic acid, prostacyclin) and vitamin K antagonists (warfarin). (Table 1) There were no differences in the use of these medications by type and size of ICU(s) served by the ECMO programs ($p>0.05$), but there were significant regional differences, with higher usage of ϵ -aminocaproic acid and recombinant human factor VIIa in North American ECMO centers, and higher usage of tranexamic acid in European and Australian/New Zealand centers.

Anticoagulation monitoring and blood product administration

Monitoring patterns for anticoagulation and thresholds for blood product administration are detailed in Table 2 and Table 3, respectively. The vast majority of respondents, 113/116 (97%), use ACT to monitor anticoagulation; the most commonly reported goal ACT range was 180–200 s by 43 of 113 (38%).

Ninety six of 117 respondents (82%) reported routine or occasional *ATIII* testing. (Table 2) The goal *ATIII* activity in a typical ECMO patient was: median 70% (range 30–100%), $n=59/96$ respondents. Ten of 96 respondents reported that their centers did not have a specified goal *ATIII* activity and 27 did not answer the question. To correct a patient's lower-than-goal *ATIII*, 46/91 (51%) use either FFP or recombinant or pooled *ATIII*, 12/91 (13%) use only FFP, 31/91 (34%) use only recombinant or pooled *ATIII* and 2/91 (2%) use neither.

Seventy five of 115 respondents (65%) reported routine or occasional *anti-factor Xa* testing (Table 2) The most commonly reported goal anti-factor Xa range was 0.3–0.7 IU/ml, by 40 of 67 respondents (60%). Other ranges reported by 10 respondents (15%) varied from as low

as 0–0.29 IU/ml to as high as 0.71–1 IU/ml. The remaining 17 of 67 respondents (25%) stated they “do not have a goal for anti-factor Xa levels”. If anti-factor Xa were lower-than-goal, respondents would increase heparin infusion rate or administer heparin bolus, 30/50 (60%), with or without FFP or ATIII administration to correct low ATIII if present; obtain more data on coagulation status via PT, aPTT, TEG, 9/50 (18%); and make individualized decisions or no changes at all, 11/50 (22%). If anti-factor Xa were higher-than-goal, respondents would decrease heparin rate, 31/46 (67%); adjust ACT range, 7/46 (15%); obtain more information on coagulation status, or consider interventions such as FFP administration or ATIII correction if low ATIII activity.

TEG use was reported as routine or occasional by 50 of 116 (43%) respondents. Of the 50 TEG users, 40 answered the follow-up question related to the type of TEG used at their center: 32/40 (80%) reported use of heparinase TEG alone or in combination with kaolin TEG or rotative TEG, 4/40 (10%) reported use of rotative TEG (thromboelastometry or ROTEM) only, 3/40 (8%) use kaolin TEG only, and 1/40 was not sure. Of the 27 respondents who further elaborated on TEG parameters used, most reported using some or all parameters (i.e., r, K, α , MA) to better define the status of the coagulation system (18/27), but no details on specific threshold were given; some only interpret and use the r time (2/27), and others do not have a protocol for TEG interpretation and/or do not use results to guide therapy (7/27).

Discussion

Our findings show that management of anticoagulation and blood product administration during ECMO is highly variable among international ECMO centers. This variability in practice patterns is likely due to a paucity of published studies to provide the groundwork for the development of evidence-based guidelines.

To our knowledge, this is the first comprehensive survey of ECMO practices of anticoagulation and blood product management. Previous ECMO program surveys(4, 5) focused on the use of ACT. This survey shows that the preferred method of point-of-care anticoagulation monitoring remains the serial measurement of ACT, as reported by 97% of respondents. However, ACT testing has several weaknesses: it can be prolonged in association with thrombocytopenia, platelet dysfunction, elevated d-dimers, low fibrinogen, other coagulation factor deficiencies, hypothermia or hemodilution(6) and can be decreased in hypercoagulable states. Further, ACT devices may yield different results, potentially confusing clinicians on adequacy of anticoagulation.(7–9) The use of ACT and common thresholds to guide therapy have not been prospectively analyzed to determine if they are associated with improved outcomes. Three respondents to this survey indicated that they do not use ACT to guide anticoagulation, but rather use aPTT and/or anti-factor IIa. Neither aPTT nor anti-factor IIa have been formally studied in ECMO. In healthy children and adults, both tests show age-related differences for a given anti-factor Xa activity of heparin. (10) Differences are more pronounced in young infants, with higher aPTT for the same anti-factor Xa.(10) aPTT is also affected by hemodilution in infants on extracorporeal support. (11) For these reasons, aPTT is likely to be used more in adult, rather than neonatal and pediatric centers.

For these reasons, many centers have moved to a more comprehensive panel of laboratory tests besides the classical ACT, PT, aPTT, fibrinogen or d-dimers. In this survey, 65% of respondents reported anti-factor Xa testing, 82% reported ATIII testing and 43% reported use of TEG during ECMO. Goal ranges for tests such as anti-factor Xa, ATIII or TEG and interventions triggered by values considered abnormal at a particular center were found to

also be variable, indicating that clinical practice has evolved in the absence of adequate evidence from observational or experimental ECMO clinical studies.

Anti-factor Xa assays determine heparin activity in the plasma and could provide an alternative to ACT for monitoring anticoagulation. In two small single-center studies, using point-of-care heparin concentration tests to guide anticoagulation during cardiopulmonary bypass led to more adequate anticoagulation, and helped reduce hemorrhage and need for transfusions when compared to ACTs.(12, 13) Heparin concentration and anti-factor Xa as monitoring tools during ECMO have only been reported in small studies. Anti-factor Xa levels were found to range between 0.2–0.6 IU/ml and up to 0.7 ± 0.2 IU/ml, and were found to have poor correlation with ACT values.(9, 14–17) Previously reported targets for anti-factor Xa during ECMO were 0.3–0.6 IU/ml(16) or 0.3–0.7 IU/ml.(1) In our survey, the most commonly reported goal for anti-factor Xa was similar: 0.3–0.7 IU/ml (60% of respondents). As many as a quarter of respondents indicated that their center does not have a clear target for anti-factor Xa. Anti-factor Xa levels are used as an adjunct test, and there are no published data on outcomes of ECMO patients monitored by anti-factor Xa compared to ACT.

ATIII is a plasma glycoprotein that forms an irreversible inactive complex with thrombin and activated factor X. This process is greatly accelerated by heparin. Adequate ATIII activity is therefore required for anticoagulation during continuous heparin infusion therapy. The target ATIII during ECMO is also not known. Respondents reported highly variable target ATIII ranges, from as low as 30% to as high as 120%. The appropriate ATIII activity during ECMO cannot be easily determined. In normal individuals, ATIII activity is lowest in neonates, and then is 10% higher compared to adult values for the rest of the childhood.(18) Normal values in means and boundaries including 95% of the population are 76% (58%–90%) in neonates and 96% (66%–194%) in adults.(18) In ECMO patients, published data are limited to a very small number of patients. In a series of 10 neonates on ECMO, median ATIII activity was found to be 19% (range: 3%–49%) immediately on ECMO, 28% (range: 17%–46%) at 6 h on ECMO and 33.5% (range: 15%–51%) at 24 h on ECMO.(19) Some ECMO centers have previously reported replacing ATIII with plasma-derived or recombinant ATIII, but the target ATIII and cutoff for replacement in ECMO patients were not detailed.(2, 14, 20, 21). In six postcardiotomy patients, investigators administered a continuous ATIII infusion to achieve a goal ATIII activity of 100% and found this to be associated with a lower incidence of hemorrhage.(20) In a different series, ATIII administration for ATIII activity <50% led to a decrease in markers of prothrombin activation and appeared to be beneficial.(22) A note of caution for this practice comes from patients on cardiopulmonary by-pass, where thrombin formation was found to be significantly reduced by ATIII administration and could in fact pose a risk for hemorrhage.(23) In addition, a randomized controlled trial in adults with septic shock who were treated with ATIII showed significantly higher rates of hemorrhage compared to placebo.(24) These data suggest that significant thrombin suppression with high-dose or continuous ATIII infusions should be approached with caution as it may be deleterious in ECMO patients. This practice will need additional investigation.

TEG use had previously been reported anecdotally by ECMO centers(2, 20, 25) and may prove to be a useful tool to monitor anticoagulation, detect hypercoagulable states and aid in the management of ECMO-related bleeding complications, but future studies are needed. In this survey, heparinase, kaolin and rotative TEG are all being reported. Of note, at the time of this survey, rotative TEG (recently referred to as ROTEM) was only licensed in Europe. In contrast to ECMO, TEG is used extensively in clinical practice for guidance of anticoagulation and anti-platelet therapy in patients with ventricular assist devices.(26) ECMO anticoagulation protocols will likely evolve combining both specific measures of

anticoagulation (e.g., heparin concentration and functional assays of heparin activity such as anti-factor Xa) and global functional tests that measure overall clot reaction, such as TEG. (2, 26)

Heparin and other coagulation-related medications

All respondents indicated use of continuous UFH infusion as the main means of anticoagulation. Direct thrombin inhibitors (e.g., argatroban, lepirudin, bivalirudin) as alternatives to UFH were used by more than half of respondents, when clinically indicated (e.g., heparin-induced thrombocytopenia). A variety of hemostatic agents, antiplatelet agents and vitamin K antagonists were also used, with regional differences that may be related to clinical choice and/or country-specific availability.

Use of heparin-bonded circuits has been proposed as a method of reducing circuit clotting. Several studies have investigated the impact of these heparin-bonded circuits on the inflammatory response, platelet preservation, fibrinolysis, blood loss and amount of blood transfusion required, during ECMO and cardiopulmonary by-pass, with evidence suggesting reduced platelet activation, decreased leukocyte and complement activation and lower pro-inflammatory cytokine production, as well as decreased blood transfusion requirements.(27–30) It is not clear, though, how these findings translate for prolonged ECMO runs and in patients of different ages, co-morbidities and indications for ECMO. In this survey, the use of heparin-bonded circuits was reported by 61% of respondents, either as tip-to-tip or for certain components. Different circuit configurations (roller vs centrifugal pump, membrane- vs hollow-fiber oxygenator, bridge vs bridgeless, type of biocompatible circuit surface coating) could also impact heparin requirements and coagulation profiles.(27, 31)

Circuit priming solutions

Many different combinations of priming solutions varying by age and geographical location were reported. FFP as part of the priming solution was reported by 50% of respondents. Addition of plasma to the circuit can overcome the problem of hemodilution affecting ACT results. Further, in CPB patients, addition of plasma improved ACT to anti-factor Xa correlation.(32, 33) This is another area that warrants further investigation.

This study has several limitations. Given the anonymous nature of this survey, we were not able to control for responses arriving from the same institution, although a duplicate check revealed no duplicates. There may also be selection bias introduced by potential systematic differences between ELSO-registered versus non-ELSO-registered ECMO centers. Non-response did not appear to be an issue for this survey, which showed relatively high response rates compared to most surveys published. The survey could not control for different practices for various age groups or for VA- vs VV-ECMO. Data on the storage age for PRBCs used for priming and for subsequent transfusion and data on ATIII and medication doses and titration were not collected. This study did not assess outcomes associated with different methods for anticoagulation employed by responding centers. This report offers a starting point for determining clinical practices and opinions among ECMO providers and provides the groundwork for ECMO anticoagulation and blood product administration guidelines and for future studies of the association between anticoagulation and blood product management and ECMO complications and outcomes.

Conclusions

The results of this survey show that ECMO anticoagulation and blood product management policies among international ELSO centers vary widely. The vast majority of ECMO centers employ ACT as the preferred anticoagulation monitoring tool. The coagulation system is

closely monitored using a variety of more specific markers such as anti-factor Xa, ATIII and TEG by a larger-than-expected number of centers. Thresholds used for blood product transfusions are equally variable, emphasizing the lack of studies in ECMO patients that could guide practice. Future studies are needed to improve standardization of these policies across institutions. While guidelines can help standardize practice, future, rigorous multicenter observational studies are needed to determine the association between anticoagulation and blood product management and ECMO complications and outcomes, followed by randomized controlled trials that will elucidate the optimal anticoagulation and blood product administration practice.

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Abbreviations

ECMO	extracorporeal membrane oxygenation
ICU	intensive care unit
OR	odds ratio
CI	confidence interval
IQR	interquartile range

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Table 1

Circuit priming solutions and coagulation-related medications

Question	Responses	
Your ECMO circuit prime contains which of the following (outside of an emergency) (n=119 respondents)	Normal saline (0.9% NaCl)	29 (24%)
	PRBC	109 (92%)
	FFP	59 (50%)
	Heparin	100 (84%)
	Calcium chloride or calcium gluconate	97 (82%)
	Albumin	98 (82%)
	Sodium bicarbonate (NaHCO ₃)	90 (76%)
	Steroids	6 (5%)
	THAM	23 (19%)
	PlasmaLyte	16 (13%)
	Other ¹	12 (10%)
What is the minimum UFH infusion rate allowed by your protocol? (n=115 respondents)	0 U/kg/h ^a	35 (30%)
	1–10 U/kg/h	62 (54%)
	11–25 U/kg/h	18 (16%)
	>25 U/kg/h	0
What is the maximum UFH infusion rate allowed by your protocol? (n=115 respondents)	No upper limit	83 (72%)
	50–75 U/kg/h	21 (18%)
	76–100 U/kg/h	8 (7%)
	101–125 U/kg/h ^b	3 (3%)
In the last six months, have you used non-UFH anticoagulation? (n=117 respondents)	Yes	10 (8%)
	No	107 (90%)
What non-UFH anticoagulation do/can you use in your ICU? (n=107 respondents)	Argatroban	48 (45%)
	Bivalirudin	10 (9%)
	Lepirudin	6 (6%)
	We never use any other pharmacologic anticoagulation besides UFH	50 (47%)
	Other	0
Do you ever use any of the products below for management of anticoagulation/hemorrhage/thrombosis in ECMO patients? (n=94 respondents)	e-aminocaproic acid	63 (67%)
	Recombinant human factor VIIa	63 (67%)
	Tranexamic acid	21 (22%)
	Aprotinin	13 (14%)
	Other ²	10 (11%)

UFH: unfractionated heparin; PRBC: packed red blood cells; FFP: fresh frozen plasma; THAM: tromethamine;

¹ Other (number of respondents): fresh whole blood (1), platelets (1), Hartman's solution (2), mannitol (1), lactated Ringer's solution (3), Normosol (4);

² Other: acetylsalicylic acid (4), warfarin (2), prostacyclin (2), serine protease inhibitors (1), dipyridamole (1)

^aNo in-depth data were collected on patient characteristics and duration of off-heparin ECMO, but respondents commented that this is mainly employed for brief periods of time in post-operative patients.

^b6 of 8 respondents reporting maximum UFH infusion rate of 76–100 U/kg/h and 2 of 3 respondents reporting maximum UFH infusion rate of 101–125 U/kg/h were from ECMO programs caring solely for neonatal and pediatric patients.

Table 2Laboratory monitoring during ECMO^{*}

Parameter	Responses	
ACT goal (sec) (n=116 respondents)	Minimum ACT goal, mean (SD)	183 (13), range 140–220
	Maximum ACT goal, mean (SD)	210 (15), range 170–240
	We do not follow ACT (n=3 respondents)	
CBC monitoring frequency (n=119 respondents)	Every 1–3 h	1 (1%)
	Every 4–5 h	12 (10%)
	Every 6–8 h	55 (46%)
	Every 9–12 h	31 (26%)
	>12 h apart	20 (17%)
PT/aPTT monitoring frequency (n=116 respondents)	Every 4–5 h	12 (10%)
	Every 6–8 h	41 (35%)
	Every 9–12 h	20 (17%)
	>12 h apart	36 (31%)
	Not monitored	7 (6%)
Fibrinogen monitoring frequency (n=119 respondents)	Every 4–5 h	8 (7%)
	Every 6–8 h	31 (26%)
	Every 9–12 h	25 (21%)
	>12 h apart	52 (44%)
	Only as needed	3 (3%)
D-dimer monitoring frequency (n=117 respondents)	Never	25 (21%)
	Every 6–8 h	6 (5%)
	Every 9–12 h	10 (9%)
	>12 h apart	27 (23%)
	Only as needed	49 (42%)
Free hemoglobin monitoring frequency (n=117 respondents)	Never	24 (21%)
	Every 1–6 h	1 (1%)
	Every 7–12 h	9 (8%)
	>12 h apart	47 (41%)
	Only as needed	36 (31%)
LDH monitoring frequency (n=112 respondents)	Never	17 (15%)
	Every 1–6 h	10 (9%)
	Every 7–12 h	10 (9%)
	>12 h apart	32 (29%)
	Only as needed	43 (38%)
Factor VIII monitoring frequency (n=115 respondents)	Never	50 (43%)
	Every 1–6 h	0

Parameter	Responses	
	Every 7–12 h	3 (3%)
	>12 h apart	1 (1%)
	Only as needed	61 (53%)
ATIII measurements (n=117 respondents)	Routinely	60 (51%)
	Occasionally	36 (31%)
	Never	21 (18%)
ATIII monitoring frequency (n=89 respondents)	Every 1–8 h	7 (8%)
	Every 9–12 h	17 (19%)
	Every 13–24 h	45 (51%)
	Only as needed	20 (22%)
Anti-factor Xa measurements (n=115 respondents)	Routinely	46 (40%)
	Occasionally	29 (25%)
	Never	40 (35%)
Anti-factor Xa monitoring frequency (n=66 respondents)	Every 1–8 h	15 (23%)
	Every 9–12 h	12 (18%)
	Every 13–24 h	27 (41%)
	Only as needed	12 (18%)
TEG measurements (n=116 respondents)	Routinely	21 (18%)
	Occasionally	29 (25%)
	Never	66 (57%)

* All parameters refer to a typical ECMO patient at the respondent's ECMO center; ACT: activated clotting time; SD: standard deviation; CBC: complete blood count; ECMO: extracorporeal membrane oxygenation; LDH: lactate dehydrogenase; AT: antithrombin; TEG: thromboelastogram

Table 3

Transfusion thresholds in ECMO patients*

Question	Responses		
	Pediatric-only programs (n=81)	Adult-only and mixed adult and pediatric programs (n=40)	p-value
What is the low hematocrit threshold (%) you use for PRBC transfusion in a typical ECMO patient?, median (range)	35 (25 – 40)	30 (20 – 40)	<0.001
What is your typical platelet threshold (cells/microL) for platelet transfusion in an otherwise uncomplicated ECMO run?, median (range)	100,000 (50,000 – 200,000)	100,000 (20,000 – 100,000)	0.034
What is your typical low fibrinogen threshold (mg/dL) for which you would administer FFP or cryoprecipitate?, median (range)	150 (60 – 200)	145 (50 – 200)	0.33