Supplemental material

Antithrombin replacement during veno-venous ECMO: results of a survey among 16 Italian Centres

In October 2017 we conducted a survey to better understand how antithrombin deficiency during veno-venous ECMO is currently managed in the 16 Centres forming the Italian network for treatment of the acute respiratory failure ("Rete specializzata nell'insufficienza respiratoria acuta" – ReSpIRA). The survey was distributed to local ECMO-program coordinators or directors (listed in the main manuscript) using a web-based instrument (SurveyMonkey.com®). Response rate was 100%. Results are reported below.

- Question 1: How many subjects are treated with veno-venous ECMO each year in your Centre?

Answer	n	%
0-9 subjects per year	7	44
10-19 subjects per year	4	25
20-29 subjects per year	3	19
> 30 subjects per year	2	13

- Question 2: What is the drug of choice for anticoagulation during veno-venous ECMO in your Centre?

Answer	n	%
Unfractionated heparin	16	100
Bivalirudin	0	0
Argatroban	0	0
Other	0	0

- Question 3: How is anticoagulation routinely monitored and what is the usual target for anticoagulation during veno-venous ECMO in your Centre? (more than one answer possible)

Answer	n	%
Activated partial thromboplastin time (aPTT), sec	9	56
aPTT, ratio	7	44
Activated clotting time (ACT), sec	6	38
Thromboelastography (TEG®), min	2	13
Thromboelastometry (ROTEM®), min	0	0
Anti-factor Xa assay, U/ml	0	0

Centre	Variable	Target
1	aPTT, ratio ACT, sec	1.5-2.0 180-210
2	ACT, sec	180-200
3	aPTT, ratio ACT, sec	2.0 190-200
4	aPTT, sec	50-70
5	aPTT, ratio	1.8-2.2
6	aPTT, ratio	1.5-2.1
7	aPTT, sec	40-50
8	aPTT, sec	45-60
9	aPTT, ratio	1.5-1.8
10	aPTT, sec	60
11	aPTT, sec	50-60
12	aPTT, sec aPTT, ratio ACT, sec R (TEG®), min	50 1.5 170 <8
13	aPTT, sec ACT, sec	50-60 180-200
14	aPTT, ratio	2.0-3.0
15	aPTT, sec ACT, sec R (TEG®), min	50-80 180-220 10-15
16	aPTT, sec	40-50

- Question 4: Is circulating antithrombin activity routinely measured during veno-venous ECMO in your Centre?

Answer	n	%
Yes, once a day	12	75
Yes, more than once a week but less than once a day	1	6
Yes, once a week	3	19
Yes, if heparin resistance is suspected	0	0
No	0	0

- Question 5: Which drug is used to increase the circulating antithrombin activity during veno-venous ECMO in your Centre?

Answer	n	%
Antithrombin concentrate	9	56
Recombinant antithrombin	7	44
Fresh frozen plasma	0	0
None	0	0

- Question 6: Is antithrombin routinely replaced just because its circulating activity is lower than a critical value (please specify) during veno-venous ECMO in your Centre?

Answer	n	%
Yes, if antithrombin activity is <40%	1	8
Yes, if antithrombin activity is <60%	3	23
Yes, if antithrombin activity is <70%	5	39
Yes, if antithrombin activity is <80%	1	8
Yes, if antithrombin activity is <90%	2	15
Yes, if antithrombin activity is <100%	1	8
No, the decision to administer antithrombin also depends on the level of anticoagulation and/or the dose of the anticoagulant drug	3	19
No, we do not routinely replace antithrombin	0	0

- Question 7: For Centres where antithrombin is routinely administered - How is antithrombin administered during veno-venous ECMO in your Centre?

Answer	n	%
As a bolus (in few minutes)	7	44
As extended infusion (in few hours)	7	44
As continuous infusion	2	13

- Question 8: For Centres where antithrombin is routinely administered - What is the rule for stopping antithrombin replacement during veno-venous ECMO in your Centre?

Answer	n	%
Attainment of antithrombin activity ≥70%	2	13
Attainment of antithrombin activity ≥80%	1	6
Attainment of antithrombin activity ≥90%	3	19
Attainment of antithrombin activity ≥100%	6	37
Attainment of a pre-specified anticoagulation target	2	13
We administer antithrombin but we do not measure antithrombin activity thereafter	2	13

- Question 9: For Centres where antithrombin is routinely administered – Why is antithrombin replaced during veno-venous ECMO in your Centre? (more than one answer possible)

Answer	n	%
To prevent heparin resistance	4	25
To correct heparin resistance	7	44
To reach/maintain the anticoagulation target more easily	9	56

Antithrombin decreases inflammation and protects the endothelium	1	6

- Question 10: For Centres where antithrombin is not routinely administered - Why is antithrombin not replaced during veno-venous ECMO in your Centre? (more than one answer possible)

Answer	n	%
Because it does not prevent heparin resistance	0	0
Because it does not correct heparin resistance	0	0
Because it does not help reach/maintain the anticoagulation target	0	0
Because it is too risky (for instance, bleeding)	0	0
Because it is too expensive	0	0
Other	0	0