

Supplemental Digital Content

Anti-Xa and aPTT concordance and outcomes in adults undergoing ECMO: a secondary analysis of the pilot HELP-ECMO randomised trial

TABLE S1. Comparison of main patients characteristics and outcome between those with mainly discordant paired with aPTT relatively lower than anti-Xa (classified discordant ‘low’) and between those with mainly discordant paired with aPTT relatively higher than anti-Xa (classified discordant ‘high’).

Variables	Discordant ‘low’ n = 9	Discordant ‘high’ n = 15	P
Age, year	35 [23 - 46]	40 [31.5 - 62]	0.46
Gender, male	8 (88.9)	10 (66.7)	0.35
Weight, kg	80 [76 - 85]	80 [72.5 - 85.5]	0.44
APACHE III	46.5 [31.7 - 60.3]	71 [45.5 - 98.75]	0.07
Heparin dose	35067 [20476 - 49637]	21650 [12206 - 24690]	0.016
Heparin resistance	5 (55.6)	1 (6.7)	0.015
Days on ECMO	12 [8 – 18]	8 [7 – 16]	0.38
Never weaned of ECMO	1(11.1)	5 (33.3)	0.45
ICU mortality	7 (77.8)	10 (66.7)	0.67
Hospital mortality	7 (77.8)	9 (60)	0.66

ECMO = Extra Corporeal Membrane Oxygenation, ICU = Intensive Care Unit,

Continuous variables are expressed as median [IQR] and categorical variables are expressed as percentage.

TABLE S2: Comparison of characteristics and outcomes of patients with and without heparin resistance. Continuous variables are expressed as median [IQR] and categorical variables are expressed as percentage.

Variables	Overall n = 32	No heparin resistance n =26	Heparin resistance n = 6	P
Age, years	38 [26.8 - 57.8]	45 [30.5 - 60.8]	27 [22.3 - 33.3]	0.04
Gender, male	24 (75)	18 (69.2)	6 (100)	0.3
Weight, kg	79 [69.8 - 85.3]	78 [66, 85]	81.5 [73.5 - 92.5]	0.28
APACHE III score	57.5 [45.5 - 88.3]	64 [53.8 - 91.3]	37.5 [21.3 - 41.8]	0.001
Comorbidities				
- Immunosuppressed	4 (12.5)	4 (15.4)	0 (0)	0.57
- Respiratory failure	3 (9.4)	3 (11.5)	0 (0)	1
- Cardiovascular disease	5 (15.6)	4 (15.4)	1 (16.7)	1
- Renal failure	1 (3.1)	1 (3.8)	0 (0)	1
- Insulin dependent diabetes	1 (3.1)	1 (3.8)	0 (0)	1
Ongoing sepsis prior to ECMO	15 (46.9)	12 (46.2)	3 (50)	1
Heparin dose (UI/day)	20476 [11176 – 29904]	14000 [10518 - 22823]	43002 [35393 - 50501]	<0.001
Group of randomization, n (%)				0.65
- 'Low dose heparin' group	16 (50)	14 (53.8)	2 (33.3)	
- 'Therapeutic anticoagulation' group	16 (50)	12 (46.2)	4 (66.7)	
ECMO type				
- VV ECMO	23 (71.9)	17 (70.8)	6 (100.0)	0.290
- VA ECMO	9 (28.1)	9 (36)	0 (0)	0.145
Indications for VV ECMO				
- Asthma	2 (6.2)	2 (7.7)	0 (0)	0.27
- Bacterial or viral pneumonia	9 (28.1)	3 (11.5)	1 (16.7)	
- Lung Transplantation	3 (9.3)	1 (3.8)	0 (0)	
- Other respiratory disorders	9 (28.1)	5 (19.2)	4 (66.7)	
Indications for VA ECMO				
- Acute cardiomyopathy	2 (6.2)	2 (7.7)	0 (0)	n.a.
- AMI	1 (3.1)	1 (3.8)	0 (0)	
- Heart Transplantation	3 (9.4)	3 (11.5)	0 (0)	
- Myocarditis	1 (3.1)	1 (3.8)	0 (0)	
- Other	2 (6.2)	2 (7.7)	0 (0)	
Outcomes				
ECMO outcomes				
Days on ECMO	8 [5.5 - 14]	7.5 [5 - 10.5]	18 [14.3 - 18]	0.006
Weaning (n, %)				
No	7 (21.9)	6 (23.1)	1 (16.7)	1
Yes	24 (75)	19 (73.1)	5 (83.3)	
ICU mortality	23 (71.9)	19 (73.1)	4 (66.7)	1
Hospital mortality	22 (68.8)	18 (69.2)	4 (66.7)	1

APACHE = Acute Physiology and Chronic Health Evaluation, ECMO = Extra Corporeal Membrane Oxygenation, ICU = Intensive Care Unit, VA = Veno arterial, VV = Veno venous.

TABLE S3: Comparison of biological parameters between heparin resistance states and no heparin resistance states in patients randomized in the ‘therapeutic anticoagulation’ group (n = 16).

Variables**	No heparin resistance n = 317	Heparin resistance n = 25	p*
aPTT (seconds)	59 [50 - 67]	42 [36 - 48]	< 0.001
Anti-Xa (IU/L)	0.33 [0.13 - 0.5]	0.28 [0.06 - 0.38]	< 0.001
Lowest Hb (g/L)	80 [74, 90]	88 [82, 92]	0.06
Highest Hb (g/L)	94 [88, 102]	98 [93, 101]	0.046
Highest plasma free Hb (g/L)	5 [3, 8]	7 [5, 11]	0.83
Lowest corrected ionised calcium (mmol/L)	1.11 [1.04, 1.19]	2.28 [1.09, 2.34]	0.73
Highest Urea (mmol/L)	11 [8, 14]	13 [10, 15]	0.77
Highest Bilirubin (µmol/L)	12 [9, 18]	26 [9.3, 27]	0.006
Lowest Arterial pH	7.36 [7.3, 7.43]	7.36 [7.34, 7.42]	
Highest D-dimer (mg/L)	113 [33, 161]	180 [169, 217]	< 0.001
Highest INR	1.2 [1.1, 1.3]	1.2 [1.1, 1.3]	0.54
Lowest INR	1.2 [1, 1.3]	1.2 [1.1, 1.2]	0.35
Highest Fibrinogen (g/L)	4.5 [3.2, 5.8]	5.8 [5.4, 6.9]	0.5
Lowest Fibrinogen (g/L)	4.7 [3.8, 6.1]	5.1 [4.1, 6.9]	0.12
Highest PT (sec)	14.90 [13.9, 16.17]	15.8 [14.7, 16.2]	0.81
Lowest PT (sec)	15.3 [13.9, 16.2]	15.4 [14.7, 15.8]	0.77
Highest platelet count (G/L)	141 [93.8, 226]	153 [97, 182]	0.76
Lowest platelet count (G/L)	151.5 [84.8, 241]	153 [97, 182]	0.95
Daily heparin dose, UI/24h	21600 [12000, 31800]	48800 [42900, 60000]	0.02
aPTT/anti-Xa Discordance (n, %)			
- Concordant aPTT/anti-Xa	190 (59.9)	16 (64)	< 0.001
- aPTT relatively lower than anti-Xa	31 (9.8)	9 (36)	
- aPTT relatively higher than anti-Xa	96 (30.3)	0 (0)	

aPTT: activated Partial Thromboplastin Time, Hb: Haemoglobin, INR: International Normalized Ratio, PT: Pro-Thrombin time.

**highest and lowest values are for the day of the heparin resistance episode

FIGURE S1. Scatter plot represented paired aPTT/anti-Xa in standard dose group (therapeutic anticoagulation). Each paired value was classified in three groups: ‘aPTT

comparable to anti-Xa' (blue circle); 'aPTT relatively lower than anti-Xa level' (green square) and 'aPTT relatively higher than anti-Xa level' (red diamond).

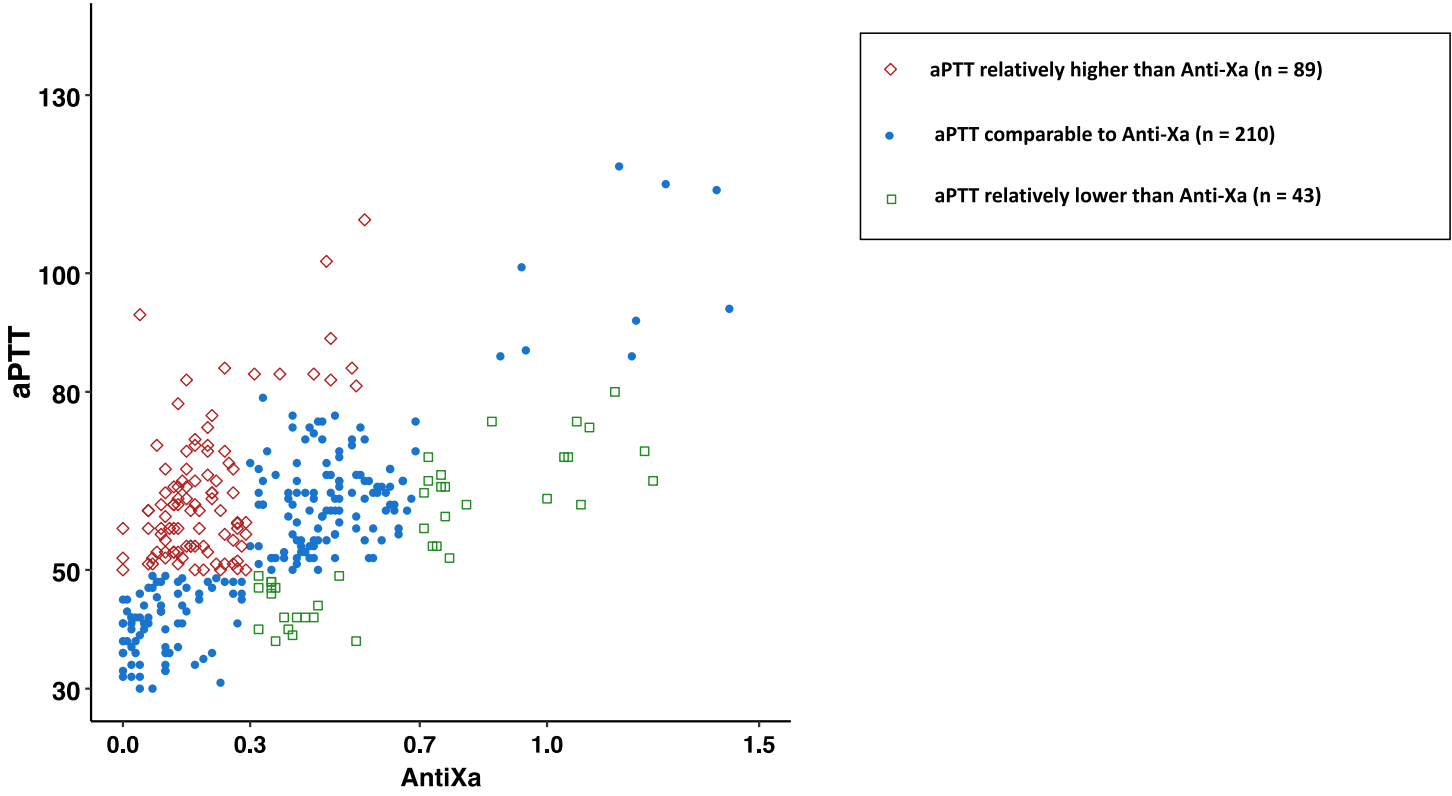


FIGURE S2. Scatter plot represented paired aPTT/anti-Xa in low dose group. Each paired value was classified in three groups: 'aPTT comparable to anti-Xa' (blue circle); 'aPTT relatively low to anti-Xa level' (green square) and 'aPTT relatively high to anti-Xa level' (red diamond).

