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Città della Salute e della Scienza di Torino

UNIVERSITÀ DEGLI STUDI DI TORINO

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SMART MEETING ANESTHESIA RESUSCITATION INTENSIVE CARE
MAY 24-28 2021

HEMORRHAGIC AND THROMBOTIC COMPLICATIONS IN A COHORT OF PATIENTS TREATED WITH VENO-VENOUS ECMO FOR COVID-19 RELATED ARDS IN TURIN.

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BACKGROUND

It has been reported that COVID-19 is often associated with a hypercoagulability status [1], while Extra Corporeal Membrane Oxygenation (ECMO) can expose both to thrombotic and hemorrhagic risk [2]. To better understand the relationship between the coagulatory anomalies induced by COVID-19 and those induced by ECMO we analyzed the cohort of patients treated with ECMO at the referral center in Turin.

METHODS

Clinical data of all consecutive adult patients requiring veno-venous ECMO due to COVID-19 related ARDS in 'Città della Salute e della Scienza' Hospital (Turin, Italy), between February and December 2020, were collected retrospectively, from day 0 (ECMO placement day) to fourteen days later. The anticoagulation protocol consisted of a bolus of 50-100 IU/kg of unfractionated heparin (UFH) at ECMO placement, followed by a continuous infusion titrated to an activated clotting time (ACT) of 180-200 seconds [3].

RESULTS

Thirtyfive patients were enrolled and 91% of them reported coagulopathies (Figure 1). Severe bleeding occurred in 29 patients, 2 patients underwent hemorrhagic shock and 2 died for a fatal hemorrhagic stroke. Most frequent bleeding sites were patients' airways (57%), ECMO cannulation sites (60%) and vascular accesses (66%). Deep venous thrombosis was documented in 14% of patients, while pulmonary embolism in 6%. ECMO oxygenator failure due to membrane clotting and thrombosis of a cannula occurred in 9 and 2 patients, respectively. Daily cumulative dose of heparin decreased from ECMO implantation to day 14; hemoglobin, platelets count and fibrinogen values decreased significantly over the time, while d-dimer increased (Table 1).

FIGURE 1: COAGULOPATHIES IN COVID-19

	N = 35
Deep venous thrombosis, n (%)	5 (14)
Pulmonary thrombo-embolism, n (%)	2 (6)
ECMO cannula thrombosis, n (%)	2 (6)
Oxygenator failure, n (%)	9 (26)
Bleeding, n (%)	29 (83)
Hemorrhagic shock	2 (6)

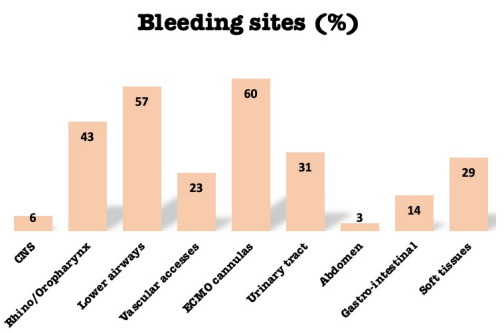

TABLE 1. COAGULATION PARAMETERS

	Laboratory range	Day 0	Day 1	Day 3	Day 7	Day 14	p value
ACT max, sec		187,5 (160,3 - 212,8)	189 (176 - 218)	182,5 (167,8 - 195,8)	183 (168,5 - 201,5)	185 (161 - 203,5)	0,938
Hb, g/dL	13.5-18.0	10,5 (9.4 – 11.8)	9,2 (8.3 – 10.1)	8,5 (7.7 – 9.9)	8,7 (8 – 9.7)	8 (7.5 – 8.6)	< 0.001
Hct, %	40-52	33,2 (29.5 - 36)	29,4 (25.5 – 32.8)	25,95 (23.75 – 30.4)	26,8 (24.98 – 30.4)	25,45 (23.9 – 27.2)	< 0.001
Platelets, x10³/L	140-450	249 (202 - 301)	227 (158 – 302)	161,5 (112.8 – 209.5)	118,50 (68.8 – 155)	98 (60.3 – 165.3)	< 0.001
INR	0.80-1.20	1,24 (1.15 – 1.32)	1,22 (1.15 – 1.28)	1,17 (1.09 – 1.23)	1,18 (1.1 – 1.26)	1,23 (1.11 – 1.31)	0,365
aPTT ratio	0.80-1.18	1,77 (1.28 – 2.32)	1,96 (1.58 – 2.32)	1,68 (1.42 – 2.04)	1,77 (1.31 – 2.08)	1,53 (1.02 – 2.15)	0,163
D-dimer, ng/mL	<510	2254 (1311 - 5549)	2435 (1461 – 5702)	4512 (1718 – 8958)	15538 (5123 – 33714)	18483 (7459 – 28387)	0,012
Fibrinogen, mg/dL	200-400	527 (372 - 783)	491 (275 – 750)	510 (260 – 706)	347 (228 – 592)	266 (197 – 386)	0,004
Antithrombin III, %	80-120	87 (65.5 – 99.5)	80 (72 – 89.5)	84 (72.5 – 95)	84 (63 – 107)	87,50 (62.75 – 112)	0,479
UFH daily-dose, x10³ IU			31.6 (21.96 – 36.72)	30.24 (20.8 – 38.52)	30 (18.6 – 34.56)	14.93 (0 – 27.6)	< 0.001

Data are expressed as median (IQR).

CONCLUSIONS

The cohort of COVID-19 patients treated with vv-ECMO developed more bleeding events than historically observed in not-COVID-19 patients treated with ECMO (83% vs 30-50%, respectively), and reported a lower rate of pulmonary embolism (6% vs 16%). [2.4] Despite a formal monitoring of thrombotic events was not always performed, it should also be noted that the D-dimer values increased significantly from day 0 to day 14.
Finally, although a reduced daily cumulative dosage of UFH was used to reach the lower limit of the anticoagulant range, ACT values remained stable and high (> 180 seconds) over the time, resulting in continuous bleeding episodes.
Given that high bleeding rates in COVID-19 patients treated with ECMO have been highlighted by other authors [5], further investigations are needed to define the best coagulation management in this context in order to balance thrombotic and hemorrhagic risk.

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