Thrombosis in patients with COVID-19

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ORIGINAL

High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study

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Primary Outcome

The primary end-point:

Comparison between **Thrombotic events** in patients with **COVID-19 ARDS** and **non- COVID-19 ARDS.**

Methods

- Between **March 3rd** and **March 31st 2020**, **all patients** referred for **ARDS** due to **SARS-CoV-2** were **prospectively included** on admission in **four intensive care units** in **two centres** of a **French tertiary hospital**. **There was no exclusion criteria**
- A **historical prospective cohort** of “non-COVID-19 ARDS” patients included between 2014 and 2019 was **used for the comparison** of COVID- 19 ARDS to non- COVID-19 ARDS

Table 1 Characteristics of COVID-19 ARDS and non-COVID-19 ARDS

	Population before matching ($n=383$)			Population after matching ($n=222$)		
	Non-COVID-19 ARDS ($n=233$)	COVID-19 ARDS ($n=150$)	p-value	Non-COVID-19 ARDS ($n=145$)	COVID-19 ARDS ($n=77$)	p-value
Age—median, IQR	74 [63; 81]	63 [53; 71]	< 0.001	72 [61; 80]	68 [61; 75]	0.593
Male—*n* (%)	164 (70.4)	122 (81.3)	0.02	112 (77.2)	63 (81.8)	0.426
Medical history—*n* (%)						
Malignancies/hemopathies	31 (13.4)	9 (5.0)	0.02	14 (9.7)	6 (7.8)	0.678
Cardiovascular diseases	143 (61.4)	72 (48)	0.01	85 (58.6)	42 (55.6)	0.753
Thrombo-embolic event	13 (5.6)	8 (5.3)	0.92	9 (6.2)	7 (9.1)	0.42
Cerebrovascular diseases	23 (10)	7 (4.7)	0.06	8 (5.5)	5 (6.5)	0.788
Immure diseases	13 (5.6)	4 (2.7)	0.17	7 (4.8)	4 (5.2)	0.951
Diabetes	51 (21.9)	30 (20)	0.66	29 (20)	17 (22.1)	0.589
Chronic liver disease	21 (9)	4 (2.7)	0.01	7 (4.8)	3 (3.9)	0.816
Chronic renal disease	38 (16.3)	6 (4.0)	< 0.001	14 (9.7)	5 (6.5)	0.438
Respiratory disease	49 (21.0)	21 (14)	0.07	36 (24.8)	11 (14.3)	0.207
Baseline SAPS II—median, IQR	61 [49; 76]	49 [37; 64]	< 0.001	54 [45; 69]	53 [46; 67]	0.560
Baseline SOFA—median, IQR	11 [9, 13]	8 [5, 10]	< 0.001	10 [8, 13]	9 [7, 12]	0.204
PaO_2/FO_2 on ICU admission (mmHg)—median, IQR	142 [93; 195]	125 [97; 170]	< 0.02	118 [89; 174]	135 [99; 181]	0.520
Invasive mechanical ventilation—*n* (%)	233 (100)	150 (100)	1	145 (100)	77 (100)	1
Baseline heparin treatment—*n* (%)						
Prophylactic dosing[a]	188 (80.7)	105 (70)	0.27	110 (75.9)	60 (77.9)	0.768
Therapeutic dosing	45 (19.3)	45 (30)	0.02	35 (24.1)	17 (22.1)	0.697
ECMO—*n* (%)	10 (4.3)	12 (8.1)	0.124	7 (4.8)	4 (5.2)	0.952
ECMO duration (days)—median, IQR	8 [5.3; 10.8]	7 [4.3; 11]	0.642	10 [7.0; 11.5]	6.5 [4.5; 9]	0.527

SOFA, sequential organ failure assessment; SAPSII, simplified acute physiology score II

[a] Prophylactic dosing was 4000 UI/day for low molecular weight heparin or if contra-indicated, unfractioned heparin at 5–8 U/kg/h

Results

- **150 patients** included in study
- **Median age** was **63** [53; 71] years
- **male-to-female** ratio was **122:28**
- **64** clinically relevant **thrombotic complications** were diagnosed in 150 patients during their ICU stay, **mainly pulmonary embolisms**

- **100 CTPAs** Performed on **99 patients..**
- **25** Patients had **pulmonary embolus**
- **24 men**, mean **age 62** years old

- **15 CTB** and **10 MRI brain** scans performed
- **4** showed **ischemic strokes**
- In one patient, there was a complete occlusion of the right internal carotid artery without any sign of ischemic stroke
- **2** patients had a **left cerebellar ischemic stroke** on **MRI**

Table 3 Outcomes of COVID-19 ARDS and non-COVID-19 ARDS

	Population before matching ($n = 383$)				Population after matching ($n = 222$)			
	Non-COVID-19-ARDS ($n = 233$)	COVID-19-ARDS ($n = 150$)	OR [95% IC]	*p*-value	Non-COVID-19-ARDS ($n = 145$)	COVID-19-ARDS ($n = 77$)	OR [95% IC]	*p*-value
Thrombo-embolic complications—*n* (%)	14 (6)	27 (18)	3.4 [1.7–7.3]	< 0.001	7 (4.8)	9 (11.7)	2.6 [1.1–6.1]	0.04
Pulmonary embolisms—*n* (%)	3 (1.3)	25 (16.7)	15.2 [4.5–80.4]	< 0.001	3 (2.1)	9 (11.7)	6.2 [1.6–23.4]	0.01
Deep vein thrombosis—*n* (%)	3 (1.3)	3 (2)	1 [0.1–9.2]	1	2 (1.4)	0 (0)	–	–
Myocardial infarction—*n* (%)	6 (2.6)	0 (0)	0 [0–1.3]	0.09	2 (1.4)	0 (0)	–	–
Cerebral ischemic attack—*n* (%)	1 (0.4)	2 (1.3)	3.1 [0.2– 185.5]	0.68	0 (0.0)	0 (0)	–	–
Limb ischemia—*n* (%)	0 (0)	1 (0.7)	Inf [0.0–Inf]	0.78	0 (0.0)	0 (0)	–	–
Mesenteric ischemia—*n* (%)	3 (1.3)	1 (0.7)	0.5 [0.0–6.5]	0.98	2 (1.4)	1 (1.3)	0.96 [0.09–9.8]	0.97
Nb of RRT filter per dialyzed patient—median, IQR	1 [2–1]	3 [2–7]	–	< 0.001	2.0 [1.0–2.5]	3.0 [2.0–6]	–	0.03
Nb of RRT filter per day of RRT—median, IQR	0.3 [0.3; 0.5]	0.7 [0.5; 1]	–	< 0.001	0.3 [0.3; 0.4]	0.7 [0.5; 1]	–	< 0.001
ECMO oxygenator thrombosis—*n* (%)	1/10 (10)	2/12 (16.7)	–	0.59	1/7 (14.3)	0/4 (0)	–	–
Hemorrhagic complications—*n* (%)	1 (1.8)	4 (2.7)	2.4 [0.27–28.5]	0.6	2 (1.4)	0 (0)	–	–

ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy

- Baseline **elevated D Dimers**
- **PT, aPTT and AT** were within **normal ranges**, and **fibrinogen was higher** (7.0 g/L vs. 5.6)
- **no COVID-19** patient **met criteria for DIC**
- The mechanisms involved in thrombosis remains unclear. Endothelial inflammation was obvious, with **very high levels of vWF:Ag and FVIII**

Conclusion

- **Despite anticoagulation**, a **high number** of patients with **ARDS** secondary to **COVID-19 develop** life-threatening **thrombotic complications.**

Limitations

- Study has **not** been **able** to **describe** the **pathophysiological hypothesis** leading to the high incidence of clinically relevant thrombosis in COVID-19 patients
- **Large number of COVID-19** patients were **still intubated at the time of data collection**, the **incidence** of thrombotic complications is **probably under-estimated**

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Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum

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Abstract

Study Design: Guidance Document

- Shared experiences of medical providers managing COVID-19 from early stages across the globe
- Expert opinions from the Anticoagulation Forum Board of Directors
- Known best practices that have long-served as the evidence-based foundation of anticoagulation management in the pre-COVID-19 era.

Should acutely ill hospitalized patients with confirmed or highly suspected COVID-19 receive venous thromboembolism (VTE) prophylaxis?

- YES
- 25% of Covid Patients developed DVT compared to 5–15% of medically hospitalised patients

What intensity of VTE prophylaxis should patients with COVID-19 receive?

- For all non-critically ill hospitalized patients (i.e., not in an ICU) with confirmed or highly suspected COVID- 19, we recommend standard dose VTE prophylaxis
- For critically ill patients (i.e., in an ICU) with confirmed or highly suspected COVID-19, we suggest increased doses of VTE prophylaxis
- For patients that are improving and transferring out of the ICU to the medical ward, it is reasonable to deescalate to standard VTE prophylaxis dosing

Should patients with confirmed COVID-19 receive VTE prophylaxis after hospital discharge?

- We suggest that extended VTE prophylaxis is not necessary for all patients with COVID-19 who are being discharged from the hospital
- We suggest that a multidisciplinary discussion occur at or near the time of discharge to determine if a patient has ongoing VTE risk factors, may benefit from extended post-hospital VTE prophylaxis, and has ensured access to VTE prophylactic medications

Should biomarkers, such as D-dimer, be serially measured to trigger changes in care?

- Based on currently available evidence, we suggest against daily monitoring of d-dimer for the purpose of guiding anticoagulant therapy. D-dimer measurement may be used as a marker of illness severity and prognosis.
- We suggest against intensification of anticoagulant dosing based only on biomarkers, such as d-dimer. However, acutely worsening clinical status in conjunction with laboratory value changes, such as rising D-dimer, may necessitate further thromboembolic workup or empiric treatment.

Should thrombolytic therapy be used in patients with COVID-19?

- We recommend against use of thrombolytics in patients with COVID-19 outside of a clinical trial setting unless there is another clinical indication for thrombolysis, such as ST elevation myocardial infarction, acute ischemic stroke, or high-risk (massive) PE with hemodynamic compromise

Take Home message

- High risk of Pulmonary embolus in patients with Covid 19
- Critically ill patients should be put on therapeutic dose clexane