Thrombosis Research 191 (2020) 9–14

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy

Corrado Lodigiani[a,b,*], Giacomo Iapichino[c], Luca Carenzo[c], Maurizio Cecconi[b,c], Paola Ferrazzi[a], Tim Sebastian[d], Nils Kucher[d], Jan-Dirk Studt[e], Clara Sacco[a], Bertuzzi Alexia[f], Maria Teresa Sandri[g], Stefano Barco[d,h], on behalf of the Humanitas COVID-19 Task Force

[a] Center for Thrombosis and Hemorrhagic Diseases, Humanitas Clinical and Research Hospital, Rozzano, Milano, Italy
[b] Department of Medical Sciences, Humanitas University, Milano, Italy
[c] Department of Anaestesia and Intensive Care, Humanitas Clinical and Research Center, Rozzano, Milano, Italy
[d] Clinic for Angiology, University Hospital Zurich, Zurich, Switzerland
[e] Division of Medical Oncology and Hematology, University Hospital Zurich, Zurich, Switzerland
[f] Department of Oncology, Humanitas Clinical and Research Hospital, Rozzano, Italy
[g] Laboratory Medicine Division, Humanitas Clinical and Research Hospital, Rozzano, Milano, Italy
[h] Center for Thrombosis and Hemostasis, University Medical Center, Johannes Gutenberg University Mainz, Mainz, Germany

Background

- It has been postulated that the high mortality observed among COVID-19 patients may be partly due to unrecognized pulmonary embolism (PE) and pulmonary in situ thrombosis.
- However, few data are available on the rate and characteristics of thromboembolic complications in hospitalized patients with COVID-19.

Aim of the study

- To describe the rate of venous and arterial thromboembolic complications in hospitalized patients with COVID-19.

Methods

- Retrospective cohort study including consecutive adult symptomatic patients with laboratory-proven COVID-19 who have been admitted to a large university hospital (Humanitas Clinical and Research Hospital, Rozzano, Milan, Lombardy, Italy) since February 2020 to April 2020.
- The primary outcome was any thromboembolic complication: venous thromboembolism (VTE) including venous thrombosis (DVT) and pulmonary embolism (PE), and cardiovascular events including ischemic stroke, and acute coronary syndrome (ACS)/ myocardial infarction (MI).
- The secondary outcome was overt disseminated intravascular coagulation (DIC).

Results

- 388 consecutive patients.
- Median age 66 years, 68% men, 16% requiring intensive care (ICU).
- Thromboprophylaxis was used in 100% of ICU patients and 75% of those on the general ward.
- Thromboembolic events occurred in 28 patients corresponding to a cumulative rate of 21% (27.6% ICU, 6.6% general ward). Half of the thromboembolic events were diagnosed within 24 h of hospital admission. 44 patients underwent VTE imaging tests and VTE was confirmed in 16 (36%). Computed tomography pulmonary angiography (CTPA) was performed in 30 patients (7.7%), and pulmonary embolism was confirmed in 10 (33% of CTPA).
- The rate of ischemic stroke and ACS/MI was 2.5% and 1.1%, respectively.
- Overt DIC was present in 8 (2.2%) patients.

Baseline characteristics of COVID-19 patients.

	Intensive care unit (n = 61)		General ward (n = 327)		Total (N = 388)	
Age (years), median (Q1-Q3)	61 (55–69)		68 (55–77)		66 (55–75)	
Men	49/61	80.3%	215/327	65.7%	264/388	68.0%
Body mass index (kg/m2)						
≤25	20/57	35.1%	110/306	35.9%	130/361	36.0%
25–30	20/57	35.1%	126/306	41.2%	144/361	39.9%
≥30	17/57	29.8%	70/306	22.9%	87/361	24.1%
Overall duration of hospitalization (days), median (Q1-Q3)	18 (14–24)		9 (6–13)		10 (7–15)	
Cardiovascular risk factors						
Arterial hypertension on treatment	27/61	44.3%	156/327	47.7%	183/388	47.2%
Diabetes mellitus on treatment	11/61	18.0%	77/327	23.5%	88/388	22.7%
Dyslipidemia on treatment	7/61	11.5%	69/327	21.1%	76/388	19.6%
Chronic renal dysfunction	9/61	14.8%	52/327	15.9%	61/388	15.7%
Smoking	3/61	4.9%	42/327	12.8%	45/388	11.6%
Active cancer	2/61	3.3%	23/327	7.0%	25/388	6.4%
Solid	1		16		17	
Hematological	1		9		10	
Ongoing cancer therapy	1/61	1.6%	10/327	3.1%	11/388	2.8%
Hormonal therapy	1		3		4	
Chemo/immuno-therapy	0		5		5	
Radiotherapy	0		2		2	
History of cancer	0/61	0%	2/327	0.6%	2/388	0.5%
Chronic obstructive pulmonary disease	1/61	1.6%	34/327	10.4%	35/388	9.0%
Prior thromboembolic events						
Coronary artery disease	7/61	11.5%	47/327	14.4%	54/388	13.9%
Prior stroke	1/61	1.6%	19/327	5.8%	20/388	5.2%
Peripheral atherosclerosis	5/61	8.2%	48/327	14.7%	53/388	13.7%
Prior venous thromboembolism	0/61	0.0%	12/327	3.7%	12/388	3.1%
Use of co-medications						
Aspirin	17/61	27.9%	77/320	24.1%	93/379	24.5%
Vitamin K antagonists	0/61	0%	16/329	4.9%	16/388	4.1%
Direct oral anticoagulants	2/61	3.3%	15/329	4.6%	17/388	4.4%
ACE-inhibitors	6/61	9.8%	47/329	14.3%	53/388	13.7%

Venous and arterial thromboembolic events in hospitalized COVID-19 patients.

	Intensive care unit			General ward			Total		
Thromboembolic events	n	% of closed cases (n = 48)	% of imaging tests performed*	n	% of closed cases (n = 314)	% of imaging tests performed*	n	% of closed cases (n = 362)	% of imaging tests performed
At least one thromboembolic event	8	16.7% (95%CI 8.7%–29.6%)	–	20	6.4% (95%CI 4.2%–9.6%)	–	28	7.7% (95%CI 5.4%–11.0%)	–
VTE	4	8.3%	22%	12	3.8%	46%	16	4.4%	36%
PE (± DVT)	2	4.2%	25%	8	2.5%	36%	10	2.8%	33%
Isolated pDVT	1	2.1%	7%	3	1.0%	44%	4	1.1%	21%
Isolated dDVT	0	–	–	1	0.3%	13%	1	0.3%	13%
Catheter-related DVT	1	2.1%	50%	0	–	–	1	0.3%	50%
Ischemic stroke	3	6.3%	–	6	1.9%	–	9	2.5%	–
ACS/MI	1	2.1%	–	3	1.0%	–	4	1.1%	–

ACS, acute coronary syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; pDVT, proximal deep vein thrombosis; dDVT, distal DVT; PE, pulmonary embolism; VTE, venous thromboembolism.

Conclusions

- Hospitalized patients with COVID-19 were characterized by a high rate of thromboembolic complications.
- The high number of arterial and, in particular, venous thromboembolic events diagnosed within 24 h of admission and the high rate of positive VTE imaging tests among the few COVID-19 patients tested suggest that there is an urgent need to improve specific VTE diagnostic strategies and investigate the efficacy and safety of thromboprophylaxis in ambulatory COVID-19 patients.