REUE | Original Article

Risk of thromboembolic events after recovery from SARS-CoV-2 infection

Enrique González-Revuelta[1,2], Héctor Lago-Gancedo[1,2], Borja Camacho-Montes[1], Sonia Paola Leiva-Bisbicuth[1,2], Marta Iglesias-Vela[3], Jesús Seco-Calvo[4]

BACKGROUND. SARS-CoV-2 infection is associated with a high incidence of thromboembolic complications. However, whether or not a prothrombotic state persists after recovery is unknown.

MATERIAL AND METHODS. We undertook a case-control comparison of records from November 1, 2020, to March 31, 2021. Case records for patients treated for thromboembolic episodes in hospital emergency departments were selected; control patients were treated for other conditions in the same period. We recorded whether or not case and control patients had a history of recovery from COVID-19. Bivariate logistic regression was used to explore risk.

RESULTS. Records for 179 cases and 390 controls were selected. A majority of case patients had cerebrovascular stroke (30.2%) or acute coronary syndrome (21.2%). Only 17 cases (9.5%) and 390 controls (8.9%) had recently recovered from COVID-19. These data suggest an odds ratio of 1.064 (95% CI, 0.58-1.96) for COVID-19 exposure as a predictor of thromboembolic episodes, although the model was underpowered (R^2 = 0.028). The effect size was small for all variables, although the effect size for severity of SARS-CoV-2 infection was higher (0.2).

CONCLUSIONS. Our findings show that patients who have recovered from COVID-19 do not have a significantly higher risk of thromboembolic events than patients who have not recently recovered from this infection. Patients with a recent history of COVID-19 do not need to receive preventive anticoagulant treatment for longer periods than other patients.

Keywords: COVID-19. Thromboembolism. Anticoagulants.

Riesgo tromboembólico en pacientes que han superado la infección por sars-cov-2

INTRODUCCIÓN. La infección por SARS-CoV-2 ha presentado una alta frecuencia de episodios tromboembólicos como complicación. Sin embargo, los efectos ya superada la fase aguda continúan siendo un interrogante, desconociéndose si el efecto protrombótico persiste.

MATERIAL Y MÉTODO. Estudio de casos y controles que definió como casos los tromboembolismos atendidos en urgencias hospitalarias entre el 1 noviembre de 2020 y el 31 de marzo de 2021. Se comparó con una serie de controles seleccionados entre las consultas a urgencias en el mismo periodo con el fin de conocer, atendiendo al antecedente de COVID-19, el riesgo protrombótico de la misma. Finalmente, se realizó un modelo predictivo sobre estos episodios mediante regresión logística binaria.

RESULTADOS. Se seleccionaron 179 casos y 390 controles. La mayoría de los casos se debieron a accidente cerebrovascular y síndrome coronario agudo (30,2 y 21,2%, respectivamente) y 17 (9,5%) presentó antecedente de COVID-19 superada recientemente. De los 390 controles, 35 (8,9%) había padecido la infección. Estos datos arrojaron una OR de 1,064 (IC 95% de 0,58-1,96), así como un modelo de escaso poder predictivo (R^2 = 0,028). El tamaño del efecto fue pequeño en todas las variables del modelo, si bien en la gravedad con la que se padeció la COVID-19, el tamaño del efecto fue medio (0,2).

CONCLUSIONES. El riesgo protrombótico en pacientes que ya han superado la enfermedad por COVID-19 no es significativamente mayor. Su manejo clínico no exigiría de anticoagulación profiláctica durante periodos prolongados.

Palabras clave: COVID-19. Tromboembolismo. Anticoagulantes.

Author Affiliations: [1]Medicina de Familia y Comunitaria. G.A.P. León, Spain. [2]Grupo de trabajo SEMESMIR-Castilla y León, Spain. [3]Servicio de Urgencias. Complejo Asistencial Universitario de León, Spain. [4]Instituto de Biomedicina (IBIOMED). Universidad de León, Spain.
Corresponding Author: Enrique González Revuelta. Residente de Medicina de Familia y Comunitaria. Complejo Asistencial Universitario de León. C/ Altos de Nava, s/n. 24071 León, Spain.
E-mail: egonzalezrev@saludcastillayleon.es
Article Information: Received: 10-12-2022. Accepted: 27-12-2022. *Online:* 5-1-2023.
Editor in Charge: Guillermo Burillo Putze.

Introduction

Severe acute respiratory syndrome due to SARS-CoV-2 was declared in December 2019 in the Chinese city of Wuhan. On January 30, 2020, the outbreak of COVID-19 was determined to be a public health emergency of international concern.[1-3]

An association has been observed between this infection and an increased incidence rate of thromboembolic events, thus highlighting the need to establish treatment for such events.[4,5] Frequent episodes of venous thromboembolism (VTE) and pulmonary embolism (PE) have been reported in patients with COVID-19, which could complicate the clinical course of these patients. Moreover, episodes of mesenteric ischemia or acute limb ischemia have been reported, related to the systemic inflammatory state also triggered by SARS-CoV-2 infection.[6-9]

In the most symptomatic cases, this disease culminates in a diffuse inflammatory response with high plasma cytokine levels such as IL-2, IL-7, IL-10, granulocyte colony-stimulating factor, and TNF-alpha, among others.[10] This promotes a prothrombotic inflammatory state through activation of coagulation factor VII, overexpression of tissue factor in endothelium and platelets, alteration of the plasminogen activator inhibitor, and activation of protein C, which promotes fibrin generation and limits fibrinolysis, leading to hypoxic vasocclusion and even direct viral activation of immune cells.[11-15]

On the other hand, persistent SARS-CoV-2 antigenicity has been detected in the GI tract, both upper and lower, even 6 months after infection. Simultaneously, the European Observatory on Health Systems and Policies, promoted by the World Health Organization (WHO), has observed persistence of symptoms up to 12 weeks post-infection in some patients.[16]

Similarly, multiple organ symptoms after COVID-19 have been reported in a notable number of patients[17]. The spectrum of these signs ranges from cough and dyspnea to prolonged asthenia, headache, palpitations, chest pain, joint pain, physical limitations, depression, or insomnia. The November 2020 Lancet–Chinese Academy of Medical Sciences conference[18] warned that dysfunctions and complications from SARS-CoV-2 infection could persist in some discharged patients for at least 6 months. The so-called "long COVID" or "persistent COVID" is an emerging and still poorly understood health problem.[19-21]

The aim of this study is to determine whether SARS-CoV-2 infection continues to represent an increased risk for the occurrence of thromboembolic events in patients who have surpassed the acute phase of the disease.

Material and methods

We conducted a retrospective observational case-control study. Cases included patients treated in the emergency department (ED) with a diagnosis of thromboembolic episode between November 1st, 2020, and March 31st, 2021, identified through the electronic system of *Hospital de León* (León, Spain). The thromboembolic episodes considered were acute coronary syndrome or acute myocardial infarction (ACS/AMI), pulmonary embolism (PE), deep vein thrombosis (DVT), mesenteric ischemia, mesenteric infarction (MI), ischemic stroke, transient ischemic attack (TIA), and acute limb ischemia (ALI).

For each case, at least 2 controls were selected from the same database and period, with diagnoses other than the abovementioned conditions. Controls were matched by age with a maximum difference of 2 years. Patients who had experienced thromboembolic events in the 6 months prior to their ED visit were excluded.

For both groups, the exposure factor was the presence of a "coronavirus disease" diagnosis in the 6 months prior to the ED episode, according to discharge data from primary care. The severity of the infection was recorded based on whether hospitalization or intensive care unit (ICU) admission was required, or if management was outpatient. Additionally, the time elapsed between discharge from COVID-19 and the onset of the thromboembolic episode was recorded.

Sociodemographic variables included age and sex. Thromboembolic and cardiovascular risk factors—defined dichotomously—were past medical history of heart failure, hypertension, diabetes mellitus, atrial fibrillation, peripheral vascular disease, prior stroke, active cancer, use of antiplatelet or anticoagulant therapy, oral contraceptive use, pregnancy or hormonal contraception, lupus or antiphospholipid syndrome, and other hematological diseases with a prothrombotic profile.

Statistical analysis

Statistical analysis was performed using IBM-SPSS Statistics for Macintosh, version 28.0. Comparative analysis between case and control distributions was conducted to test for sample normality using the Shapiro–Wilk test. Data were expressed as mean ± standard deviation (SD) or as percentages with confidence intervals (CI). Parametric chi-square tests were used for categorical variables and Student's t-tests for quantitative variables. A P value < .05 was considered statistically significant. The odds ratio (OR) was calculated to estimate the risk of previous COVID-19 infection for developing thromboembolic events. To establish a predictive model for each studied variable, a multivariate logistic regression analysis was performed. The effect size was interpreted using Cohen's w for categorical variables and OR values transformed into Cohen's d/w, with non-significant results defined as < 1.68.

This study was approved by the Ethics Committee for Clinical Research (CEIC) of the León and Bierzo Health Areas (record no. 2178). Given the study design, patient consent was waived, as data collection ensured anonymity.

Results

A total of 569 patients were included in the study, of whom 179 were cases (with at least 1 thromboembolic episode) and 390 were controls. The description of the sample, distribution of variables, and intergroup differences are shown in Table 1. There were no significant sociodemographic or clinical differences between groups, except for diabetes mellitus (P = .046), which was more frequent in the case group.

Among the 179 cases, 95 (53%) were men, with a mean age of 71.7 years (SD, 15.7). Of these, 21.2% had ACS; 40 (22.3%), PE; 29 (16.2%), DVT; 54 (30.2%), stroke or TIA; 9 (5%), mesenteric infarction; and 9 (5%), acute limb ischemia (Figure 1). Seventeen (9.5%) had previously experienced SARS-CoV-2 infection; of these, 76.5% had mild disease. The mean time between COVID-19 infection and the thromboembolic episode was 35.4 days (SD, 22.9). In the control group, 191 (49%) were men with a mean age of 71.5 years (SD, 15.9). Prior SARS-CoV-2 infection occurred in 8.9% of these patients; among them, 57.1% had mild disease, 34.3% required hospitalization, and 8.6% required intensive care (Table 1).

Regarding thromboembolic risk associated with SARS-CoV-2 infection, no significant increase was observed in the case group, with an OR of 1.064 (95% CI, 0.58–1.96) (Table 2).

Analysis of the thromboembolic risk associated with previous COVID-19 infection showed that 17 of the 179 cases had a prior infection vs 33 in the control group. Therefore, there are no data to confirm that post-acute SARS-CoV-2 infection significantly increases the likelihood of thromboembolic events.

Effect size estimation showed small effects across all variables in the model, with the largest corresponding to COVID-19 severity, approaching 0.2 (a medium effect) (Table 3).

Finally, logistic regression analysis for predicting thromboembolic episodes yielded a low predictive capacity ($R^2 = 0.028$), with non-significant values for all studied variables (Table 4).

Discussion

Our results show that the prothrombotic risk in patients who have already recovered from COVID-19 is not significantly higher, and therefore their management would not require prophylactic anticoagulation for prolonged periods.

According to several authors, during the acute phase of the disease there is some degree of association with an increased rate of thromboembolic events involving both

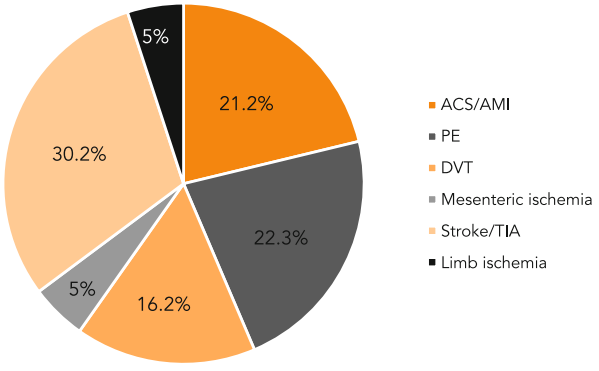

Figure 1. Frequency of thromboembolic episodes studied.
ACS: acute coronary syndrome; AMI: acute myocardial infarction; PE: pulmonary embolism; DVT: deep vein thrombosis; TIA: transient ischemic attack.

Table 1. Sociodemographic and clinical description of the sample

	Cases	Controls	*P*
Sex			
Male	95 (53%)	191 (49%)	
Female	84 (47%)	199 (51%)	
Age (years)	71.7 (SD 15.7)	71.52 (SD 15.9)	.831
Type of thrombosis			
ACS	38 (21.2%)		
PE	40 (22.3%)		
DVT	29 (16.2%)		
Mesenteric ischemia	9 (5%)		
Stroke/TIA	54 (30.2%)		
Acute limb ischemia	9 (5%)		
HF			.634
Yes	27 (15%)	65 (17%)	
No	152 (85%)	325 (83%)	
AF			.702
Yes	28 (16%)	66 (17%)	
No	151 (84%)	324 (83%)	
HTN			.164
Yes	108 (60%)	211 (54%)	
No	71 (40%)	179 (46%)	
DM			.046
Yes	52 (29%)	79 (20%)	
No	127 (71%)	309 (80%)	
Previous stroke			.972
Yes	13 (7.3%)	28 (7%)	
No	166 (92.7%)	362 (93%)	
PVD			.604
Yes	19 (10.6%)	36 (9%)	
No	160 (89.4%)	354 (91%)	
Antiplatelet therapy			.078
Yes	33 (18.4%)	50 (13%)	
No	146 (81.6%)	340 (87%)	
Anticoagulant therapy			.521
Yes	40 (22.3%)	78 (20%)	
No	139 (77.7%)	312 (80%)	
Active cancer			.645
Yes	8 (5%)	21 (5%)	
No	171 (95%)	369 (95%)	
Hematologic disease			.325
Yes	3 (1.7%)	3 (0.8%)	
No	176 (98.3%)	387 (99.2%)	
Hormonal contraception			.498
Yes	0	1	
No	179 (100%)	389 (~100%)	
Lupus/Antiphospholipid syndrome			.579
Yes	1 (0.6%)	4	
No	178 (99.3%)	386	
Pregnancy			
Yes	0	0	
No	179	390	
Previous COVID-19 infection			.41
Yes	17 (9.5%)	35 (9%)	
No	162 (90.5%)	355 (91%)	
Severity of COVID-19 infection			
Outpatient	13 (76.5%)	20 (57.1%)	
Hospitalization	4 (23.5%)	12 (34.3%)	
ICU	0	3 (8.6%)	

*Significance levels correspond to bivariate contrasts between groups (Pearson's Chi-square test for independent samples).
ACS: acute corona y syndrome; PE: pulmonary embolism; DVT: deep vein thrombosis; HF: heart failure; AF: atrial fibrillation; HTN: hypertension; DM: diabetes mellitus; PVD: peripheral vascular disease; ICU: intensive care unit.

Table 2. Thromboembolic risk in patients with resolved COVID-19 infection

	COVID-19 Negative	COVID-19 Positive	Total
Control	355	35	390
	68.7%	67.3%	68.5%
Case	162	17	179
	31.3%	32.7%	31.5%
Total	517	52	569
	100%	100%	100%

*Odds ratio (OR) for Case/Control = 1.064.

venous and arterial circulation.[4,5] There is a higher frequency of VTE, AMI, and stroke, which often occur despite prophylaxis and sometimes even with therapeutic anticoagulation. These findings led, in clinical practice, to the widespread prescription of anticoagulant drugs both in hospitalized and outpatient patients, as reflected in clinical practice guidelines for these conditions.[4,5]

As a result, recommendations have been established for managing thromboprophylaxis in COVID-19 patients, both in hospital and outpatient settings. However, evidence in this regard remains limited, and there is no clear guidance on the duration for which prophylaxis should be maintained after recovery from the acute phase.[22,23] Therefore, and consistent with previously published findings, a recent meta-analysis[7] reported a 33% prevalence of thromboembolic events in these patients, rising to 50% among those admitted to ICUs. Similarly, it has been confirmed that during the clinical course of SARS-CoV-2 infection, the prevalence of thromboembolic complications is high. The persistence of some post-infection symptoms has been reported as well, raising the question of whether the prothrombotic risk also persists.[18-21]

In our study, we found that more than half of the thrombotic events corresponded to coronary syndromes and strokes, whereas in most previously reviewed studies, DVT or PE were the predominant thrombotic complications.[24] In the same line, a multicenter study conducted in emergency departments of Spanish hospitals found a higher frequency of pulmonary embolism with an OR of 4.53 (95% CI, 4.03–5.10) in patients with acute COVID-19, and significantly lower frequencies of ACS, DVT, stroke, or GI bleeding (OR, 0.44, 95% CI, 0.36–0.53; OR, 0.66, 95% CI, 0.52–0.84; OR, 0.47, 95% CI, 0.40–0.56; OR, 0.59, 95% CI, 0.47–0.74, respectively).[25]

In our own analysis, we obtained an OR of 1.064 (95% CI, 0.58–1.96), which does not support that SARS-CoV-2 infection confers a higher risk of thromboembolic events in patients who have surpassed the acute phase of the disease.

Finally, the results obtained from the multivariate analysis did not allow us to establish a reliable predictive model for identifying factors most closely associated with the occurrence of thrombotic events in the studied patients. Therefore, broader studies are still required to explore this question further.[26]

Regarding the limitations of this study, we must first highlight that it was conducted in a single health care center and used a retrospective design, which limits the generalizability of its findings. Additionally, the study period was influenced by the epidemiological context of that time. The timeframe analyzed preceded the COVID-19 vaccination campaigns, meaning that none of the included subjects were protected by this strategy. However, this circumstance underscores the clinical relevance of our results, as they can guide therapeutic management in mild cases—both in vaccinated individuals and in those who decline vaccination—indicating that prolonged prophylactic anticoagulation would not be necessary.

Table 3. Estimation of the effect size of the variables used in the model

Variable	Cohen's W	Odds Ratio	RR
Sex	0.04 (0-0.12)	0.85 (0.6-1.21)	0.95 (0.67-1.34)
HF	0.02 (0-0.1)	0.89 (0.55-1.45)	0.96 (0.62-1.51)
AF	0.02 (0-0.1)	0.91 (0.56-1.47)	0.97 (0.62-1.51)
HTN	0.06 (0-0.14)	1.29 (0.9-1.85)	1.08 (0.76-1.54)
DM	0.1 (0-0.18)	1.60 (1.07-2.4)*	1.18 (0.82-1.68)
Previous stroke	0.00149 (0-0.02)	1.01 (0.51-2)	1 (0.56-1.78)
PVD	0.02 (0-0.1)	1.17 (0.65-2.10)	1.05 (0.64-1.72)
Antiplatelet therapy	0.07 (0-0.16)	1.54 (0.95-2.49)	1.16 (0.78-1.73
Anticoagulant therapy	0.03 (0-0.11)	1.17 (0.76-1.80)	1.05 (0.71-1.55)
Active cancer	0.02 (0-0.1)	0.82 (0.36-1.89)	0.94 (0.46-1.93)
Hematologic disease	0.04 (0-0.12)	2.2 (0.44-11)	1.37 (0.55-3.46)
Hormonal contraception	0.03 (0-0.11)	–	–
Lupus/Antiphospholipid syndrome	0.02 (0-0.11)	0.54 (0.06-4.89)	0.86 (0.13-5.58)
Previous COVID-19 infection	0.00843 (0-0.08)	1.06 (0.58-1.96)	1.02 (0.61-1.71)
COVID-19 severity	0.17 (0-0.41)	–	–

*There are statistically significant differences in the distribution of diabetes mellitus between the 2 groups studied.
ACS: acute coronary syndrome; PE: pulmonary embolism; DVT: deep vein thrombosis; HF: heart failure; AF: atrial fibrillation; HTN: hypertension; DM: diabetes mellitus; PVD: peripheral vascular disease.

Table 4. Binary logistic regression model

	B	Standard Error	Wald	Sig.	Exp(B)
HF	–.288	.278	1.071	.301	.750
AF	–.295	.329	.802	.371	.745
HTN	.193	.201	.922	.337	1.213
DM	.325	.216	2.270	.132	1.385
Previous stroke	–.128	.374	.117	.733	.880
PVD	–.068	.339	.040	.842	.935
Antiplatelet therapy	.415	.278	2.223	.136	1.514
Anticoagulant therapy	.344	.301	1.307	.253	1.411
Active cancer	–.216	.432	.251	.617	.805
Hematologic disease	.656	.852	.593	.441	1.927
Hormonal contraception	–20.208	40192.970	.000	1.000	.000
Lupus / Antiphospholipid syndrome	–.432	1.134	.145	.703	.649
Previous COVID-19 infection	.072	.315	.052	.819	1.075
Constant	–.995	.155	41.125	< .001	.370

Model fit: Cox–Snell R^2 = 0.02; Nagelkerke R^2 = 0.02
HF: heart failure; AF: atrial fibrillation; HTN: hypertension; DM: diabetes mellitus; PVD: peripheral vascular disease.

Several clinical practice guidelines on the management of patients with severe SARS-CoV-2 infection have included antithrombotic and anticoagulant drugs as part of the therapeutic regimen, due to the hypercoagulable nature of the disease. Nevertheless, uncertainty has persisted regarding how long the prothrombotic risk remains and, therefore, for how long such treatments might be beneficial. Based on our results, once the most acute phase of infection has been overcome, the risk of developing a thrombotic episode does not appear to increase, suggesting that continuing anticoagulant therapy long-term may not be justified[23,27].

ARTICLE INFORMATION

Conflict of Interest Disclosures: None reported.

Funding: The authors declare the non-existence of funding in relation to this article.

Ethical responsibilities: The authors have confirmed the maintenance of confidentiality and respect for the patient rights, agreement of publication, and transfer of rights to Revista Española de Urgencias y Emergencias.

Article not commissioned by the Editorial Board and with external peer review.

Note of the editors: This is a BOWMAN-generated English translation of the officially indexed Spanish-language article, which should be cited as Rev Esp Urg Emerg. 2023;2:19-23. In this translated version, the editors have supervised the process; however, it cannot be ruled out that some errors resulting from the artificial intelligence translation process may have gone unnoticed.

Acknowledgments: The authors thank all the Family and Community Medicine residents of León for their involvement in research activities and their tireless scientific curiosity.

REFERENCES

1. World Health Organization. Coronavirus Disease (COVID 19) situation report. World Health Organization. [Internet] 2021. (Accessed 18 April 2022). Available at: http://www.who.int/emergencies/diseases/novel-coronavirus-2019.
2. Puerta-Alcalde P, García-Vidal C. El perfil del paciente COVID-19 atendido en los servicios de urgencias españoles durante la pandemia de 2020. Emergencias. 2020;32:225-6.
3. Núñez-Gil IJ, Estrada V, Fernández-Pérez C, Fernández-Rozas I, Martín-Sánchez FJ, Macaya C. Curva pandémica COVID-19, sobrecarga sanitaria y mortalidad. Emergencias. 2020;32:293-5.
4. Panigada M, Bottino N, Tagliabue P, Grasseli G, Novembrino C, Changtarankul V, et al. Hipercoagulability of COVID19 patient in intensive care unit: a report of tromboelastrography findings and other paramenters of hemostasis. J Thromb Haemost. 2020;18:1738-42.
5. McBane RD. Thromboembolism and the Pandemic. JACC. 2020;76:2073-5.
6. Avila J, Long B, Holladay D, Gottlieb M. Thrombotic complications of COVID 19. Am J Emergency Med. 2021;39:213-8.
7. Kefale B, Tegegne G, Tadege M. Prevalence and Risk Factors of Thromboembolism among Patients with Coronavirus Disease-19: A Systematic Review and Meta-Analysis. Clin and Apl Thomb/hemost. 2020;26:1-13.
8. Sakr Y, Giovini M, Leone M, Pizzili G, Kortgen A, Bauer M, et al. Pulmonary embolism in patients Open Access with coronavirus disease-2019 (COVID-19) pneumonia: a narrative review. Ann Intensive Care. 2020;10:124.
9. Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thormbosis in patients with severe SARS-COV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020;46:1089-98.
10. Ye Q, Wang B, Mao J, The pathogenesis and treatment of the "cytokine Storm" in COVID 19. J Infect. 2020;80:607-13.
11. Fox SE, Armakbekov A, Harbert JL, Li G, Quincy-Brown J, Van der Heide RS. Pulmonary and cardiac pathology in African American patients with COVID19: an autopsy series from New Orleands. Lancet. 2020;8:681-6.
12. Toshiaki I, Jerrold HL, Marcel L, Tachil J. Coagulopathy in COVID19. J Thromb Haemost 2020;18:2103-9.
13. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA. 2020;180:1-11.
14. Colling ME, Kanthi Y. COVID–19-associated coagulopathy: An exploration of mechanisms. Vasc Med. 2020;25:471-8.
15. Barnes B, Adrover J, Baxter-Stoltzfus A, Borczuk A, Cools-Lartigue J, Crawford JM, et al. Targeting potential drivers of COVID-19: Neutrophil extracellular traps. J Exp Med. 2020; 217(6):e20200652.
16. Gaebler C, Wang Z, Lorenzi J, Muecksch F, Finkin S, Tokuyama M, et al. Evolution of antibody immunity to SARS-COV2. Nature. 2021;591:639-44.
17. WHO. Long therm effectos of COVID19. World Health Organization. [Internet] 2021. (Accessed 18 April 2022). Available at: https://www.who.int/docs/default-source/coronaviruse/risk-comms-updates/update-36-long-term-symptoms.pdf.
18. The Lancet. Facing up to Long COVID. Lancet. 2020;396:1861.
19. Chen JY, Zhang AD, Lu HY, Wang FF, Li ZC. CHADS2 versus CHA2DS2-VASc score in assessing the stroke and throm- boembolism risk stratification in patients with atrial fibrillation: a systematic review and meta-analysis. J Geriatr Card. 2013;10:258-66.
20. Mazzaccaro D, Giacomazzi F, Giannetta M, Varriale A, Scaramuzzo R, Modafferi A, et al. Non-Overt Coagulopathy in Non-ICU Patients with Mild to Moderate COVID-19 Pneumonia. J Clin Med. 2020;1781.
21. Perez-Copete J, Esteve-Pastor MA, Roldán V, Valdés M, Marín F. Escalas de evaluación del riesgo tromboembólico y hemorrágico en la fibrilación auricular. Rev Esp Cardiolo. 2016;16:25-32.
22. Carbonell AP, Vargas MF, Vallejo OG, Lerín AG, Ferriols MA, Morant JP, et al. COVID-19 y tromboprofilaxis: recomendaciones para nuestra práctica clínica en atención primaria. Semergen. 2020;46:479-86.
23. Vivas D, Roldán V, Esteve-Pastor MA, Roldán I, Tello-Montoliu A, Ruiz-Nodar JM, et al. Recomendaciones sobre el tratamiento antitrombótico durante la pandemia COVID-19. Posicionamiento del Grupo de Trabajo de Trombosis Cardiovascular de la Sociedad Española de Cardiología. Rev Esp Cardiol. 2020;73:749-57.
24. Malas MB, Naazue UBm Eksayed N, Mathkouthi A, Marmor R, ClaryB. Thromboembolism risk of COVID-19 is high ans associated with higher risk of mortality: A systematic review and meta-analysis. EClinicalMedicine 2020:29:100639.
25. Miró O, Llorens P, Jiménez S, Piñera P, Burillo-Putze G, Martín A, et al. Frequency of five cardiovascular/hemostatic entities as primary manifestations of SARS-CoV2 infection: Results of the UMC-19-S2. Int J Cardiol. 2021;330:268-72.
26. Del Castillo JG. Claves en la interpretación de los modelos pronósticos en el paciente COVID-19. Emergencias. 2021;33:251-3.
27. Gerotziafas GT, Catalano M, Colgan MP, Pecsvarady Z, Wautrecht JC, Fazeli B, et al. Guidance for the Management of Patients with Vascular Disease or Cardiovascular Risk Factors and COVID-19: Position Paper from VAS-European Independent Foundation in Angiology/Vascular Medicine. Thromb Haemost. 2020;120:1597-698.