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ABSTRACT

Background: Hospitalized patients with COVID-19 and raised D-dimer levels have high rates of venous thromboembolism (VTE). Methods: We used data from hospitalized patients with COVID-19 that were tested for pulmonary embolism (PE) or deep vein thrombosis (DVT) because of raised D-dimer levels. We aimed to identify patients at increased risk for VTE. Results: From March 25 to July 5th, 2020, 1,306 hospitalized patients with COVID-19 and raised D-dimer levels underwent testing for VTE in 12 centers. In all, 171 of 714 (24%) had PE, and 161 of 810 (20%) had DVT. The median time elapsed from admission to VTE testing was 12 days, and the median time from D-dimer measurement to testing 2 days. Most patients with VTE were men (62%), mean age was 62 ± 15 years, 45% were in an intensive care unit. Overall, 681 patients (52%) received VTE prophylaxis with standard doses, 241 (18%) with intermediate doses and 100 (7.7%) with therapeutic doses of anticoagulants. On multivariable analysis, patients with D-dimer levels >20 times the upper normal range (19% of the whole cohort) were at increased risk for VTE (odds ratio [OR]: 3.24; 95%CI: 2.18–4.83), as were those with a platelet count <100,000/μL (OR: 4.17; 95%CI: 1.72–10.0). Conclusions: Hospitalized patients with COVID-19 and D-dimer levels >20 times the upper normal range were at an increased risk for VTE. This may help to identify what patients could likely benefit from the use of higher than recommended doses of anticoagulants for VTE prophylaxis.
VTE based on clinical index of suspicion only, and against systematic screening using doppler ultrasonography of the lower limbs or chest CT-scan [16,17].

However, they note that clinicians should have a low threshold for testing in patients with a reasonable degree of clinical suspicion for VTE. Moreover, the preliminary ISTH guidance on the detection and treatment of conglutopathy in COVID-19 suggests that patients with raised D-dimer levels should be admitted to hospital [18] and some authors have advocated the use of screening programs, at least in patients with raised D-dimer levels [8,19,20].

The RIETE (Registro Informatizado de Enfermedad Tromboembólica) Registry is an ongoing, multicenter, international, observational registry of consecutive patients with objectively confirmed acute VTE (ClinicalTrials.gov identifier: NCT02832245). Since March 25, 2020, the Steering Committee of RIETE agreed to prospectively incorporate new data elements related to patients with COVID-19 [21]. The current study describes the results of a call to recruit data from hospitalized patients with COVID-19 that underwent diagnostic tests for VTE (either deep vein thrombosis [DVT] or pulmonary embolism [PE]) because of raised D-dimer levels. Our aim was to identify what patients were at increased risk for VTE.

2. Methods

2.1. Patients

For this study, we retrospectively analyzed data from the RIETE-Testing registry, which collected information on hospitalized patients with COVID-19 and raised D-dimer levels (ClinicalTrials.gov identifier, NCT04380792). All patients or their healthcare proxies provided written or oral consent for participation in the registry in accordance with local ethics committee requirements. The study analyzed data from 12 hospitals located in 4 countries (Spain, Italy, 2, United States and Germany 1 each). The study used the presence or absence of confirmed VTE as the primary endpoint. The RIETE investigators used medical record review to assess vital status. Unlike prior RIETE studies, the RIETE-Testing study has distinctions for patient enrollment criteria compared with the original RIETE registry [22]. Unlike the original RIETE registry (which is still ongoing), the RIETE-Testing study included only hospitalized patients with COVID-19, with or without confirmed VTE.

2.2. Study design

The investigators enrolled patients hospitalized for COVID-19 (confirmed by positive polymerase chain reaction testing of a nasopharyngeal sample or from tracheal aspirate in intubated patients) who had raised D-dimer levels between March 25 and July 5th, 2020. All patients with raised D-dimer levels during the study period were systematically investigated for VTE diagnosis, irrespectively of the presence or absence of VTE suspicion criteria. Testing included either lower limb venous compression ultrasonography (CUS) for deep vein thrombosis (DVT), or ventilation-perfusion (V/Q) scintigraphy or contrast-enhanced, helical chest computerized tomography (CT) for pulmonary embolism (PE). The time interval between obtaining blood samples for measuring D-dimer levels to VTE testing had to be < 3 days. Patients diagnosed with VTE prior to hospitalization for COVID-19, and those who developed VTE after hospital discharge were not included in the analysis. The major outcome was objectively confirmed VTE (PE, DVT, or both).

2.3. Variables of interest

Key data elements included: clinical characteristics (gender, age, body weight, mechanical ventilation), site of hospitalization (medical ward vs. an intensive care unit [ICU]), laboratory tests on the day of screening (platelet count, prothrombin time, D-dimer, fibrinogen, ferritin, creatinine), use of VTE prophylaxis (drugs, doses, duration) and the presence or absence of VTE on objective tests.

D-dimer testing was not centrally provided: levels were compared according to each hospital’s practice. Cut-off levels to define raised D-dimer were established by the Department of Clinical Chemistry at each participating site. Since the different D-dimer assays use different detection antibodies, different detection methods and often different calibrators [23–26], we requested the participating centers to provide information on the different units and normal cut-off values. Then, we compared D-dimer levels across the different centers according to how many times they exceeded the upper limit of normality in each centre.

2.4. Statistical analysis

The study reported categorical data as proportions and continuous data as mean and standard deviation (SD) or median (inter-quartile range). We compared demographics, laboratory tests, pharmacological VTE prophylaxis, and 30-day mortality according to patients’ disposition status: hospitalized in a medical ward or in an intensive care unit (ICU). We used unpaired two-tailed t-tests or the Mann-Whitney U test (for those variables found not to follow a normal distribution) for comparisons in the distributions of continuous variables between medical ward and ICU patients, and chi-squared or Fisher’s exact tests to compare the categorical data between the two groups. The risk to develop VTE was assessed with Cox proportional hazard model. We selected the following covariates in regression models for adjustment: sex, age, body weight, hospital status (in medical ward or ICU), platelet count, fibrinogen levels, D-dimer levels and use of VTE prophylaxis. Finally, we calculated the association between D-dimer levels (given as multiples of upper normal range) and VTE diagnosis (either DVT or PE). We calculated and compared the c-statistics, sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio of different multiples of the upper normal range of D-dimer. We conducted statistical analyses with the use of SPSS (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

3. Results

From March 25 to July 5th, 2020, 1,306 hospitalized patients with COVID-19 and raised D-dimer levels were tested for VTE: 639 underwent helical CT-scan, 75 ventilation perfusion lung-scan and 810 lower limb CUS (218 were screened for both, PE and DVT). In all, 171 of 714 patients undergoing chest CT-scan or V/Q lung scan (24%) had confirmed PE, and 161 of 810 patients undergoing CUS (20%) had confirmed DVT. The rates of PE and DVT largely varied among participating centers, as did the proportion of patients with D-dimer levels above 10 times the upper limit of normality (Table 1). In general, the highest rates of VTE were found in those centers where a highest proportion of patients had D-dimer levels above 10 times the upper normal limit, and vice versa.

The median time elapsed from COVID-19 diagnosis to testing for VTE was 16 days (interquartile range [IQR]: 7–22) in patients testing positive for VTE and 11 days (IQR: 5–19) in those testing negative. The median time elapsed from hospital admission to testing was 14 days (IQR: 7–21) in patients with VTE and 10 days (IQR: 5–19) in those without VTE. The median time from D-dimer measurement and testing was 2 days. Most patients (62%) were men, mean age was 62 ± 15 years, 45% were in the ICU and 39% were on mechanical ventilation.

Overall, 681 patients (52%) had received VTE prophylaxis with low-molecular-weight heparin (LMWH) or direct oral anticoagulants (DOACs) at standard doses, 241 (18%) at intermediate doses, and 100 (7.7%) at therapeutic doses (Table 2). Moreover, 86 patients (6.6%) received unfractionated heparin, 7 (0.5%) vitamin K antagonists and 6 (0.5%) received fondaparinux. In 186 patients (14%) there was no available information on the drugs, doses and/or duration.

There were no differences in the clinical characteristics (sex, age, body weight) of patients with- or without VTE, but patients with VTE were more likely to be in an ICU than in a medical ward, and more likely
were on mechanical ventilation (Table 3). There were no significant differences in mean levels of platelet count, prothrombin time, fibrinogen, ferritin or creatinine clearance between patients with- or without VTE, but patients with VTE were more likely to have D-dimer levels above 10- or even 20 times the upper normal level than those without VTE (Table 3). The proportion of patients with confirmed DVT, PE or VTE (both DVT or PE) progressively increased as the levels of D-dimer (given as multiples of the upper normal range) also increased (Fig. 1). Patients receiving standard doses of VTE prophylaxis had similar rates of PE (odds ratio [OR]: 0.87; 95%CI: 0.56–1.37) or DVT (OR: 0.94; 95%CI: 0.55–1.66) than those on intermediate doses, but had lower rates of PE (OR: 0.32; 95%CI: 0.19–0.55) or DVT (OR 0.28; 95%CI: 0.15–0.51) than those receiving therapeutic doses (Table 2).

The 30-day mortality rate in patients with VTE was significantly higher than in those without VTE (OR: 1.63; 95%CI: 1.10–2.43). When separately analyzed however, the mortality rate was non-significantly higher in patients with PE than in those without PE (OR: 1.46; 95%CI: 0.87–2.42), or in patients with DVT than in those without DVT (OR: 1.64; 95%: 0.99–2.67).

On multivariable analysis, patients with D-dimer levels above 20 times the upper normal range were at an increased risk for VTE (OR: 3.24; 95%CI: 2.18–4.83), as were those with a platelet count <100,000/μL (OR: 4.17; 95%CI: 1.72–10.0) (Table 4). Patients with D-dimer levels above 10 times the upper normal range were not at a significantly higher risk for VTE (OR: 1.45; 95%CI: 0.97–2.18).

Finally, we calculated the association between D-dimer levels (given as multiples of upper normal range) and VTE diagnosis. As it could be expected, the sensitivity of D-dimer levels to detect VTE progressively decreased as the threshold value increased, and the specificity increased (Table 5). The cut-point associated with the best AUC value was 10 times higher the upper normal range (c-statistics: 0.67; 95%CI: 0.63–0.70).
inter-quartile range.

Standard deviation; ICUs, intensive care units; VTE, venous thromboembolism; IQR,  

Abbreviations:

D-dimer levels, admission in the ICUs or in medical wards, and in the  

incidence rates in different centers (ranging from 1.3% to 87%). These  

DVT had positive  

Proportion of patients testing positive for DVT, PE or VTE, according to  

Comparisons between patients with- or without VTE: *p < 0.05; †p < 0.01; ‡p < 0.001.  

Comparisons between patients with- or without VTE: *p < 0.05; †p < 0.01; ‡p < 0.001.  

univariate and multivariate analyses for venous thromboembolism.

| Venous thromboembolism | Univariate | Multivariate |
|------------------------|------------|--------------|
| Clinical characteristics |            |              |
| Male gender            | 1.24 (0.93–1.67) | – |
| Age >65 years           | 1.10 (0.83–1.46) | – |
| Body weight ≤80 kg     | 0.93 (0.69–1.26) | – |
| Admitted in ICUs       | 2.66 (1.99–3.56)2 | 1.28 (0.90–1.83) |
| Laboratory tests       |            |              |
| Platelet count <100,000/μL | 0.46 (0.21–1.02)  | 4.17 (1.72–10.0) |
| Fibrinogen >600 mg/dL   | 1.12 (0.84–1.49) | – |
| Prothrombin time >13 s | 1.09 (0.81–1.48) | – |
| D-dimer levels >2 x upper limit | Ref. | Ref. |
| D-dimer levels >10 x upper limit | 1.97 (1.36–2.86)2 | 1.45 (0.97–2.18) |
| D-dimer levels >20 x upper limit | 4.72 (3.28–6.81)2 | 3.24 (2.18–4.83) |
| Ferritin levels >1,000 ng/mL | 1.56 (1.14–2.13)2 | 0.78 (0.56–1.08) |
| VTE prophylaxis         |            |              |
| Standard doses          | Ref.       | Ref.         |
| Intermediate doses      | 1.24 (0.84–1.83) | 0.81 (0.51–1.27) |
| Therapeutic doses       | 3.05 (1.92–4.84)4 | 1.68 (0.99–3.06) |
| Other/not reported      | 1.45 (1.01–2.07)4 | 0.67 (0.36–1.09) |

Abbreviations: ICU, intensive care unit; VTE, venous thromboembolism; Ref., reference.  

a p < 0.05.  
b p < 0.01.  
c p < 0.001.  

Table 5  

Prognostic values of different multiples of the upper range of D-dimer to detect VTE.  

| Patients, N | PE (n=1,090) | DVT (n=783) | VTE (n=486) | DVT+PE (n=210) |
|-------------|--------------|-------------|-------------|----------------|
| c-statistics | 0.57         | 0.64        | 0.67        | 0.62           |
| Sensitivity | 95.7         | 83.0        | 63.3        | 35.3           |
| Specificity | 18.1         | 45.5        | 69.8        | 89.4           |
| PPV          | 26.3         | 31.8        | 39.1        | 50.5           |
| NPV          | 93.2         | 89.7        | 86.1        | 81.9           |
| PLR          | 1.2 (1.1–1.2) | 1.5 (1.4–1.7) | 2.1 (1.8–2.5) | 3.3 (1.9–5.9) |
| NLR          | 0.2 (0.1–0.4) | 0.4 (0.3–0.5) | 0.5 (0.5–0.6) | 0.7 (0.7–0.8) |

Abbreviations: VTE, venous thromboembolism; PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio.  

dooses of VTE prophylaxis.  

Our study has a number of limitations that should be considered. First, we cannot know how many patients were truly asymptomatic, since hospitalized patients with COVID-19 often present with dyspnea, hypoxemia and acute respiratory distress syndrome. Second, some patients in our study underwent CT-scan, some V/Q scan and some CUS. Since patients were generally not subjected to both tests for PE and DVT, we do not know if patients with a negative test indeed did not have VTE, or did not have PE plus DVT. Third, local protocols (VTE prophylaxis, threshold for testing and choice of testing) may have resulted in major bias, as reflected by the wide ranges in VTE prevalence. Fourth, we did not include into the analysis concomitant diseases (such as cancer, chronic heart disease, chronic lung disease, anemia) or concurrent medications (antiplatelets, corticosteroids, …) that may also have influenced the risk for VTE. Finally, though only D-dimer levels above 20 times the upper normal range achieved significant multivariable analysis, it had a lower c-statistics than levels above 10 times the upper range. Further studies are needed, with more patients, to ascertain what the optimal D-dimer threshold could be.  

We conclude that hospitalized patients with COVID-19 and D-dimer  

Fig. 1. Proportion of patients testing positive for DVT, PE or VTE, according to D-dimer levels.  

Abbreviations: PE, pulmonary embolism; DVT, deep vein thrombosis; SD, standard deviation; ICUs, intensive care units; VTE, venous thromboembolism; IQR, inter-quartile range.  

In our study, 24% of patients tested for PE and 20% of those tested for DVT had positive findings. However, there was a large variability in the incidence rates in different centers (ranging from 1.3% to 87%). These differences may likely be due to differences in the intensity of the rise of D-dimer levels, admission in the ICUs or in medical wards, and in the proportion of patients receiving standard-, intermediate- or therapeutic
levels above 20 times the upper normal limit had a 3-fold higher risk to develop VTE than those with less raised levels. This may help to identify what patients could likely benefit from the use of intermediate- or therapeutic doses of anticoagulants for VTE prophylaxis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Manuscripts Submitted to Biomedical Journals: All authors had full access to the data presented in this manuscript.

Appendix 1

This article is original work that has not been previously published in any substantial part and is not under consideration for publication elsewhere. All authors have read and approved this manuscript. All authors meet the criteria for authorship stated in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals. All authors had full access to all data and hold final responsibility for the decision to submit this manuscript for publication.

Appendix 2

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References

[1] J. Helms, C. Tscuquard, F. Severac, F. Leonard-Lorant, M. Ohana, X. Delabranche, et al., High risk of thrombosis in patients in severe SARS-Co-V-2 infection: a multicenter prospective cohort study, Intensive Care Med. 46 (6) (2020) 1089–1098.

[2] C. Lodigiani, G. Iapichino, L. Carenzo, M. Cecconi, P. Ferrariz, T. Sebastian, et al., Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy, Thromb. Res. 191 (2020) 9–14.

[3] F.A. Klok, M. Kruip, N.J.M. van der Meer, M.S. Arbous, D. Gomers, K.M. Kaut, et al., Incidence of thrombotic complications in critically ill ICU patients with COVID-19, Thromb. Res. 191 (2020) 145–147.

[4] S. Middeldorp, M. Coppens, T.F. van Haaps, M. Foppen, A.P. Vlaar, M.C.A. Müller, et al., Incidence of venous thromboembolism in hospitalized patients with COVID-19, J. Thromb. Haemostasis 18 (8) (2020) 1995–2002.

[5] S. Cai, S. Chen, X. Li, S. Liu, F. Wang, Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia, J. Thromb. Haemostasis 18 (6) (2020) 1421–1424.

[6] J.P. Liñós, M. Leclerc, C. Chochos, J.M. Monzali, M. Ramakers, M. Arozov, et al., High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients, J. Thromb. Haemostasis 18 (7) (2020) 1743–1746.

[7] G. Grandmain, A. Andrey, D. Périard, R.P. Engelberger, G. Carrel, S. Doll, et al., Systematic screening for venous thromboembolic events in COVID-19 pneumonia, TH Open 4 (2020) e113–e115.

[8] M. Arrifoni, G. Danic, G. Gaurier, P. Gicquel, D. Bautéille, F. Rafi, et al., Systematic assessment of venous thromboembolism in COVID-19 patients receiving thromboprophylaxis: incidence and role of D-dimer as predictive factors, J. Thromb. Thrombolysis 50 (1) (2020) 211–216.

[9] A. Spyropoulou, J.I. Weitz, Hospitalized COVID-19 patients and venous thromboembolism: A perfect storm, Circulation 142 (2020) 129–132.

[10] D. Zhang, X. Feng, D. Zhang, C. Jiang, H. Mei, J. Wang, et al., Deep vein thrombosis in hospitalized patients with COVID-19 in Wuhan, China: prevalence, risk factors, and outcome, Circulation 142 (2020) 114–128.

[11] B. Ren, F. Yan, Z. Deng, Z. Zhang, L. Xiao, M. Wu, L. Cai, Extremely high incidence of lower extremity deep vein thrombosis in 48 patients with severe COVID-19 in Wuhan, Circulation 142 (2020) 181–183.

[12] J. Poissy, J. Goutay, M. Caplan, E. Parmentier, T. Duburcq, F. Lassalle, et al., Pulmonary embolism in patients with COVID-19: awareness of an increased prevalence, Circulation 142 (2020) 184–186.

[13] J.A. Hüpstensteer, E.L. Burnham, S.E. Jolley, Prevalence of venous thromboembolism in critically ill patients with COVID-19, Br. J. Haematol. 190 (3) (2020) e134–e137.

[14] D. Wichmann, J.P. Sperhake, M. Lütgehetmann, S. Steurer, C. Edler, A. Heinemann, et al., A European wide screening of patients under anticoagulation therapy and COVID-19, Thromb. Res. 188 (2020) 209–211.

[15] J.F. Llitjos, M. Leclerc, C. Chochois, J.M. Monsallier, M. Ramakers, M. Auvray, et al., Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy, Thromb. Res. 191 (2020) 9–14.

[16] A.C. Spyropoulou, J. Connors, B. Hunt, D. Giannis, J. Douketis, Scientific and Standardization Committee: clinical guidance on the diagnosis, prevention and treatment of venous thromboembolism in hospitalized patients with COVID-19, J. Thromb. Haemostasis (2020), https://doi.org/10.1111/j.1538-7836.2020.04793.x.

[17] L.K. Moores, T. Tritschler, S. Brosnan, M. Carter, J.F. Collen, K. Doerschug, et al., Prevention, diagnosis, and treatment of VTE in patients with COVID-19: Chest guideline end expert panel report, Chest 158 (3) (2020) 1143–1163.

[18] L.K. Moores, T. Tritschler, S. Brosnan, M. Carter, J.F. Collen, K. Doerschug, et al., Prevention, diagnosis, and treatment of VTE in patients with COVID-19: Chest guideline end expert panel report, Chest 158 (3) (2020) 1143–1163.

[19] J. Thachil, N. Sando, G. Alanga, M. Cattaneo, M. Levi, et al., ISTH interim guidance on recognition and management of coagulopathy in COVID-19, J. Thromb. Haemostasis 18 (5) (2020) 1023–1026.

[20] M.R. Aryal, R. Gouarn, A. Donato, R. Pathak, V.R. Bhat, A. Katel, P. Kouis, Venous thromboembolism in COVID-19: towards an ideal approach to thromboprophylaxis, screening, and treatment, Curr. Cardiol. Rep. 22 (2020) 52.

[21] A.T. Obi, G.D. Barnes, T.W. Wakefield, S. Brown, J.L. Eliason, E. Arndt, et al., Practical diagnosis and treatment of suspected venous thromboembolism during COVID-19 pandemic, J. Vasc. Surg. Lymphat. Disord 8 (2020) 526–534.

[22] C. Fernández-Capitán, R. Barba, C. Díaz-Pedroche, P. Sigüenza, P. Demelo-Rodríguez, C. Siniscalchi, et al., Prevalence, characteristics, treatment patterns and outcomes among patients with venous thromboembolism during hospitalization for COVID-19, Semin. Thromb. Haemost. Oct 21 (2020), https://doi.org/10.1055/s-0040-1718402 (in press).

[23] B. Bkdéli, D. Jiménez, M. Hawkins, S. Ortiz, P. Prandoni, B. Brenner, et al., Rationale, design and methodology of the computerized registry of patients with venous thromboembolism (RIETE), Thromb. Haemostasis 118 (2018) 214–224.

[24] G. Lippi, A. Tripodi, A.M. Simundic, E.F. Favalaro, International survey on D-dimer test reporting: a call for standardization, Semin. Thromb. Haemost. 41 (2015) 287–293.

[25] E.J. Favalaro, J. Thachil, Reporting of D-dimer data in COVID-19: some confusion and potential for misinformation, Clin. Chem. Lab. Med. 58 (2020) 1191–1199.

[26] C. Longstaff, D. Acock, J.D. Oulton, L. Jennings, S. Kitchen, N. Mutch, et al., Harmonisation of D-dimer: A call for action, Thromb. Res. 137 (2016) 219–220.

[27] R.S. Riley, A.R. Gilbert, J.B. Dalton, S. Pai, R.A. McPherson, Widely used tests and clinical applications of D-dimer assay, Lab. Med. 47 (2) (2016) 90–102.