DOI: 10.1002/emp2.12530

ORIGINAL RESEARCH

Revised: 11 May 2021

Infectious Disease

Risk of venous thromboembolism in a Swedish healthcare system during the COVID-19 pandemic: A retrospective cross-sectional study

Jens Wretborn MD¹ I Matthias Jörg MD¹ Patrik Benjaminsson Nyberg MD, PhD¹ Daniel B. Wilhelms MD² I

¹ Department of Emergency Medicine, Local Health Care Services in Central Östergötland, Region Östergötland, Linköping, Sweden

² Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden

Correspondence

Jens Wretborn, MD, Department of Emergency Medicine, Linköping University Hospital, 581 85 Linköping, Sweden. Email: jens.wretborn@med.lu.se

Funding and support: This work was supported by 2 public grants from Region Östergötland to Daniel B Wilhelms (LIO-532001 and LIO-700271). The funding body had no role in the design, data collection, analysis, or writing of this study.

Abstract

Objective: The objective of this study was to investigate the risk and prevalence of venous thromboembolism (VTE) for patients undergoing a diagnostic test for VTE with confirmed COVID-19 infection compared with patients with no COVID-19 infection. **Methods:** This was a retrospective cross-sectional study of patients in an integrated

healthcare system in Sweden, covering a population of 465,000, with a diagnostic test for VTE between March 1 and May 31 in the years 2015 to 2020. Risk for VTE with COVID-19 was assessed by logistic regression, adjusting for baseline risk factors.

Results: A total of 8702 patients were included, and 88 of those patients tested positive on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction test. A positive SARS-CoV-2 test did not increase the odds for VTE (odds ratio, 0.97; 95% confidence interval [CI], 0.55–1.74) and did not change when adjusting for sex, previous VTE, previous malignancy, Charlson score, hospital admission, intensive care, or ongoing treatment with anticoagulation (odds ratio, 0.72; 95% CI, 0.16–3.3). The prevalence of VTE was unchanged in 2020 compared with 2015 to 2019 (16.5% vs 16.1%, respectively), and there was no difference in VTE between the SARS-CoV-2 positive, negative, or untested groups in 2020 (15.9%, 17.6%, and 15.7%, respectively; P = 0.85).

Conclusions: We found no increased prevalence of VTE in the general population compared with previous years and no increased risk of VTE in patients who were SARS-CoV-2 positive, suggesting that SARS-CoV-2 status should not influence VTE workup in the emergency department. The prevalence of VTE was high in patients with SARS-CoV-2 treated in the intensive care unit (ICU), where the suspicion for VTE should remain high.

KEYWORDS

deep venous thrombosis, emergency department, prevalence, pulmonary embolism, SARS-CoV-2, venous thromboembolism

Supervising Editor: Nicholas Johnson, MD.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2021 The Authors. JACEP Open published by Wiley Periodicals LLC on behalf of American College of Emergency Physicians



1 | INTRODUCTION

1.1 | Background

In the ongoing COVID-19 pandemic, reports have shown an increased risk of venous thromboembolism (VTE), including both pulmonary embolism (PE) and deep venous thrombosis (DVT),¹⁻⁵ and international guidelines recommend prophylactic anticoagulation for all hospitalized patients with COVID-19.⁶ The majority of reports on VTE in COVID-19 have been carried out in the intensive care unit (ICU) and show a prevalence of VTE of 20% to 30%.¹⁻³ This is higher than cohorts of non-selected ICU patients where the prevalence of VTE is closer to 10%.⁷⁻¹⁰ However, studies on ICU patients with severe sepsis and viral infections such as H1N1 influenza have shown a prevalence of VTE of 37% and 44%, respectively.^{11,12} The prevalence of VTE in hospitalized non-ICU patients with COVID-19 is 3% to 4%,13-15 similar to studies on internal medicine patients with prophylactic anticoagulation.¹⁶ However, and relevant to emergency medicine, the VTE risk and prevalence in outpatients with known or suspected COVID-19 is less studied.¹⁷ Watchmaker et al studied PE incidence at 6 New York City hospitals during April 2020 and found 87 patients diagnosed with PE compared with 34 during the same period the previous year.¹⁸ On the contrary, Freund et al studied PE prevalence in patients undergoing computed tomography pulmonary angiography (CTPA) in 6 emergency departments (ED) in Europe and found no increased prevalence or risk of VTE in patients with COVID-19.¹⁹ Similarly, in a single center study of 324 admitted patients (50% COVID-19), Pizzi et al found no increase in DVT or PE in patients who were COVID-19 positive compared with patients with no COVID-19 infection.²⁰

1.2 | Importance

The mixed results on the risk of VTE provides a challenge for the emergency physician when assessing pretest probability in patients with known or suspected COVID-19. If COVID-19 were an independent risk factor for VTE in outpatients, traditional approaches to risk stratification and diagnostic testing may need to be modified.

1.3 | Goals of this investigation

The goal was to investigate if COVID-19 was associated with an increased risk of VTE in patients undergoing testing for VTE in a regional healthcare system in Sweden.

2 | METHODS

2.1 Study design and setting

In this retrospective observational study, we evaluated the risk and prevalence of VTE during the first 3 months, March 1 to May 31, of the

The Bottom Line

In a cohort of 8700 patients in Östergötland, Sweden, who were tested for venous thromboembolism (VTE), there was no difference in incidence found among those with a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test in the year 2020 compared with 2015 to 2019, implying that SARS-CoV-2 status alone should not dictate VTE workup in the emergency department, and other risk factors should be considered.

COVID-19 pandemic in the county of Östergötland (Region Östergötland, Sweden). The county has a population of 465,000 (December 31, 2019), and healthcare is provided by a central, publicly funded healthcare system. There is 1 rural community hospital, 1 urban community hospital, and 1 academic tertiary care hospital. All hospitals, outpatient clinics, and primary care centers in the county use the same electronic health records (EHRs), and all diagnostic studies of VTE are performed within the healthcare system. In the first months of the pandemic, only patients admitted to a hospital for suspected COVID-19 were tested, and the prevalence of COVID-19 in the general population was largely unknown. The cumulative incidence of confirmed cases in the county by the end of the study period in 2020 was 424 per 100,000, and the mortality rate was 42 per 100,000. Approximately 618 patients with confirmed COVID-19 had been admitted or were still in a hospital by May 31, 92 of whom were in intensive care, and the healthcare system was under considerable strain.

2.2 | Selection of participants

Adult patients (≥18 years of age) who underwent a diagnostic test for suspected VTE during the calendar months of March, April, and May 2015 to 2020 were included. Follow-up investigations, tests performed on referred patients from another healthcare system, and planned but non-performed tests were excluded.

2.3 | Exposures

The exposure was COVID-19 infection, defined as a positive polymerase chain reaction (PCR) test up to 14 days before or 7 days after the diagnostic test for VTE. This timeframe was chosen a priori to account for the delay from symptom onset to deterioration²¹ and delay to PCR test in the beginning of the pandemic. All patients with at least 1 diagnostic test for VTE during 2020 were matched with the regional severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) database of real-time PCR (RT-PCR) results. PCR was the diagnostic criteria for COVID-19 used in our system, and patients with a high probability for COVID-19 despite a negative PCR were tested repeatedly. PCR data were extracted from the healthcare system's central diagnostic laboratory, the only authorized SARS-CoV-2 laboratory during this period.

2.4 | Measurements

Additional known risk factors for VTE were extracted from the EHR. In-hospital care on a ward or in the ICU was defined as a minimum of 24 hours of care, as tests related to the ED presentation may be deferred up to 24 hours. Anticoagulant treatment was defined as treatment with a B01A class drug²² >7 days before the diagnostic test. Risk factors for VTE were age (continuous), sex (male/female), previous VTE (yes/no), malignancy (yes/no), ward care (yes/no), intensive care (yes/no), and Charlson score (continuous), and data were extracted from the EHR. The EHR has partial coverage of diagnoses before 2008 and full coverage thereafter. Mortality at 30 days was defined as allcause mortality based on the Swedish national civil registration registry.

2.5 | Outcomes

The outcome was a diagnosis of VTE by CTPA or ultrasound. Written study reports were extracted from the picture archiving and communication system for all CTPA and ultrasound for DVT. Findings of PE were coded as positive for any contrast defect in a subsegmental or more central pulmonary artery. Any additional finding classified as definitive or probable PE by the attending radiologist was coded as PE positive. DVT was diagnosed with complete compression ultrasound or 3-point compression ultrasound of the leg.²³ Isolated muscle vein thrombosis and thrombophlebitis were classified as negative examinations. Patients with multiple tests of the same modality on the same day were classified as duplicates and combined to a single test. The reports were classified as positive or negative independently by J.W. and M.J. All positive or ambiguous reports and differences in classification were reviewed by J.W., M.J., and P.B.N. and solved through full consensus. Interrater reliability was not systematically assessed. A subset of diagnostic tests were done in the department of clinical physiology and were already classified as positive or negative.

2.6 Analysis

Descriptive data were reported as percentage, mean with standard deviation (SD), or median with interquartile range (IQR). Prevalence was reported by separate diagnoses, for example, the prevalence of PE was CTPA-positive tests compared with all performed CTPA. Logistic regression was used to investigate the crude and adjusted risks for a VTE by COVID-19 status. Prevalence was compared with the chi-squared test with pre-defined subgroup analysis for PE and non-PE VTE, mainly DVT. Patients with no RT-PCR test results in 2020 were treated as a separate subgroup to avoid bias based on test availability.

WILEY

We performed a sensitivity analysis for the timing of COVID-19 diagnosis by running all possible time frames up to 30 days before or after the diagnostic test. We also performed analysis to test the robustness by incrementing the number of positive VTE cases in the SARS-CoV-2– positive cohort until there was a statically significant difference compared with the SARS-CoV-2–negative cohort.

Based on historical data, about 500 VTE tests are performed each month in the system. A sample size calculation with the chi-square goodness-of-fit test for 2 categorical variables with a conservative effect size of 0.1 (α = 0.05, power = 0.8) required 785 samples. A total of 3 months of data collection, March 1 through May 31, were collected to account for a possible decrease in tests during the initial period of the pandemic. To assess differences in VTE testing practice due to the pandemic, 5 years of historical data were included that was not considered in the sample size calculation.

Data were imported into Pandas (version 0.23)²⁴ and analyzed with Python using the Scipy library (version 1.17)²⁵ and Statsmodels library (version 0.12).²⁶

2.7 Ethical considerations

This study was carried out in accordance with the Declaration of Helsinki.²⁷ Ethical approval was granted by the Swedish Ethical Review Authority with permit reference 2020–02701, and the study was pre-registered on May 26, 2020, at ClinicalTrials.gov with identifier NCT04400877. The study has been conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting observational trials.

3 | RESULTS

There were 9973 diagnostic tests for VTE performed during the study period. After the exclusion of ineligible tests and a reduction for duplicate tests, a total of 8702 tests were included in the analysis (Figure 1).

The cohort of patients that performed a diagnostic test for VTE in 2020 was well matched with patients from 2015 to 2019. However, the subgroup of patients with a positive SARS-CoV-2 test were more often men, had a higher prevalence of previous VTE and a lower prevalence of malignancy, and were more likely to be treated in or admitted to a ward or an ICU compared with the 2020 and 2015 to 2019 cohorts (Table 1). The prevalence of any VTE, PE, and DVT in the full cohort was 16.2%, 17.5%, and 15.2%, respectively. There was no difference in prevalence of VTE in 2020 compared with 2015 through 2019 (16.5% vs 16.1%; difference, 0.4%; 95% confidence interval [CI], –1.8% to 2.4%; Appendix).

COVID-19 infection was confirmed for 88 diagnostic tests, and 14 of these had positive findings of VTE, 12 had positive findings of pulmonary embolisms, and 2 had positive findings of DVTs. There was no significant difference in the prevalence of VTEs between the confirmed SARS-CoV-2-positive, SARS-CoV-2-negative, or untested groups in 2020 (15.9%, 17.6%, and 15.7% of tests in each group, respectively;

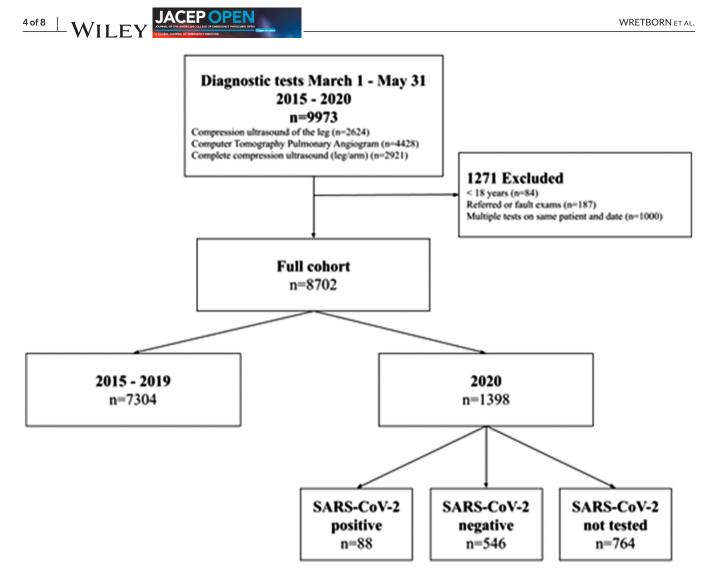


FIGURE 1 Flowchart of diagnostic tests included in the study. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

P = 0.85; Table 2). The prevalence of VTEs in patients diagnosed on the ward and as outpatients was lower in the SARS-CoV-2–positive group compared with the group confirmed negative (Table 3). There was a high prevalence of VTEs in the cohort of patients treated in the ICU before their diagnostic test (7/10; 70%). No patients in the ICU with negative or those with no SARS-CoV-2 test were diagnosed with VTE during the study months in 2020 compared with 39% (n = 9/23) from 2015 through 2019 (Table 3)

A positive SARS-CoV-2 test decreased the risk of VTE compared with a negative SARS-CoV-2 test (odds ratio [OR], 0.97; 95% CI, 0.55– 1.73) in an unadjusted analysis. The OR for VTE decreased (0.72; 95% CI, 0.16–3.3) when adjusting for previous VTE, previous malignancy, intensive care, in-hospital care, sex, age, Charlson score, and ongoing treatment with anticoagulation.

In a test of robustness, the difference in the prevalence of VTE became statistically significant after adding 14 patients to the SARS-CoV-2-positive and VTE-positive group. This would correspond to an increase in prevalence of 100% compared with our findings. There was no difference in VTE prevalence irrespective of time frame for classifying a patient as COVID-19 positive, between 1 and 30 days before

and after the diagnostic test with a consistently lower prevalence in the COVID-19 group (mean difference, 1.84%; SD, 0.8).

3.1 | Limitations

This was a retrospective observational study, and the results are limited to the variables we were able to control for. We used the risk factors for PE and DVT defined by Wells et al,^{28,29} but were not able to obtain physiologic data or referring physicians' assessments at the time of the diagnostic test to adjust for all the criteria in the conventional diagnostic tools.^{29,30} However, we believe that we have been able to adjust for the majority of confounders for VTE when evaluating infection with SARS-CoV-2 as a possible risk. This is supported by the results of our adjusted regression model, which show a significant association between VTE, previous VTE, and admission to an ICU, and a negative association with ongoing treatment with oral anticoagulation.

Only patients who had a diagnostic test for suspected VTE were considered in this study, hence this is a select cohort of patients, which limits the generalizability. However, there was no increased prevalence **TABLE 1**Epidemiology data of patients who have done a diagnostic test for venous thromboembolism in 2015 to 2019, 2020 and thesubgroup of patients who were SARS-CoV-2 positive

	2015-2019	2020 ^a	SARS-CoV-2 positive
Cohort			
Ν	7304	1398	88
Age, y	64.9	64.4	62.6
Female, n (%)	4172 (57.1)	794 (56.8)	34 (38.6)
BMI, kg/m ² (n)	27.8 (5144)	28.3 (934)	28.7 (64)
Risk factor			
Ongoing anticoagulation, n (%)	2557 (35.0)	449 (32.1)	22 (25.0)
Previous VTE, n (%)	698 (9.6)	124 (8.9)	13 (14.8)
Previous malignancy, n (%)	1430 (19.6)	271 (19.4)	10 (11.4)
Charlson score, median (IQR)	4 (2-6)	4 (1-6)	3 (1-5)
Treatment			
Admitted to ward, n (%) c	1625 (22.2)	374 (26.8)	30 (34.1)
Ward care, n (%) ^b	1258 (17.2)	219 (15.7)	41 (46.6)
ICU admission, n (%) ^c	96 (1.3)	37 (2.6)	7 (8.0)
ICU care, n (%) ^b	23 (0.3)	18 (1.3)	10 (11.4)
Ventilator treatment, n (%)	47 (0.6)	25 (1.8)	8 (9.1)
Outcome			
VTE positive, n (%)	1179/7304 (16.1)	230/1398 (16.4)	14/88 (16.0)
PE positive, n (%)	610/3416 (17.9)	124/779 (15.9)	12/78 (15.4)
30-day mortality, n (%)	173/7304 (2.4)	47/1398 (3.4)	8/88 (9.1)

BMI, body mass index; IQR, interquartilerange; PE, pulmonary embolism; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VTE, venous thromboembolism.

^aIncludes the SARS-CoV-2-positive group.

^bMore than 24 hours of care before a diagnostic test for VTE.

^cAdmission within 24 hours of diagnostic test for VTE.

TABLE 2Difference in the prevalence of VTE between patientswho were SARS-CoV-2 positive, SARS-CoV negative, and not tested in2020

	Positive	Negative	Untested 2020
VTE ^a	15.9% (14/88)	17.6% (96/546)	15.7% (120/764)
PE	15.4% (12/78)	16.2% (71/439)	15.6% (41/262)
DVT	15.4% (2/13)	21.6% (25/116)	16.1% (82/509)

DVT, deep venous thrombosis; PE, pulmonary embolism; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VTE, venous thromboembolism.

Data in parenthesis denotes the number of test positive (VTE/PE/DVT) by the total number of investigations done for each test and SARS-CoV-2 status group.

^aTest for PE and DVT on the same day were combined.

of VTE in the cohort except for patients in intensive care. If there were a true increase of VTE from COVID-19, irrespective of other risk factors, we would expect to see a signal when the incidence of COVID-19 was rising in the community.

SARS-CoV-2 status was missing from a significant proportion of patients undergoing testing for VTE in 2020, which limits the gener-

alizability of the results. We did not have the resources to chart review these patients to adjudicate a probability of COVID-19. However, the untested cohort resembled the cohort from 2015 to 2019 in terms of VTE prevalence and risk factors (Table 1).

We may have missed a few PEs by not including chest computed tomography (CT) or scintigraphy. However, any finding associated with PE on chest CT would warrant a definitive workup including CTPA, whereas scintigraphy is rarely performed in our system. In addition, tests for cerebral venous sinus thrombosis were not included because of resource limitations. We based the classification of PE on the radiology report and not an independent read of the image data. Although this may have introduced a subjective interpretation, it reflects the actual practice in Sweden where non-radiologists rely on the report by the radiologists for the diagnosis of PE.

4 DISCUSSION

An infection with SARS-CoV-2 virus confirmed on RT-PCR was not associated with an increased risk of VTE in patients undergoing a diagnostic test for VTE in a large, integrated healthcare system in Sweden. WILEY

TABLE 3	Prevalence of VTE	by SARS-CoV-2 resu	It and admission status
---------	-------------------	--------------------	-------------------------

	SARS-CoV-2 positive	SARS-CoV-2 negative	Untested 2020	2015-2019
ICU ^a	70% (7/10)	0% (0/4)	0% (0/4)	30% (7/23)
Ward ^a	10% (3/31)	20% (21/108)	20% (12/64)	20% (210/1239)
Outpatient	10% (4/47)	20% (75/434)	20% (108/696)	20% (962/6042)
ICU admission ^b	0% (0/7)	20% (4/26)	0% (0/4)	20% (18/96)
Ward admission ^b	10% (3/30)	20% (49/262)	40% (30/82)	30% (484/1625)

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VTE, venous thromboembolism.

Data in parenthesis denotes the number of test positive (VTE/PE/DVT) by the total number of investigations done for each test and SARS-CoV-2 status group. ^aMore than 24 hours of care before a diagnostic test for VTE.

^bAdmission within 24 hours of a diagnostic test for VTE.

We found no increase in prevalence of VTE in 2020 compared with 2015 to 2019, andno difference between patients who were SARS-CoV-2 positive, negative, or untested during 2020. This is similar to the results by Freund et al, who found no association between a confirmed diagnosis of COVID-19 and a PE in 3253 patients undergoing CTPA for suspected PE in the ED,¹⁹ and the results by Pizzi et al, who found no increased prevalence of VTE in admitted patients with COVID-19.²⁰ However, there was a high prevalence of VTE in patients with confirmed COVID-19 in the ICU, similar to previous reports.^{1–3}

COVID-19 did not increase the odds for VTE compared with a negative test when adjusting for known risk factors and ongoing treatment with anticoagulation. This indicates that patients with COVID-19 being investigated for VTE may be risk stratified using conventional tools. Although the OR for COVID-19 suggested a lower risk for VTE, the CIs were wide, indicating the need for a larger study to confirm these results. Intensive care was associated with a high prevalence of VTE, which is in line with previous studies, and the suspicion for VTE should generally be higher in these patients.^{1–3}

For the emergency physician, determining pretest probability before performing a test is central to the correct use of diagnostic testing. Based on our results, COVID-19 status had little influence on the risk for VTE when adjusting for classical risk factors, such as previous VTE or malignancy. The high prevalence of VTE in the ICU group was for patients treated in the ICU for >24 hours and thus less relevant to the emergency physician. For patients primarily seen in the ED, the outpatient and admission groups, the prevalence of VTE was consistently lower in the COVID-19 group, which strengthens our results.

There was a high prevalence of VTE at 70% (7/10), most of them being PE (6/7), in the ICU subgroup with confirmed SARS-CoV-2 infection. Because of the pandemic, the ICU cohort for 2020 is likely different from the ICU cohorts between 2015 and 2019, with a more homogenous group of patients with severe acuterespiratory distress syndrome, limiting comparability. Although the number of patients investigated was small in this group, the results are comparable with previous studies^{1,3} and support the notion that VTE is a relevant problem for patients with severe COVID-19 in the ICU.⁶ In hospitalized, non-intensive care patients and outpatients with COVID-19, the VTE prevalence was lower compared withpatients with no COVID-19 infection and the 2015 to 2019 cohort. This may be attributed to increased testing in the beginning of the pandemic because of concerns for VTE.^{1,2,31} In addition, most elective surgery for non-malignant causes was either postponed or canceled to free up intensive care resources as well as to reduce the need for postoperative intensive care. Because recent surgery is a risk factor for VTE, this might have reduced the prevalence of VTE in the general population. On the contrary, most non-emergent outpatient clinics and primary care appointments were cancelled or deferred to telemedicine meetings, which may have led to a higher threshold to test for VTE and an increased prevalence in the 2020 group. It is difficult to quantify the impact of these changes but compared with data from 2015 to 2019, there are no large differences in VTE prevalence in 2020, suggesting a limited impact of the pandemic on the testing practice for VTE.

This comprehensive study includes all patients diagnosed with VTE in the whole county of Östergötland with 465,000 inhabitants during the first 3 months of the pandemic. The national voluntary recommendation not to travel during the initial months of the pandemic was comparable to a national lockdown that substantially limited the movement and possibility of seeking care in another healthcare system, which is uncommon even under normal circumstances, and further strengthens our results.

We found no increased risk of VTE in patients with SARS-CoV-2 undergoing a diagnostic test for VTE in an integrated healthcare system in Sweden during the first 3 months of the COVID-19 pandemic. The prevalence of VTE was heterogeneous within the cohort, and lower in patients with COVID-19 in general, except for ICU patients. There was no general increase in prevalence of VTE compared with 2015 to 2019. Our results suggest that COVID-19 should not influence the pretest probability for VTE when considering the workup for VTE in the ED. The results should be confirmed in a larger study.

ACKNOWLEDGMENTS

We acknowledge the help of Erik Onelöw, Section for Bioinformatics, Region Östergötland, Sweden, in compiling the study data set. We also acknowledge Charlotte Brage, Department of Radiology, and Christina Svensson, Department of Clinical Physiology, both at Region Östergötland, for their help in extracting diagnostic data.

CONFLICT OF INTEREST

All authors have completed the International Committee of Medical Journal Editors uniform disclosure form at www.icmje.org/coi_ disclosure.docx and declare no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years, and no other relationships or activities that could appear to have influenced the submitted work.

AUTHOR CONTRIBUTIONS

Jens Wretborn, Matthias Jörg, Patrik Benjaminsson Nyberg, and Daniel B. Wilhelms conceived and designed the study. Daniel B. Wilhelms obtained funding and supervised the study. Jens Wretborn and Matthias Jörg collected the data. Jens Wretborn, Matthias Jörg, and Patrik Benjaminsson Nyberg abstracted study reports. Jens Wretborn analyzed the data and performed statistical analysis. Jens Wretborn drafted the manuscript, and all authors contributed substantially to its revision. Jens Wretborn takes responsibility for the paper as a whole. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

PRE-REGISTRATION

The study was pre-registered on May 26, 2020, at ClinicalTrials.gov with identifier NCT04400877.

ORCID

Jens Wretborn MD ^D https://orcid.org/0000-0002-0549-6805 Matthias Jörg MD ^D https://orcid.org/0000-0002-1805-5283 Daniel B. Wilhelms MD ^D https://orcid.org/0000-0001-6347-3970

REFERENCES

- Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res.* 2020;191:145-147.
- Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost*. 2020;18(6):1421-1424.
- Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. *Intensive Care Med.* 2020;46(6):1089-1098.
- Leonard-Lorant I, Delabranche X, Severac F, et al. Acute pulmonary embolism in COVID-19 patients on CT angiography and relationship to D-Dimer levels. *Radiology*. 2020;296(3):E189-E191.
- Poissy J, Goutay J, Caplan M, et al. Pulmonary Embolism in COVID-19 patients: awareness of an increased prevalence. *Circulation*. 2020;142(2):184–186.
- Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 2020;18(5):1023-1026.
- Muscedere JG, Heyland DK, Cook D. Venous thromboembolism in critical illness in a community intensive care unit. J Crit Care. 2007;22(4):285-289.
- Cook D, Crowther M, Meade M, et al. Deep venous thrombosis in medical-surgical critically ill patients: prevalence, incidence, and risk factors. Crit Care Med. 2005;33(7):1565-1571.
- Cook D, Attia J, Weaver B, McDonald E, Meade M, Crowther M. Venous thromboembolic disease: an observational study in medical-surgical intensive care unit patients. *J Crit Care.* 2000;15(4): 127-132.
- PROTECT Investigators for the Canadian Critical Care Trials Group and the Australian and New Zealand Intensive Care Society Clinical

JACEP OPEN

Trials Group, Cook D, Meade M, et al. Dalteparin versus unfractionated heparin in critically ill patients. 2011;364(14):1305-1314.

- Kaplan D, Casper TC, Elliott CG, et al. VTE incidence and risk factors in patients with severe sepsis and septic shock. *Chest.* 2015;148(5):1224-1230.
- 12. Obi AT, Tignanelli CJ, Jacobs BN, et al. Empirical systemic anticoagulation is associated with decreased venous thromboembolism in critically ill influenza A H1N1 acute respiratory distress syndrome patients. *J Vasc Surg Venous Lymphat Disord*. 2019;7(3): 317-324.
- Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res.* 2020;191:9-14.
- 14. Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost*. 2020;18(8):1995-2002.
- Criel M, Falter M, Jaeken J, et al. Venous thromboembolism in SARS-CoV-2 patients: only a problem in ventilated ICU patients, or is there more to it? *Eur Respir J.* 2020;56(1):2001201.
- Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. prophylaxis in medical patients with enoxaparin study group. N Engl J Med. 1999;341(11):793-800.
- Jiménez D, García-Sanchez A, Rali P, et al. Incidence of VTE and bleeding among hospitalized patients with coronavirus disease 2019: a systematic review and meta-analysis. *Chest.* 2021;159(3):1182-1196.
- Watchmaker JM, Goldman DT, Lee JY, et al. Increased incidence of acute pulmonary embolism in emergency department patients during the COVID-19 pandemic. *Acad Emerg Med.* 2020;27(12):1340-1343.
- Freund Y, Drogrey M, Miró Ò, et al. Association between pulmonary embolism and COVID-19 in ED patients Undergoing CTPA: the PEPCOV international retrospective study. *Acad Emerg Med.* 2020;27(9):811-820.
- 20. Pizzi R, Gini G, Caiano L, et al. Coagulation parameters and venous thromboembolism in patients with and without COVID-19 admitted to the emergency department for acute respiratory insufficiency. *Thromb Res.* 2020;196:209-212.
- Chen J, Qi T, Liu L, et al. Clinical progression of patients with COVID-19 in Shanghai, China. J Infect. 2020;80(5):e1-e6.
- Norwegian Institute of Public Health. WHO Collaborating Centre for Drug Statistics Methodology, guidelines for ATC classification and DDD assignment 2020. https://www.whocc.no/atc_ddd_methodology/who_international_working_group/. Published 2019. Accessed July 29, 2020.
- 23. Needleman L, Cronan JJ, Lilly MP, et al. Ultrasound for lower extremity deep venous thrombosis. *Circulation*. 2018;137(14):1505-1515.
- McKinney W. Data structures for statistical computing in python. In: Jones E, Millman J eds. Proceedings of the 9th Python in Science Conference (Vol. 445). Austin, TX: Python for Scientific Computing; 2010:51-56.
- Millman KJ, Aivazis M. Python for scientists and engineers. Computing in Sci Eng. 2011;13(2):9-12.
- Seabold S, Perktold J. Econometric and statistical modeling with python. In: Jones E, Millman J eds. Proceedings of the 9th Python in Science Conference (Vol. 445). Austin, TX: Python for Scientific Computing; 2010:92–96.
- World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-2194.
- Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med. 2003;349(13):1227-1235.

29. Wolf SJ, McCubbin TR, Feldhaus KM, Faragher JP, Adcock DM. Prospective validation of wells criteria in the evaluation of patients with suspected pulmonary embolism. *Ann Emerg Med.* 2004;44(5):503-510.

CEPO

- Kline JA, Courtney DM, Kabrhel C, et al. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. J Thromb Haemost. 2008;6(5):772-780.
- Llitjos J-F, Leclerc M, Chochois C, et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. *J Thromb Haemost*. 2020;18(7):1743–1746.

APPENDIX: PREVALENCE BY TEST MODALITY AND YEAR

How to cite this article: Wretborn J, Jörg M, Benjaminsson Nyberg P, Wilhelms DB Risk of venous thromboembolism in a Swedish healthcare system during the COVID-19 pandemic: A retrospective cross-sectional study. *JACEP Open*. 2021;2:e12530. https://doi.org/10.1002/emp2.12530

Test	Year	Prevalence, %	Comparison (mean of other years), %	Difference, %	95% CI	Р
VTE	2015	17.8	15.9	1.91	-0.002198 to 0.040316	0.08
VTE	2016	16.4	16.2	0.19	-0.019701 to 0.0235	0.89
VTE	2017	16.6	16.1	0.53	-0.01547 to 0.0261	0.64
VTE	2018	15.3	16.4	-1.11	-0.031112 to 0.008991	0.31
VTE	2019	14.7	16.5	-1.75	-0.03729 to 0.002361	0.10
VTE	2020	16.5	16.1	0.31	-0.018085 to 0.02429	0.80
PE	2015	19.7	17.1	2.65	-0.006363 to 0.059272	0.11
PE	2016	16.8	17.6	-0.85	-0.040435 to 0.023471	0.65
PE	2017	18.9	17.2	1.66	-0.014955 to 0.048243	0.32
PE	2018	17.4	17.5	-0.09	-0.03087 to 0.028999	0.99
PE	2019	16.5	17.7	-1.23	-0.042746 to 0.018245	0.47
PE	2020	15.9	17.9	-1.94	-0.048116 to 0.00933	0.22
DVT	2015	16.1	14.9	1.20	-0.015628 to 0.039532	0.42
DVT	2016	15.9	15.0	0.90	-0.020041 to 0.038089	0.57
DVT	2017	14.5	15.3	-0.75	-0.034555 to 0.019455	0.63
DVT	2018	13.7	15.5	-1.74	-0.044227 to 0.00942	0.24
DVT	2019	14.0	15.4	-1.40	-0.040174 to 0.01211	0.33
DVT	2020	17.1	14.8	2.24	-0.008887 to 0.05359	0.16

Cl, confidence interval; DVT, deep venous thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.