Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Cardiovascular Imaging* author instructions page.

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Frequency of Pulmonary Embolism in Patients With COVID-19

Several reports have highlighted a high incidence of pulmonary embolism (PE) in patients with coronavirus disease-2019 (COVID-19) (1–4). However, patients with severe illness, particularly those in the intensive care unit, have increased D-dimer levels and high risk of venous thromboembolism. It is not clear whether the high risk of PE reported in some series simply reflects severe illness, or whether COVID-19 itself confers a particularly high risk of thromboembolism. We thus set out to evaluate the rate of PE in patients with COVID-19 compared with control subjects who were tested but found to be negative for the virus.

This retrospective study was approved by the Institutional Review Board of our hospital system. Patients in our health care system who received COVID-19 reverse transcriptase polymerase chain reaction testing between March 1, 2020, and May 1, 2020, and underwent computed tomography pulmonary angiography (CTPA) within 7 days prior to and 14 days after the testing were included. Radiology reports and D-dimer levels within 1 day of the CTPA were retrieved from the electronic medical record. Clinical pre-test probability of PE was derived from order indications. The presence of an endotracheal tube was extracted from radiology reports. CTPA reports were recorded as positive for PE, negative, or nondiagnostic. Nondiagnostic studies were excluded.

Statistical analysis was performed with JMP Pro version 15 (SAS Institute, Cary, North Carolina). Differences between categorical variables were analyzed with 1-tailed Fisher exact test and continuous variables with 1-tailed Student's *t*-test. Multivariable logistic regression was used to evaluate determinants of a positive CTPA. Confidence intervals (CIs) for area under the receiver-operating characteristic curves were generated by bootstrapping.

A total of 709 CTPAs were identified; 13 nondiagnostic studies were excluded, leaving 696 CTPAs from 674 patients. The median age was 63 (range 17 to 100) years, 352 patients (52%) were female, and 167 (25%) were COVID-19-positive. Pre-test probability was available for 475 CTPAs (68%): of COVID-19-negative patients, 33 (9%) were low risk, 152 (43%) intermediate risk, and 169 (48%) high risk; of COVID-19-positive patients, 6 (5%) were low risk, 74 (61%) intermediate risk, and 41 (34%) high risk. The 167 patients with COVID-19 represent 3% of the total number (n = 5,816) of patients who were COVID-19-positive in our health care system in that time frame.

Of 170 CTPAs in patients with COVID-19, 20 (11.8%) were positive for PE, compared with 45 of 526 CTPAs (8.6%) in patients without COVID-19 (p = 0.14) (**Table 1**). Of patients intubated at the time of CTPA, 7 of 23 patients with COVID-19 (30.4%) had PE, compared with 6 of 33 patients without COVID-19 (18.2%) (p = 0.22). For CTPAs done within 1 day of COVID-19 testing, 14 of 99 patients with COVID-19 (14.1%) had PE versus 29 of 375 patients without COVID-19 (7.7%) (p = 0.04). PEs were located in the main pulmonary arteries in 11 patients (17%), lobar in

TABLE 1 Relationship of COVID-19 and Intubation to PE

	Positive CTPA
COVID-19 positive	20/170 (11.8)
Intubated	7/23 (30.4)
Not intubated	13/147 (8.8)
Within 1 day of COVID-19 test	14/99 (14.1)
COVID-19 negative	45/526 (8.6)
Intubated	6/33 (18.2)
Not intubated	39/493 (7.9)
Within 1 day of COVID-19 test	29/375 (7.7)

Values are n/N (%).
COVID-19 = coronavirus disease-2019; CTPA = computed tomography pulmonary angiography; PE = pulmonary embolism.

18 (28%), segmental in 26 (41%), and subsegmental in 9 (14%). There was no significant difference by COVID-19 status ($p = 0.08$).

The average D-dimer level for patients with COVID-19 was 2,616 ng/ml versus 2,354 ng/ml for patients without COVID-19 ($p = 0.12$). D-dimer was predictive of PE in both groups, with area under the receiver-operating characteristic curves of 0.825 (95% CI: 0.687 to 0.922) for patients with COVID-19 and 0.810 (95% CI: 0.727 to 0.875) for patients without COVID-19. Multivariable logistic regression analysis for diagnosis of PE showed that among age, sex, COVID-19 status, intubation, and D-dimer, the only significant variable was D-dimer (range odds ratio: 36.1; $p < 0.0001$).

Our results show that COVID-19 status did not predict PE, with the biggest risk factor being elevated D-dimer. We found substantially lower rates of PE in our COVID-19-positive cohort (12%) than those reported in other studies (22% to 30%) (1,2,4). This may be related to higher severity of disease in those studies. Indeed, in the subgroup of intubated patients in our study, the rate of PE was 30%, which is comparable to the 21% in a study focused exclusively on patients with COVID-19 who were in intensive care (3). Among our intubated patients, those with COVID-19 did have a higher rate of PE than those without COVID-19, but this did not reach statistical significance. However, the number of intubated patients in our study was quite low, limiting our statistical power. It is possible that the prothrombotic state reported in patients with COVID-19 is associated with greater severity of disease, leading to the sickest patients having higher rates of PE. Of note, patients with severe pandemic H1N1 influenza were also shown to have an increased rate of PE (5).

We did find a greater risk of PE within 1 day of COVID-19 testing. It may be that patients with COVID-19 are given more prophylactic anticoagulation than non-COVID-19 cases are, leading to a lower risk of PE later in their disease course. Alternatively, it is possible that the small numbers of patients with CTPAs later in the disease course precluded detection of a difference at later time points.

This study has several limitations, most notably that it is retrospective. The population was selected for patients who underwent CTPAs, which itself introduces bias. However, we do note that our PE rates are lower those in other reports, suggesting that our study is likely less biased than some others. Finally, we did not record use of anticoagulation, which would affect the risk of developing thromboembolism. However, the practice guidelines in our hospital system recommend routine prophylactic anticoagulation for all inpatients with COVID-19.

In summary, we found that the risk of PE was much lower than previously reported in patients with COVID-19, although there was an increased risk of PE around the time of polymerase chain reaction test positivity. There is mounting evidence of a prothrombotic state in patients with COVID-19. However, it remains to be elucidated whether COVID-19 produces a unique prothrombotic pathophysiology or simply drives thrombosis through severe inflammation.

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