Increased Pulmonary Embolism Incidence and Mortality in Patients Subsequently Diagnosed with COVID-19: An Analysis of Health Insurance Claims Data

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There are increasing data prompting that SARS-CoV-2 infection and the COVID-19 pandemic are directly or indirectly associated with acute thromboembolic events. While the incidence of acutely ischaemic limb events in heterogeneous cohorts varied widely in the available literature, multiple studies have revealed that deep vein thrombosis (DVT) and pulmonary embolism (PE) occur more often in patients suffering from COVID-19.

In a prospective cohort study of the first 80 deaths with ante- or post-mortem polymerase chain reaction (PCR) confirmed SARS-CoV-2 infection in Hamburg, Germany, no evidence of arterial thrombosis was apparent, but DVT and PE were found in 40% and 21% of the cases, respectively. Systematic reviews and meta-analyses including up to 65 000 patients noted venous thromboembolism in 21% of the patients. Hence, to date, interdisciplinary consensus documents recommend prophylactic heparin to prevent venous thromboembolism in hospitalised patients. In previous studies, the present authors reported declining admission rates for major cardiovascular emergencies as well as increased mortality in patients with confirmed SARS-CoV-2 infection. However, these two studies did not specifically include patients admitted to hospitals with either DVT or PE. The current study aimed to determine whether the hospital admission rate with venous thromboembolism increased during the COVID-19 pandemic and how SARS-CoV-2 infection interacts with these conditions.

Data from Germany’s second largest insurance fund, BARMER, were used, including medical care provided to approximately 13.2% of Germany’s population (9.14 million between 2017 and 2020). The BARMER cohort has been used widely for health service research and contains reliable inpatient diagnoses with regular sample validation of internal and external validity. For the current retrospective observational study, patients were included with an index hospital stay for PE or DVT between 1 January 2017 and 31 March 2021. Besides date of primary diagnosis (by month and year), data were collected on patients’ age (in years), dichotomised sex, any confirmed SARS-CoV-2 infection, and inpatient death. The hospital incidence of DVT or PE was calculated as a ratio of admitted persons and the entire insured population in a defined period. To address seasonal effects, the corresponding periods were compared: March through June 2017 — 2019 (pre-COVID-19) vs. March 2020 through June 2020 (first wave), and October through March 2017 — 2019 (pre-COVID-19) vs. October 2020 through March 2021 (second wave). Parametric confidence intervals (CI) for the change in hospital incidence were computed assuming Poisson distributed counts. Relative risks and attributable fractions were calculated to quantify the increase in PE associated with the COVID-19 pandemic.

In total, 63 874 eligible patients (59.6% women, mean age 70.1 years) with 25 374 patients treated primarily for DVT and 38 500 treated primarily for PE were included. During the first and second waves, a total of 1 781 (2.8%, 95% CI 2.7 — 2.9%) confirmed SARS-CoV-2 infections were reported among eligible patients (67 666 SARS-CoV-2 infected during the study period among all hospitalised patients in the entire insured BARMER cohort) (Fig. 1).

During the first and second pandemic waves, the number of patients admitted with DVT decreased by $-13.6\%$ (95% CI $-17.5\%$ — $-9.6\%$, $p < .001$) and $-6.4\%$ (95% CI $-9.7\%$ — $-2.9\%$, $p < .001$), respectively. There was no change in admission of patients with PE during the first wave ($+0.04\%$, 95% CI $-3.6\%$ — $3.8\%$) but an increase of $+14.7\%$ (95% CI $11.6\%$ — $17.9\%$, $p < .001$) during the second wave of the COVID-19 pandemic.

The hospital incidence of DVT per 100 000 persons ranged between values of 5.9 in April 2020 and 8.2 in January 2021. Over the whole period, 5% of all cases could be attributed to COVID-19. The hospital incidence of PE per 100 000 persons ranged between values of 9.9 in April 2020...
and 15.3 in January 2021. Over the whole period, 12% of all cases could be attributed to COVID-19.

The overall in hospital mortality in patients treated for DVT was 4.9% and thereby 2.99 times higher (95% CI 2.27 – 3.89, \( p < .001 \)) in patients with confirmed SARS-CoV-2 infection vs. those not infected (12.8% vs. 4.9%). In total, 12.8% of deaths could be attributed to the virus. The overall in hospital mortality in patients treated for PE was 14.1% and thereby 1.76 times higher (95% CI 1.57 – 1.97, \( p < .001 \)) in patients with confirmed SARS-CoV-2 infection vs. those not infected (22.8% vs. 12.9%). In total, 8.5% of deaths could be attributed to the virus.

The results of the current study confirm previous reports from observational studies and systematic reviews of the existing literature suggesting an association between SARS-CoV-2, DVT, and PE, while adding a large population based cohort from Germany. Furthermore, there is preliminary evidence for excess mortality in SARS-CoV-2 positive patients with PE. Unfortunately, the reasons for the observed differences between pandemic waves remain unknown. It appears possible that the healthcare use behaviour of the population changed during the pandemic, but also that a shift of the infected populations, for example caused by virus variants, contributed to the observed development. Although the current analysis of health insurance claims was limited to aggregated monthly based data and could neither address stage migration nor non-registration or non-presentation, these results together with the available literature suggest that further evidence is necessary to identify the underlying factors leading to higher rates of thromboembolic events and excess mortality in affected patients.

CONFLICT OF INTEREST AND FUNDING

None.

REFERENCES


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