



Review Article

Impact of COVID 19 on Hospitalization for Thromboembolic Diseases in Germany

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Abstract

Objectives: We compared hospitalization rates for thrombotic venous and arterial disease in 2020 and 2021 of the COVID-19 pandemic with the 3-year period from 2017 to 2019 before.

Patients and Methods: Lists of hospitalizations with principal diagnoses of Pulmonary Embolism (PE), Deep Vein (DVT), Sinus Vein (SVT) and Portal Vein Thrombosis (PVT), Budd-Chiari-Syndrome (BCS), Myocardial Infarction (MI), Embolic Stroke (ES), and acute Peripheral Embolism and Thrombosis (PET) were provided by the Federal Statistical Office in Germany.

Results: The number of hospitalizations was fairly constant before the COVID-19 pandemic for PE, PVT, BCS, MI, and ES; those for DVT and PET were trending downward; and those for SVT were trending upward. In 2020, absolute number of all hospitalizations was 13.8% lower than the average from 2017 to 2019. Contrary to this trend, hospitalized cases for SVT, BCS, and ES were within the 95%-CI of the 3 years before COVID-19, and they were lower for PE, DVT, PVT, MI, and PET. In 2021, absolute number of all hospitalizations was 14.6% lower. Contrary to this trend, the absolute number of hospitalizations for PE, SVT, and ES was above the upper limit of the 95%-CI of the 3 years before COVID-19.

The increase in PE in 2021 occurred in the 50- to 80-year age groups, and the decrease in MI and PET in the 70- and 85-year age groups. The increase in SVT affected all age groups.

Conclusion: The analysis shows that the COVID-19 pandemic does not affect all venous and arterial diseases equally.

Keywords: Pulmonary Embolism; Deep Vein Thrombosis; Sinus Vein Thrombosis; Portal Vein Thrombosis; Budd-Chiari-Syndrome; Myocardial Infarction; Embolic Stroke; Young Females

Introduction

At the beginning of 2020, SARS-CoV-2 caused a worldwide pandemic called COVID-19 [1]. A hypercoagulable state caused by COVID-19 leading to activation of coagulation cascade and Pulmonary Embolism (PE) has been described as important course of patients. In 2020 first groups reported an overall 24% (95% CI 17–32%) cumulative incidence of PE

patients with COVID-19 pneumonia, 50% (30–70%) in ICU and 18% (12–27%) in other patients [2]. Limited data suggest a high incidence of deep vein thrombosis (DVT) and PE in up to 40% of patients [3]. Prophylactic LMWH has been recommended by the International Society on Thrombosis and Haemostasis (ISTH) [4] and the American Society of Hematology (ASH) [5], but the best effective dosage is uncertain. In 2021, after introduction of specific vaccines an increase of cerebral vein/venous sinus thrombosis with thrombocytopenia syndrome after COVID-19 vaccination was reported [6–8]. Early studies have also linked coronavirus disease 2019 (COVID-19) infection with an increased risk of

ischemic stroke and acute myocardial infarction (MI) [9]. Others have reported that admissions for MI were significantly reduced during the COVID-19 pandemic, with a parallel increase in fatality and complication rates [10-12]. Numbers of hospital admissions of PAD patients were also reduced [13].

All these aspects have been described but an overview of the size of these effects on numbers of hospitalization in one specific country has not been published. Based on the German DRG-Statistic, we tried to describe the impact of COVID-19 on hospitalization rates for venous (PE, DVT, SVT, portal vein thrombosis (PVT) and Budd-Chiari-Syndrome (BCS) and arterial (MI, embolic stroke (ES) and acute peripheral embolism and thrombosis (PET)) diseases in years 2020 and 2021.

Patients and methods

The national statistics (DRG statistics) published by the Federal Statistical Office includes data from all hospitals in Germany that use the DRG system which covers more than 99%. These hospitals are legally obliged to provide extensive data on hospital treatment, including demographic data, diagnoses, comorbidities, complications, and procedures to the “Institute for the Hospital Remuneration System” (InEK), which uses the data for a yearly adaptation of the German DRG system and transmits them to the Federal Statistical Office. Since 2005 all diagnoses were coded with the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), which was adapted for Germany by the German Institute for Medical Documentation and Information (DIMDI) as ICD-10 German Modification (ICD-10-GM) in the corresponding annual version.

Compliance with Ethical Standards

This article does not contain any studies with human participants or animals performed by any of the authors. According to the occupational regulations for the North Rhine-Westphalian physicians retrospective epidemiological research projects are specifically excluded from the necessity of an ethics vote. Specific linking of cases and procedures is possible but not allowed for legal reasons.

This study does not involve human participants or animal subjects. Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research

Statistics

For the years 2017 - 2021 detailed lists of all PEs (ICD-code I26.0 + I26.9), DVTs (I80.0 – I80.9), SVTs (I67.6), PVTs (I81), BCSs (I82.0), MIs (I21.0 – I21.9), ESs (I63.1 + I63.4) and PETs (I74.2- I 74.4) documented as principal diagnosis separated in 5 years age groups were provided by the Federal Statistical Office. Calculations were done using Microsoft® Excel 2003 and Microsoft® Access 2003. As the analysis is just descriptive no statistical estimations were done.

Results

Table 1 shows the absolute number of cases with the principal diagnosis of the eight considered diseases. One can see that the number of hospitalized cases were rather constant for PE, PVT, BCS, MI and ES before COVID-19 pandemic in the years 2017 to 2019. Number of cases hospitalized for DVT and PET tend to decrease and that for SVT tend to increase already in this period.

ICD 10	2017	2018	2019	2020	2021
	Absolute number	Absolute number	Absolute number	Absolute number [estimated number]	Absolute number [estimated number]
	Mean value (95% CI)				
All hospitalizations	16,618,686	16,466,455	16,556,599	14,261,975 [16,230,128]	14,135,134 [16184728]
	16,547,247 (16,460,629 / 16,633,864)				
Venous					
Pulmonary embolism I 26.0 - I 26.9	56,727	57,070	56,651	56,076 [63,814]	61,592 [70,523]
	56,816 (56,564 / 57,068)				
Deep and superficial vein thrombosis I 80.0 – I 80.9	33,141	30,674	27,330	21,523 [24,493]	20,985 [24028]
	30381 (27082 / 33681)				

Sinus vein thrombosis I 67.6	749	812	839	836 [951]	1,180 [1,351]
	800 (748 / 852)				
Portal vein thrombosis I 81	1,277	1,379	1,303	1,228 [1,397]	1,338 [1,532]
	1,320 (1,260 / 1,380)				
Budd Chiari Syndrome I 82.0	143	126	142	128 [145]	120 [137]
	137 (126 / 148)				
Arterial					
Myocardial infarction I 21.0 - I 21.9	217,367	211,983	212,340	197,944 [225,260]	195,836 [224,232]
	213,897 (210,491 / 217,303)				
Embolic stroke I 63.1+ I 63.4	100,717	101,846	102,639	100,703 [114,600]	103,028 [117,967]
	101,734 (100,642 / 102,826)				
Arterial embolism or thrombosis I 74.2- I 74.4	16,112	15,757	15,110	13,615 [15,494]	13,469 [15,422]
	15,660 (15,085 / 16,235)				

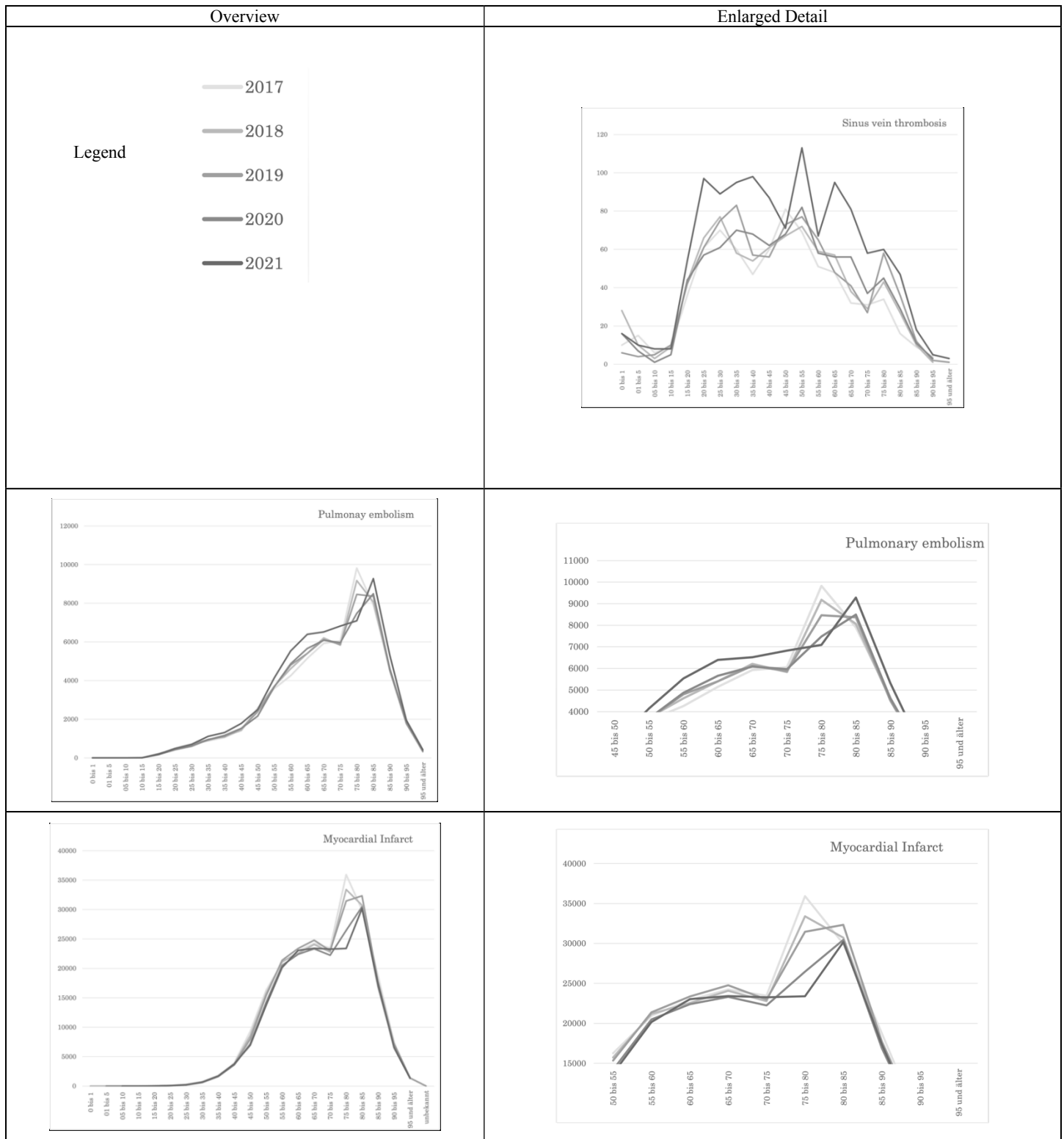
Table 1: Listed are the absolute numbers of all hospitalized cases and individual cases with the principal diagnosis of the eight diseases considered in the five years. For the three years 2017, 2018, and 2019 before the COVID-19 pandemic, we calculated the mean and 95% confidence interval (CI). For 2020 and 2021, we estimated the theoretical number of hospitalizations (in parentheses) from previous years that would have occurred in the absence of the COVID-19 pandemic by adjusting it by the percentage of the difference between that year and the mean of the three previous years.

In 2020, the first year of COVID-19 pandemic, the absolute number of all hospitalizations were 13.8% lower than mean of the years 2017 to 2019. Against this trend, hospitalized cases for SVT, PVT, BCS and ES were within the 95%-CI of the three years before COVID-19 pandemic. For PE, DVT, MI and PET it were lower. After correction by the 13.8% decrease in total number of hospitalizations, the hospitalization rates were higher than the 95%-CI for PE, SVT, PTV, MI and ES.

In 2021, the second year of COVID-19 pandemic, the absolute number of all hospitalizations were 14.6% lower than mean of the years 2017 to 2019. Against this trend, already absolute number of hospitalized cases for PE, SVT and ES were

higher than the upper limit of the 95%-CI of the three years before COVID-19. After correction by the 14.6% decrease in total number of hospitalizations, the hospitalization rates for MI were higher than the upper limit of 95%-CI.

Figure 1 shows the age distribution for some diseases over time. The increase in PE in 2021 is due to an increase in PE in the age groups from 50 to 80 years. The age group of 80 to 90 years, which is the most affected in 2017 to 2019, shows no increase. The increase in SVT spans all age groups, as is common with SVT. In contrast, the decrease in MI and PET hospitalization rates in 2020 and 2021 is primarily caused by a decrease in the age groups between 70 and 85 years.



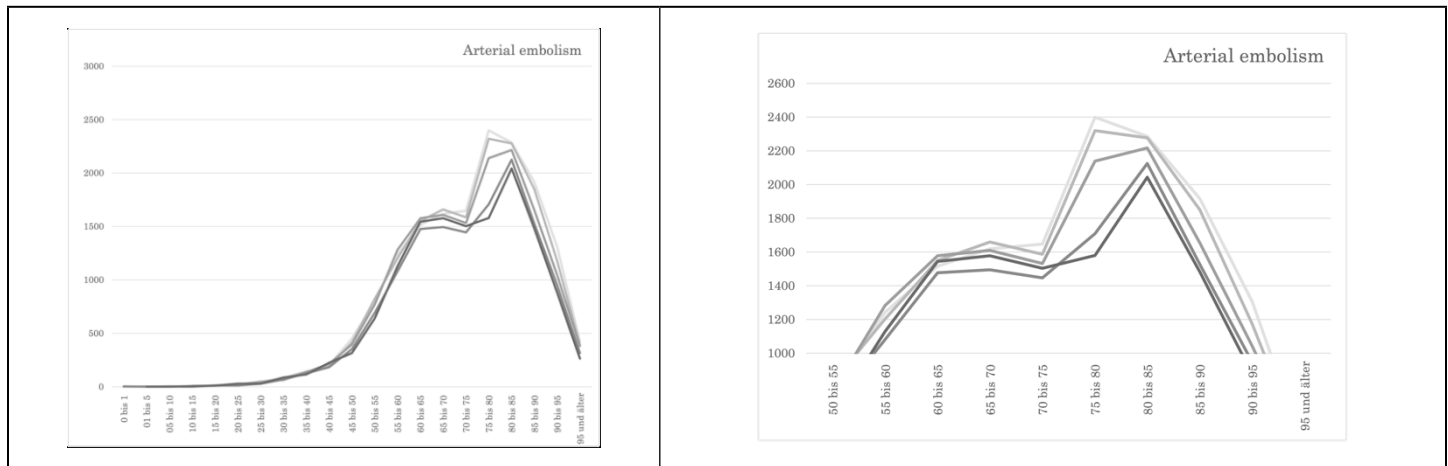


Figure 1: The graphs show the age distribution of hospitalized cases with PE, SVT, MI and PET in the years 2017 to 2021. On the left side all age groups are shown and on the right side the age groups with obvious changes are enlarged.

Discussion

The presented analysis based on the German DRG statistics shows that COVID-19 pandemic had different effects on venous and arterial diseases in 2020 and 2021 and did not impacted all diseases and all age groups in the same way.

Although primarily affecting the lungs, the SARS-CoV-2 virus also affects the cardiovascular system, both directly by the SARS-CoV-2 virus, and indirectly as a result of a systemic inflammatory cytokine storm. This includes the role of the vascular endothelium in the recruitment of inflammatory leucocytes where they contribute to tissue damage and cytokine release, which are key drivers of acute respiratory distress syndrome (ARDS), in disseminated intravascular coagulation, and cardiovascular complications in COVID-19 [14]. In addition, vaccine-induced thrombotic complications associated with the use of adenoviral vector vaccines ChAdOx1 nCoV-19 by AstraZeneca, and Ad26.COV2.S by Johnson & Johnson/Janssen, were announced shortly after the initiation of a global vaccination program. In these cases, the occurrence of thrombotic events at unusual sites-predominantly located in the venous vascular system-in association with concomitant thrombocytopenia were observed [15].

We present a unique analysis of the impact of the COVID-19 pandemic on hospitalization rates for various venous and arterial diseases during the first two years of the pandemic. Several effects must be considered when interpreting these figures:

- The number of people affected by COVID-19 in 2021 was 7.2 million, significantly higher than the 1.8 million in 2020. Therefore, the absolute hospitalization rates of COVID-19 associated diseases is expected to be greater in 2021 (<https://experience.arcgis.com>).

- The need for hospitalization depends on the severity of the condition, with less severe conditions expected to play a larger role in the overall decline in hospitalization rates in 2020 and 2021 than severe conditions such as PE, MI, or ES. Therefore, a simple estimate of theoretically hospitalized patients by adding 13.8% and 14.6%, respectively, may overstate these numbers.

- The public media have reported certain diseases with different intensity (PE in 2020 and SVT in 2021). This may have led to a change in awareness of these diseases among both the public and physicians, resulting in more frequent diagnosis of these diseases.

- In 2021, vaccination was offered for the first time. Therefore, vaccine-induced effects might not affect hospitalization rates until 2021.

- Certain age groups were vaccinated in different order and intensity. This could have an effect on hospitalization rates of different age groups.

MI, ES, and PET are serious diseases because they are life-threatening and carry a high risk of disability and amputation. With this in mind, it is striking that hospitalization rates decreased in 2020 and 2021 only for MI and PET but not for ES. One explanation for this could be that although ES is an arterial occlusion, the origin of the embolism could be venous. Similar to ES, despite a decrease in the total number of hospitalizations, the number of hospitalizations for PE and SVT remained unchanged in 2020 and actually increased disproportionately in 2021 for these three conditions. Although COVID-19 affected many more people in 2021, no such increase was seen for the arterial diseases MI and PET in 2021. Thus, the increase in hospitalization rates for PE, SVT, and ES in 2021 could be in part related to higher number of

COVID-19 infections as well to introduction of vaccination. On the other hand, the higher number of COVID-19 infections and the introduction of vaccination had no effect on hospitalization for MI, PET, PTV and BCS, obviously.

Another unexpected finding is that changes in hospitalization rates were dominated by changes in specific age groups. This is particularly evident in MI and PET, where the decrease in hospitalizations concentrated in cases aged 70 to 85 years, whereas in PE and SVT younger age groups contribute to the increase in hospitalizations. This has not been previously described in the literature, and it is unclear what proportion of these age effects are due to COVID-19 disease itself and what proportion are due to isolation strategies and vaccination campaigns.

Strength and Limitations

A major strength of this study is the large data set which includes virtually all German hospitals. This allows a unique view on the impact of COVID-19 on hospitalization rates. Moreover, to the best of our knowledge, there is currently no other publication addressing this topic from a population based viewpoint in Germany.

There are factors that limit our results. First, our ecologic study design did not allow control for confounding risk factors including obesity or life style or other infectious diseases. Second, the primary diagnosis is on the physician's own authority and strongly affects the reimbursement in the German DRG system. We do not have any information about coding quality. Third, it should be pointed out that the analysis is based on cases and not on individual patients. As a consequence, a patient may be included several times in the statistics if he had recurrent events at different times within one year. Fourth, we cannot demonstrate the effect of specific vaccines, since we lack the necessary information. Fifth, comparison of the presented data with other studies has to consider differences in study populations as well as the uncertainty about the diagnosis included.

In summary, our ecological nationwide analysis of hospitalization rates is only descriptive but provides an interesting insight into the global impact of the COVID-19 pandemic on various venous and arterial diseases in 2020 and 2021. It remains unclear why different venous and arterial diseases and specific age groups were affected in different ways. Further specific analyses are needed to clarify this.

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Conflict of interest

The authors declare that they do not have any conflict of interest

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