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Clinical outcomes and characteristics of patients hospitalized for Influenza or COVID-19 in Germany

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ABSTRACT

Objectives: Since the beginning of the severe acute respiratory syndrome coronavirus 2 pandemic, there is a discussion about the severity of coronavirus disease-2019 (COVID-19) in comparison to infections with seasonal Influenza. The objective of this study was to compare clinical and demographic characteristics of German patients hospitalized for infection with either SARS-CoV-2 or Influenza.
Methods: This study used anonymized German healthcare claims data. Patients with a confirmed COVID-19 or Influenza diagnosis, for whom a complete hospital course was available (i.e., the patient was discharged or died in hospital) were included. The data set included detailed information on patient characteristics and hospital treatment. Patients were grouped according to whether they were transferred to the intensive care unit (ICU), received mechanical ventilation (MV), or had a severe course of the disease (SD). Charlson Comorbidity Index in the eight quarters prior to hospitalization and secondary diagnoses during hospitalization were analyzed.
Results: A total of 2343 hospitalized patients with COVID-19 and 6762 hospitalized patients with Influenza were included. Fifty-four percent of the patients were male patients, with men being twice as frequent in the COVID-19 severe groups. For both diseases, patients >49 years accounted for almost three-quarters of hospital cases and hypertension, diabetes mellitus, chronic kidney disease, and chronic obstructive pulmonary disease were the most common comorbidities. The proportion of cases with ICU, MV, and SD was substantially higher for patients with COVID-19 (ICU+: 21 vs. 13 %; MV+: 15 vs. 9%; and SD +: 28 vs. 16%). Overall inhospital mortality was more than two-fold higher in COVID-19 vs. Influenza (14 vs. 6%).). The length of ventilation and hospitalization, and the proportion of patients diagnosed with acute respiratory distress syndrome, systemic inflammatory response syndrome, or acute kidney injury were considerably higher in patients with COVID-19.
Conclusions: COVID-19 resulted in higher inhospital mortality and worse clinical outcomes than Influenza. This was not attributable to demographic characteristics, preexisting comorbidities, or patient triage, because the German healthcare system had not reached its limits in the pandemic. Discussions suggesting that COVID-19 and seasonal Influenza have similar severity cannot be based on clinical evidence.

Background

Since the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, the novel respiratory disease coronavirus disease-2019 (COVID-19) has been compared with seasonal Influenza. The equating of COVID-19 with another pandemic respiratory disease with similarities in symptoms, transmission, and risk groups is obvious at first, but it tempts to underestimate the impact of the current pandemic situation and to minimize COVID-19-related outcomes. Potentially, SARS-CoV-2 appears to cause higher morbidity and mortality rates than seasonal Influenza, also due to a lack of basic immunity in the population and lack of vaccination and medication (Petersen et al., 2020; RKI, 2020a, 2020b). However, limited information is available regarding patient' characteristics and relevant outcomes of cases that require hospitalization in Germany (Böhmer et al., 2020; Karagiannidis et al., 2020; RKI, 2020a). Based on statutory health insurance (SHI) claims data, the present study compares

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unselected hospitalized patients and describes demographic characteristics as well as relevant clinical parameters such as mechanical ventilation, intensive care, and severe course of the disease in detail. Anonymized claims data of the InGef research database (FDB) provide a basis for a comparison of severe courses of hospitalized patients with Influenza in recent years in relation to the ongoing COVID-19 pandemic. The focus on hospitalized cases allows an objective evaluation, particularly of critically ill patients. We sought to generate evidence on the clinical burden of COVID-19 in an appropriately resourced health care system and to contribute to a data-based discussion and assessment of the newly emerged infectious disease. Furthermore, the description of factors associated with a severe outcome can help identify patients who may particularly benefit from future vaccines and therapies.

Methods

This observational study was based on claims data of the SHI of the FDB. The FDB contains data on health care resource utilization and the consumption of approximately 9 million anonymized insured persons between 2015 and 2020 from about 60 company and guild health insurance funds. The anonymization of the FDB ensures that individual patients, health insurance companies, and service providers can no longer be identified. A separate approval of an institutional review board or medical ethics committee was thus not required.

In accordance with the obligations of the German health system, all medical diagnoses as well as operations and procedures are documented for billing purposes. Medical diagnoses are documented in the underlying SHI claims data according to the International Classification of Diseases and Related Health Problems (10th Revision, German Modification, ICD-10-GM) (Deutsches Institut für Medizinische Dokumentation und Informatik, 2020a). The classification of operations and procedures was based on the Operation and Procedure Code (OPS) (Deutsches Institut für Medizinische Dokumentation und Informatik, 2020b). The analyzed dataset contains detailed information on demographic (age and sex as of Jan 01 of the respective year of hospital case) and clinical (OPS, discharge type, length of hospitalization, and diagnoses) patient characteristics.

For the COVID-19 analyses, we included only patients with a confirmed SARS-CoV-2 infection (main or secondary discharge diagnosis code ICD-10-GM U07.1) who were admitted to a hospital between Feb 17, 2020 and July 21, 2020. For the Influenza analysis, only patients with a confirmed infection by Influenza viruses (main or secondary diagnosis code ICD-10-GM J10) who were admitted to hospital during the Influenza seasons in the years 2017–2019 (2017 CW 40–52; 2018 CW 1–20 and 40–52; 2019 CW 1–20 and 40–52) were eligible for inclusion. Furthermore, only patients for whom the complete hospital course was available (i.e., patients were discharged or died in hospital during the study period) were selected. Subsequent hospitalizations where the patient was re-admitted on the day of discharge or the following day, were combined into one case. For patients with Influenza, in case of more than one hospitalization within the observed Influenza seasons, only the first hospitalization was analyzed. To determine baseline characteristics uniformly, only patients who were continuously insured, and therefore fully observable in the eight quarters prior to hospitalization were considered.

Based on documented ICD, OPS, and treating departments within the inpatient treatment case, cases with and without intensive care treatment (ICU+ / ICU-), cases with and without mechanical ventilation (MV+/MV-), and cases with and without severe course of the disease (SD +/ SD-) were identified. Supplement B describes the criteria used to define the subgroups (Supplement B-1) and the variables of interest (Supplement B-2) in detail. The degrees of severity are not mutually exclusive, i.e., patients can be included in more than one severity subgroup.

For each patient case, baseline characteristics, and Charlson-Comorbidity-Index (Charlson et al., 1987) were assessed based on at least one verified ambulatory diagnoses and main or secondary inpatient diagnoses as defined by ICD10-GM codes during the 8 quarters prior to hospitalization.

Based on the documented secondary diagnoses in each case, we analyzed the most frequent comorbidities and complications that occurred during the hospital stay. Further endpoints considered were case fatality rate (as inhospital death), age at death, length of hospital stay in days and length of ventilation in hours. Definitions and codes of all variables can be found in Supplement B-2

As indicators for categorical variables absolute and relative frequencies (%) and for continuous variables the median and the first and third quartiles (Q1-Q3) are reported. For data protection reasons, no measures are reported for strata with less than five patients.

Results

A total of 2343 COVID-19 cases and 6762 cases of Influenza were included in the analyses. For COVID-19, we analyzed cases from Feb 17, 2020 to July 21, 2020. For Influenza, we assessed cases from the three previous Influenza seasons (2017–2019) to gauge an average of disease severity. Baseline characteristics are presented in Table 1 and supplemental Table S1.

The median age at admission was 62 years (Q1-Q3: 48−78 years) for patients with a COVID-19 diagnosis and 68 years (Q1-Q3: 50−79 years) for patients with Influenza. Patients with COVID-19 who were ventilated or received intensive care treatment were on average 10 years older than patients with a less severe course of the disease. The differences in age for the subgroups of patients with Influenza were modest. For both infectious diseases, patients older than 49 years accounted for almost three-quarters of the hospital cases considered (73.1%, n = 1717 COVID-19 vs. 75%, and n = 5102 Influenza.). Likewise, about 54% of the patients were male (Table 1). However, for COVID-19, men were twice as likely to be in the ICU+, MV+, and SD + groups as women.

Comorbidities

For both infectious diseases hypertension, diabetes mellitus, chronic kidney disease (CKD), heart failure, and chronic obstructive pulmonary disease (COPD) are the most common comorbidities. Underlying comorbidities were slightly more frequent in patients with Influenza than in patients with COVID-19. Overall, 70% and 76% of ICU + cases, 74% and 75% of MV + cases, and 75% and 78% of SD + cases for COVID-19 and Influenza, respectively, had a documented diagnosis of hypertension in the baseline period. Heart failure and CKD occurred in one quarter of patients with Influenza and one fifth of patients with COVID-19. The differences in morbidity can be observed across all age groups (see supplemental Table S2). Overall, differences in the median Charlson Comorbidity Index for the respective total population were modest (Influenza: 2.7 Q1-Q3: 0−4 and COVID-19: 2.2 Q1-Q3: 0−4). The prevalence of the investigated relevant comorbidities was substantially higher in the ICU+, MV+, and SD + subgroups than that in ICU-, MV-, and SD- cases in patients with either COVID-19 or Influenza (see Table 1 and Supplemental table S1). Diabetes mellitus occurred in 37% of the patients with COVID-19 with severe course, while the proportion of the disease was between 19% and 22% in the groups without a severe disease progression (SD+) (see Table 1). In general, our data show a high morbidity in older

Table 1
Demographic and clinical characteristics of patients with COVID-19 and Influenza.

	COVID-19				Influenza			
Variable	Total	ICU+	MV+	SD+	Total	ICU+	MV+	SD+
% of total (N)	100 (2343)	21 (487)	15 (362)	28 (656)	100 (6762)	13 (881)	9 (610)	16 (1107)
Age in years, median (Q1-Q3)	62 (48–78)	69 (58–78)	69 (61–78)	73 (61–82)	68 (50–79)	68 (59–78)	68 59–78)	72 (61–81)
< 10, % (n)	1 (22)	<1 (<5)	0 (0)	<1 (<5)	9 (639)	2 (14)	2 (12)	1 (14)
10–19, % (n)	2 (38)	<1 (<5)	<1 (<5)	<1 (<5)	4 (250)	1 (12)	1 (5)	1 (12)
20–49, % (n)	24 (566)	8 (37)	6 (21)	6 (38)	11 (771)	8 (74)	7 (45)	7 (76)
50–69, % (n)	34 (807)	44 (216)	44 (161)	35 (231)	28 (1889)	41 (365)	44 (269)	36 (404)
70–89, % (n)	35 (820)	47 (227)	49 (177)	54 (352)	43 (2935)	45 (399)	44 (271)	50 (550)
≥ 90, % (n)	4 (90)	<1 (<5)	<1 (<5)	5 (32)	4 (278)	2 (17)	1 (8)	5 (51)
Female sex, % (n)	46 (1078)	32 (156)	26 (94)	34 (227)	47 (3165)	43 (378)	43 (261)	42 (469)
Frequent comorbidities								
Hypertension	57 (1347)	70 (343)	74 (269)	75 (489)	63 (4228)	76 (669)	75 (458)	78 (860)
Diabetes mellitus type 2	24 (566)	35 (172)	38 (138)	37 (244)	29 (1942)	39 (345)	41 (250)	40 (442)
Chronic kidney diases	19 (436)	23 (113)	26 (94)	31 (201)	24 (1598)	32 (286)	30 (183)	36 (393)
Heart failure	19 (439)	22 (107)	22 (80)	29 (193)	24 (1614)	34 (297)	34 (205)	37 (405)
Chronic obstructive pulmonary disease (COPD)	13 (306)	17 (85)	18 (66)	18 (120)	23 (1527)	35 (305)	40 (246)	33 (366)
Other diseases of the liver	14 (336)	19 (94)	20 (73)	19 (123)	14 (967)	16 (142)	17 (104)	16 (179)
Asthma bronchiale	12 (290)	13 (62)	13 (48)	12 (76)	15 (1018)	16 (139)	17 (101)	14 (155)
Atherosclerosis	12 (283)	16 (79)	16 (57)	19 (124)	15 (1044)	19 (169)	19 (117)	21 (228)
Chronic ischemic heart disease	7 (170)	8 (40)	8 (29)	11 (73)	9 (582)	11 (95)	11 (68)	11 (126)
Charlson Comorbidity Index, mean (Q1-Q3)	2.2 (0–4)	2.6 (0–4)	2.6 (1–4)	3.2 (1–5)	2.7 (0–4)	3.2 (1–5)	3.2 (1–5)	3.5 (1–5)

Baseline characteristics were determined in the 8 quarters prior to the respective analyzed hospitalization. Data are % (n), unless otherwise indicated. Data are not shown in cells that contain fewer than five patients. Abbreviations: ICU + cases in intensive care unit; MV + cases with mechanical ventilation; SD + cases with severe course of the disease; Q1-Q3: first and third quartiles; % Share in percent relative to N; and n number of cases with corresponding characteristics in the respective group.

patients with a considerably reduced burden of comorbidity in patients younger than 60 years (see supplemental Table S2).

Hospital treatment

In general, severe disease progression (SD+) was more frequent in patients with COVID-19 than in patients with Influenza (ICU+: 21 vs. 13 %; MV+: 15 vs. 9%; SD+: 28 vs. 16%) (see Table 1). This observation was more pronounced in the elderly (see Table 1). The proportion of patients with COVID-19 who were ventilated was 4% (21 of 566) of those aged 20–49 years, 20% (161 of 807) among those aged 50–69 years and 20% (178 of 910) of those aged 70 years and older. The proportion of MV for patients with Influenza was only partially age-dependent as 6% (45 of 771) of those aged 20–49 years, 14% (269 of 1889) of 50- to 69-year-olds, but 9% (279 of 3213) of those aged 70 years and older were mechanically ventilated.

For the total population, the median length of hospital stay was 8 days (COVID-19; Q1-Q3: 3–17; Influenza; and Q1-Q3: 4–14) (see Table 2). Patients with COVID-19 or Influenza who died during hospitalization were treated at a median of 11 and 12 days, respectively, (Q1-Q3: 6–21 days). COVID-19 and Influenza cases discharged after treatment were treated considerably longer than patients who died during hospitalization (see Figure 1a). This is particularly pronounced in patients with COVID-19 discharged after ventilation, who were treated for a median of 35 (discharged, Q1-Q3: 24–53) vs. 16.5 (death, Q1-Q3: 9–26) days in patients who died during the hospital stay. In the MV + group of patients with Influenza median length of hospital stay was 23.5 (Q1-Q3: 14–38) days in discharged patients vs. 14 (Q1-Q3: 8–26) days in deceased patients.

Mechanical ventilation

Almost two-thirds (73%, 268 of 362) of all ventilated patients were male, which resulted in a probability of being ventilated, which was 21% for men and 9% for women hospitalized with COVID-19. The probability of being ventilated was 10% and 8% for men and women hospitalized with Influenza, respectively.

We found substantial differences in the duration of mechanical ventilation. Patients with COVID-19 who required MV were ventilated in a median of 170 h (7 days) longer and thus more than twice as long as patients with Influenza (298 (Q1-Q3: 117–513) vs. 128 (Q1-Q3: 25–341) h). For surviving patients with COVID-19, the median duration of MV was 264 h (11 days) longer than that of non-deceased mechanically ventilated patients with Influenza (373 (Q1-Q3: 191–603) vs. 109 (Q1-Q3: 22–396) h) (see Figure 1b).

The use of extracorporeal membrane oxygenation (ECMO) was needed in 1% of total cases in both diseases (see Table 2). Whereas 9% and 7% of mechanically ventilated patients with COVID-19 and Influenza receive ECMO treatment, respectively.

Inhospital mortality

The median age at death in the total COVID-19 and Influenza population was 80 (COVID-19, Q1-Q3: 71–85) and 79 years (Influenza, Q1-Q3: 76–86), respectively. The inhospital mortality rate was considerably higher for the COVID-19 and the examined subgroups in COVID-19 disease than that of Influenza (see Table 2). Fourteen percent (n = 274) of the patients with COVID-19 died during hospital treatment, the proportion was significantly higher in the ICU+ (37%, n = 182), MV+ (47%, n = 170), and SD+ (52%, n = 338) groups (see Figure 2b and Table 2). A total of 6% (n = 412) of patients died during hospital treatment due to an Influenza infection, again the proportion was significantly higher in the ICU+ (27%, n = 236), MV+ (36%, n = 222), and SD+ (37%, n = 412) subgroups (Figure 2b-c). For COVID-19, 78% (265 of 338) of fatal cases were 70 years and older, while 70% (291 of 412) of patients who died of Influenza were older than 70 years. The mortality was 67% (237 out of 352 cases) in patients aged 70–89 years with a severe course of COVID-19 as compared to 45% (250 out of 550 cases) in the same age and subgroup in the influenza population (see Figure 2b-c). For both diseases, the percentage of male patients dying in the respective groups of severity was higher than that of females. This was particularly pronounced in the ICU + and MV + groups (see Table 2). While 41% of male patients with COVID-19 in the ICU + group died, only 30% of female patients in the same group died. Although at a lower level, figures were similar for Influenza with 31% (male patients) and 22% (female patients) dying in the ICU + group.

Table 2
Comparison of relevant outcomes and frequent secondary diagnoses for patients hospitalized with COVID-19 or Influenza.

	COVID-19				Influenza			
Variable	Total	ICU+	MV+	SD+	Total	ICU+	MV+	SD+
% of total (N)	100 (2343)	21 (487)	15 (362)	28 (656)	100 (6762)	13 (881)	9 (610)	16 (1107)
Deaths, % (n)[a]	**14 (338)**	**37 (182)**	**47 (170)**	**52 (338)**	**6 (412)**	**27 (236)**	**36 (222)**	**37 (412)**
Female, % (n)	11 (114)	30 (47)	41 (39)	50 (114)	5 (158)	22 (82)	29 (75)	34 (158)
Male, % (n)	18 (224)	41 (135)	49 (131)	52 (224)	7 (254)	31 (154)	42 (147)	40 (254)
Age at death, median (Q1-Q3:)	80 (71–85)	75 (66–82)	74 (65–81)	80 (71–85)	79 (67–86)	73 (63–81)	73 (63–81)	79 (67–86)
Age distribution of inhospital deaths, % (n)[b]								
20–49	<1 (<5)	<1 (<5)	<1 (<5)	<1 (<5)	3 (14)	6 (13)	5 (12)	13 (4)
50–69	20 (69)	32 (59)	35 (59)	20 (69)	25 (105)	36 (85)	36 (80)	25 (105)
70–89	70 (237)	64 (116)	62 (106)	70 (237)	61 (250)	54 (128)	54 (120)	61 (250)
>= 90	8 (28)	<1 (<5)	<1 (<5)	8 (28)	9 (38)	2 (5)	2 (5)	9 (38)
Length of stay in days, median (Q1-Q3)	**8 (3–17)**	**22 (12–36)**	**25 (14–41)**	**17 (9–31)**	**8 (4–14)**	**18 (11–32)**	195 **(12–34)**	**16 (9–30)**
Cases in which the patient died	11 (6–21)	16 (8–25)	165 (9–26)	11 (6–11)	12 (6–21)	14 (8–26)	14 (8–26)	12 (6–21)
Cases in which the patient was discharged	8 (2–16)	26 (15–43)	35 (24–53)	255 (14–43)	7 (4–13)	19 (12–33)	235 (14–38)	19 (12–33)
Length of ventilation in hours, median (Q1-Q3)	–	–	2975 **(117–512)**	–	–	–	**128 (25-341)**	–
Cases in which the patient died	–	–	245 (88–434)	–	–	–	1405 (40–302)	–
Cases in which the patient was discharged	–	–	373 (190–603)	–	–	–	1085 (22–395)	–
Extracorporeal membrane oxygenation (ECMO)	1 (33)	7 (32)	9 (32)	5 (33)	1 (44)	5 (44)	7 (43)	4 (44)
Frequent secondary diagnoses								
Acute kidney failure	13 (308)	46 (222)	58 (209)	39 (255)	9 (598)	35 (311)	41 (248)	33 (362)
Shock	5 (125)	24 (118)	31 (112)	19 (124)	3 (187)	20 (176)	25 (155)	16 (181)
Systemic inflammatory response syndrome (SIRS)	9 (206)	35 (172)	45 (164)	29 (189)	5 (314)	27 (234)	33 (200)	24 (271)
Acute respiratory distress syndrome (ARDS)	9 (204)	40 (197)	54 (196)	30 (199)	1 (88)	10 (88)	14 (86)	8 (88)

Data are % (n), unless otherwise indicated. Data are not shown in cells that contain fewer than five patients. Abbreviations: ICU + cases in intensive care unit; MV + cases with mechanical ventilation; SD + cases with severe course of the disease; Q1-Q3: first and third quartiles; % Share in percent relative to N; and n number of cases with corresponding characteristics in the respective group.

[a] Share in percent relative to the respective total female and male population per subgroup. N of female sex is found in Table 1.

[b] Share in percent relative to the total N of deaths per subgroup.

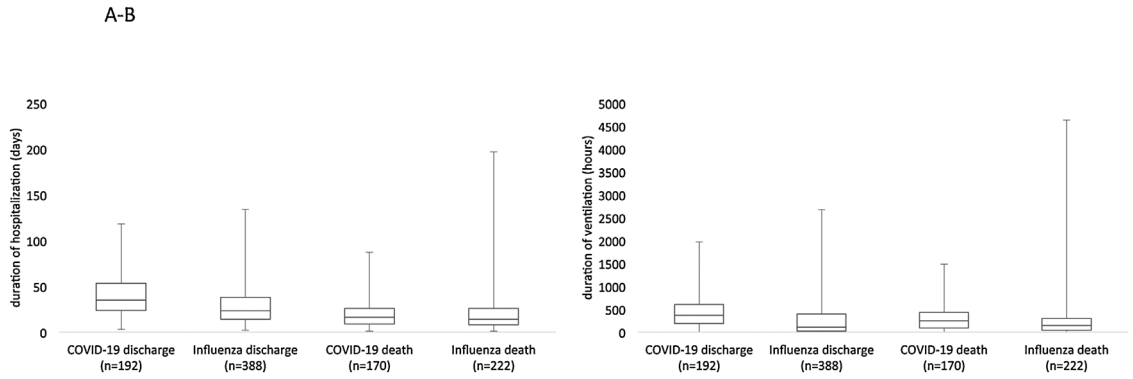

Figure 1. Duration of hospitalization (A) and mechanical ventilation (B). Duration of hospitalization (in days) by the severity group, surviving-status, and viral disease. Box plots show median and IQRs. (B) Duration of ventilation (in hours) by surviving status and viral disease. Box plots show median and IQRs.

Complications during hospitalization

Differences between patients with COVID-19 and influenza were also observed regarding complications during the hospitalization. Acute renal failure occurred in 13% (n = 308) of the considered COVID-19 cases and in 9% (n = 598) of Influenza cases (see Table 2). The proportion of affected patients was significantly higher in ICU+, MV+, and SD + cases. In the group of MV + COVID-19 cases, acute renal failure occurred in 58% (n = 209) of the patients. Most patients with a complication during the hospital treatment were ICU+, MV+, and SD + cases. Shock events occurred in 5% of patients with SARS-CoV-2 infection and 3% with Influenza, increasing to 31% (n = 112) and 25% (n = 155) of ventilated patients, respectively. Notably, 54% (n = 196) of ventilated patients with COVID-19 experienced acute respiratory distress syndrome (ARDS) as compared to 14% (n = 86) in patients with Influenza. Percentages of cases with systemic inflammatory response syndrome (SIRS) were similarly increased in ventilated COVID-19 cases (45% vs. 33%) (see Table 2).

Discussion

The presented study is among the first to objectively assess the severity of COVID-19 by comparing it to Influenza, a similar severe respiratory disease with regular seasonal or pandemic outbreaks. The epidemiological evidence obtained in this study is largely consistent with previous publications on COVID-19 (Buda et al., 2018; Karagiannidis et al., 2020; Potere et al., 2020; Richardson et al., 2020; RKI, 2020a). This particularly concerns the proportion of severe courses, the presence of comorbidities, and mortality rates. It is more challenging to compare the results of this large cohort with smaller case studies or single-centered clinical trials. Those are often biased in that they refer to data from hospitals with specialized ICU or ventilation units or hospitals located in overburdened health care systems (Arentz et al., 2020; Dreher et al., 2020; Guan et al., 2020; Rieg et al., 2020). We assume that our case mix based on claims data could roughly correspond to the total composition of hospitalized COVID-19 cases in Germany. To obtain reliable estimates for Influenza, we compare averaged data of the Influenza seasons 2017–2019, of which season 2017/2018

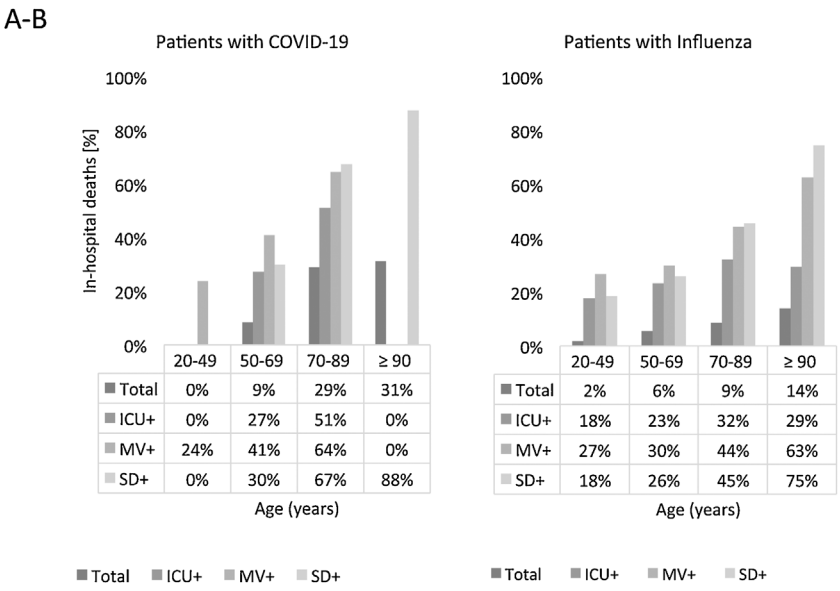

Figure 2. Inhospital death. Inhospital death by the group of severity and by age for patients with COVID-19 (B) Inhospital death by the group of severity and by age for patients with Influenza.

was particularly severe. In addition to a focus on severe cases, we distinguish between ventilated cases and cases referred to ICU. Reporting on patients' baseline characteristics in addition to outcomes and complications during the investigated hospitalization case enables a more detailed picture on groups at risk and patients who would most likely benefit from a vaccination or specific treatment.

In our study, more than two-thirds of patients hospitalized for COVID-19 or Influenza were older than 49 years. A severe course occurred in one-third of COVID-19 cases, but only in one-sixth of patients with Influenza. For both infectious diseases, the risk of intensive care (ICU+), mechanical ventilation (MV+), SD+, and inhospital death increased with age but was overall higher in COVID-19 cases. In general, patients with COVID-19 with a SD + were younger than the corresponding patients with Influenza. This finding and the strong age-dependency of severe outcomes are supported by numerous publications (Buda et al., 2018; Levin et al., 2020; RKI, 2020a; Wang et al., 2020). Interestingly, a slightly larger proportion of patients with Influenza have underlying comorbidities such as hypertension, diabetes, or COPD. In previous studies, these factors have been associated with a complicated course of Influenza infection (Lina et al., 2020; Schanzer et al., 2008; Segaloff et al., 2018). In accordance, the reported comorbidities are similarly frequent in patients with COVID-19 with severe disease progression, increase with advanced age, and might be associated with a poor outcome (Aggarwal et al., 2020; Brück, 2020; Richardson et al., 2020; Zhou et al., 2020). In fact, up to 75% of severe COVID-19 cases were previously diagnosed with hypertension and 40% with diabetes mellitus. However, the Charlson-Comorbidity Index was greater than two in both patients with COVID-19 and Influenza, which indicates that a majority of hospitalized patients were already at risk for a complicated progression.

The clinical course of COVID-19 and Influenza varies widely, ranging from asymptomatic and mild courses to severe progression with multiple organ failure and death (Guan et al., 2020; RKI, 2020c). Generally, the frequency of severe Influenza cases and the appropriate individual risk factors were shown to depend on the predominant viral strain, being higher under Influenza A(H3N2) viruses, which could not be further considered in our study (Shapshak et al., 2011). Moreover, ARDS, bacterial superinfection and septic shock, cardiovascular disorders, and acute kidney injury (AKI) are possible complications of both infectious diseases (Kluge et al., 2020; Minchole et al., 2016; Rice et al., 2012; Yang et al., 2020). Regarding the clinical outcomes and complications, it is so far uncertain in which dimensions these diseases differ.

Pronounced differences between the treatment of both diseases became apparent when looking at the severe courses. The proportion of severe cases, the percentage of ventilated patients, patients treated in an ICU, and the inhospital death rate was substantially higher in patients with COVID-19 than that in Influenza cases. In our study, 15% (n = 362) of COVID-19 and only 9% (n = 610) of Influenza cases required ventilation. This corresponds to recent studies on hospitalized patients with COVID-19 showing that between 12% and 17% of patients required MV (Karagiannidis et al., 2020; King et al., 2020; Richardson et al., 2020). The reported 9% of ventilated patients treated with ECMO is in line with published results and gives an estimate of ECMO treatment in patients with COVID-19 in Germany (Karagiannidis et al., 2020; King et al., 2020).

The distinction between patients discharged from hospital and patients who died resulted in an even clearer picture. The duration of respiratory support and the length of hospitalization is considerably higher for SARS-CoV-2 cases than for Influenza cases in the seasons 2017–2019. Our results show that COVID-19 cases are ventilated more than three times as long as Influenza cases. This is consistent with the data of Tolksdorf et al. which show 2.5 times longer ventilation of patients with COVID-19 as compared to patients with Influenza (Tolksdorf et al., 2020). It is remarkable that ventilated patients with Influenza are discharged after 23.5 days, whereas ventilated patients with COVID-19 remain in hospital for a median of 35 days.

A high case-fatality rate was reported for elderly patients with multiple comorbidities (Karagiannidis et al., 2020; RKI, 2020a). This relationship between advancing age and odds of mortality is consistent with other reports (Karagiannidis et al., 2020; RKI, 2020b; Wang et al., 2020). Furthermore, patients who received MV and/or were treated in ICU accounted for the majority of deaths in both cohorts. This is consistent with an international meta-analysis that reports a mortality rate of 34% after ICU (Potere et al., 2020), as compared to 37% in the COVID-19 cases reported here. Mortality in Influenza ICU cases was lower with 27%, which is in

line with data reported from a German sentinel study (Tolksdorf et al., 2020). A recent pre-review publication of patients admitted to a tertiary care center in Boston, USA reached similar conclusions in that mortality and morbidity are higher in COVID-19 cases than in Influenza cases (Donnino et al., 2020).

For both respiratory diseases, underlying comorbidities and advanced age are a major risk factor. In addition, male sex doubled the risk of requiring ventilation for patients with COVID-19, but only modest sex dependency was observable for Influenza infection. In this context, Takahashi et al. found that female patients mounted significantly more robust T-cell activation and a poor T cell response was associated with a poor disease outcome in male patients (Takahashi et al., 2020). In addition, we found for both diseases that men with a SD + also have a higher risk of death than that of women. Despite a lower comorbidity burden prior to infection with COVID-19 and a lower frequency of secondary outcomes of cardiovascular or pulmonary conditions, patients with COVID-19 and hereof ventilated patients, were more likely to experience acute kidney failure, shock, SIRS, or ARDS. In our study, acute kidney failure was diagnosed in 58% of ventilated patients with COVID-19, but only in 13% of the total study population. This stands in marked contrast to a meta-analysis of hospitalized patients, in which only 6% showed AKI as a secondary outcome (Potere et al., 2020). The diagnosis of ARDS as a complication of COVID-19 is found in the majority of ventilated patients and was less common in patients with Influenza. In a case study led by Arentz et al. at the Evergreen Hospital in Kirkland, Washington, an outstanding 100% of ventilated patients with COVID-19 experienced ARDS (Arentz et al., 2020). A reason for the very high number of COVID-19-related ARDS cases might be found in the higher proportion of ventilated patients and the longer ventilation duration.

To what extent outcomes of both diseases regarding, for example, long-term complications or incapacity for work are comparable, will be a focus of work in the future. Once the outpatient data are available, the FDB will offer the possibility of tracking the respective patients after hospitalization for COVID-19 or Influenza.

Conclusion

Our results suggest that despite the existence of a well-functioning health care system and its appropriate management, the early mortality of severely ill and particularly mechanically ventilated patients with COVID-19 is substantially higher than of those with seasonal Influenza. Furthermore, in coping with the COVID-19 pandemic and in comparison with seasonal Influenza, an above-average burden on hospital capacities accompanied by a long hospital duration and ventilation time must be taken into consideration.

Limitations

Our findings must be interpreted considering some limitations. First, the data shown include only hospitalized patients, so we cannot estimate the proportion of hospitalized patients in the total number of infected patients. Secondly, due to delayed data availability and the timeliness of the data, we cannot track patients after hospital discharge. Therefore, the mortality rates refer to patients who died in hospital. Thirdly, our research database includes no information on laboratory parameters, thus, we could not correlate the severe course of the disease with lab results. Finally, infection-related complications during hospitalization have been defined using the secondary diagnosis of the respective hospital cases. It is hence not possible to ascertain to what extent they can be linked to the underlying infection.

Declaration of interests

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.

Author contribution

JW and FA designed and conceptualized the study, interpretation, and revising of data and manuscript. ML, JJ, and FB worked on data analysis, interpretation and revising of data, and drafting of the manuscript.

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Ethical approval

No approval was required.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2020.11.204.

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