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Clinical characterization of hospitalized COVID-19 patients during the second wave of pandemic in the district of Rohrbach, Upper Austria

A single center retrospective study

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Summary During the peak of the second wave of the coronavirus disease 2019 (COVID-19) pandemic in November 2020, the district of Rohrbach, Upper Austria, was reported to have had the highest 7-day incidence of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) positive cases worldwide. In this study, we present the clinical characteristics of COVID-19 cases during the second wave of the pandemic in patients admitted to the only primary care hospital in the district of Rohrbach between October 2020 and February 2021. In total, 260 patients were hospitalized with a mean age of 72 years and a mortality rate of 14.6% and 13 patients (5%) were transferred to the intensive care unit (ICU). Critically ill patients (22.7%) were of older age and often lived in retirement and nursing facilities as compared to mild or moderately ill patients. Patients with a severe disease course showed significantly longer hospitalization, a worse peripheral oxygen saturation on admission and significantly higher levels of C-reactive protein (CRP), procalcitonin (PCT), lactate dehydrogenase (LDH), troponin I and D-dimer as compared to mild or moderate COVID-19 cases. These laboratory parameters might help to identify COVID-19 patients with a severe disease course. In conclusion, we could show that older, frail individuals are the most vulnerable group affected by COVID-19. Whether this trend in hospitalized patients continues with the persistence of the pandemic, the emergence of novel virus mutations, and the availability of several different vaccines is presently unclear and remains to be determined.

Keywords SARS-CoV-2 · Mortality · Laboratory features · Comorbidities · ARDS

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Introduction

An unexplained pneumonia outbreak in Wuhan, China in late 2019 was detected by the Chinese authorities as having been caused by a new type of B-coronavirus [1]. This virus was named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the World Health Organization (WHO) officially termed the disease caused by SARS-CoV-2 as coronavirus disease 2019 (COVID-19) [2]. COVID-19 rapidly spread from Wuhan to other cities in China and the entire world. By the end of February 2020, several European countries reported COVID-19 cases [3]. On 11 March the WHO officially declared the outbreak a pandemic, and governments across the world began implementing strategies to slow the infection spread, such as social distancing and complete lockdown [4]. Italy soon became the new emerging epicenter in Europe. In contrast to Italy and some other European countries, the first wave of the pandemic did not affect Austria as much as compared to the second wave.

During the first wave of the pandemic, the authorities reported 153 SARS-CoV-2 positive cases in the district of Rohrbach between March and May 2020 with

only 11 patients being hospitalized, whereas during the second wave of the pandemic between October 2020 and February 2021, 4408 COVID-19 cases were reported in the district with 260 patients being admitted to our hospital.

COVID-19 is mainly transmitted through respiratory droplets and close contact. Asymptomatic infections are a major source of transmission [5–7]. The incubation period of SARS-CoV-2 ranges from 2–14 days after virus exposure [8]. The most common symptoms include fever, cough, shortness of breath, muscle ache, headache, sore throat, and loss of taste or smell [9].

In terms of laboratory findings, many patients have a decreased number of whites blood cells (WBC) and a decreased number of lymphocytes. In most patients, C-reactive protein (CRP) and lactate dehydrogenase (LDH) levels are elevated, but procalcitonin (PCT) levels are often normal [10].

The virus spreads and invades through the respiratory mucosa triggering an immune response and induces a cytokine-release syndrome, which has been described as cytokine storm in patients with a severe progression of the disease [11]. In patients with severe COVID-19 the development of acute respiratory distress syndrome (ARDS) is characteristic and associated with high mortality, approximately 40% of patients with ARDS do not survive [9].

Computed tomography (CT) imaging is of utmost importance for the diagnosis and prognosis of COVID-19. The chest CT findings of COVID-19 may include ground-glass opacities (GGO), crazy-paving pattern, consolidation, and other findings of viral pneumonia [12–14]. Chest CT can be used to evaluate the severity of lung involvement. The CT findings are related to the time course and often show different imaging signs with progression [12].

In the early phase of the disease, there are multiple interstitial changes, especially in the peripheral portions of the lungs. In severe cases, lung consolidation can occur, but pleural effusions are rare [12].

In the present study, we describe the clinical and radiologic findings of COVID-19 patients admitted to our hospital during the second wave of the pandemic from October 2020 until February 2021, in which the district was reported to have had the highest 7-day incidence of SARS-CoV-2 positive cases worldwide (1475 cases/100,000 inhabitants, 17 November 2020) [15–17]. By 20 November 2020, 1196 SARS-CoV-2 positive individuals were reported to the authorities in the district (2.1% of the population!) [18]. The 7-day incidence of SARS-CoV-2 positive cases was 736/100,000 inhabitants in Upper Austria and 543/100,000 inhabitants all over Austria by that point of time.

Methods

Setting

This study was performed at the Klinikum Rohrbach, the only primary care teaching hospital located in the district of Rohrbach, Upper Austria. The hospital has 196 beds and provides basic medical and surgical care with a department for internal medicine, a department for surgery and for trauma surgery. The hospital also has a pediatric ward, a department for gynecology and obstetrics, a department of radiology and a department for anesthesiology and intensive care for an average of 11,000 inpatients (10,791 inpatients in 2019) and 50,000 outpatients (49,436 outpatients in 2019).

Study design

We conducted a retrospective data analysis of the clinical and demographic characteristics of all hospitalized COVID-19 cases during the second wave of pandemic admitted to our hospital between October 2020 and February 2021. The study was approved by the Institutional Review Committee and all data were collected retrospectively.

Data collection

The following data were collected from medical records: patient characteristics, such as age, gender, comorbidities (arterial hypertension, coronary heart disease, diabetes mellitus, chronic obstructive pulmonary disease), laboratory features (leukocytes, lymphocytes, CRP, PCT, LDH, hypersensitive troponin I, D-dimer), peripheral oxygen saturation on admission, and length of hospitalization. Once a suspected case was admitted to the hospital, a nucleic acid test (PCR, GeneXpert, Cepheid, Sunnyvale, CA, USA) was carried out immediately by a nasopharyngeal swab and analysis in our laboratory to confirm positivity for SARS-CoV-2. A native thin-section chest CT was performed on every COVID-19 patient on admission.

COVID-19 patients were clinically classified into three major categories: first, mild disease course in patients requiring no oxygen support, second, moderate disease course in patients requiring oxygen support, and, third, severe/critically ill patients with either fatal outcome or survival and requirement of high flow oxygen therapy (Airvo), continuous positive airway pressure (CPAP) ventilation or invasive ventilation. We assessed the qSOFA score (respiratory rate, altered mental status, systolic blood pressure) as well as peripheral oxygen saturation and heart rate to determine the degree of illness and to check for clinical deterioration. Patients received additional treatment with methylprednisolone, antibiotic therapy or antithrombotic prophylaxis with low-molecular weight

heparin when clinically indicated. A subset of patients also received remdesivir.

Statistical analysis

Continuous variables are represented by median and quartile ranges (P25 and P75), categorical variables are represented by numbers (percentages).

Mann-Whitney U-test and Krustkal Wallis test were used for nonnormal distribution variables. The χ^2 or Fisher's exact test were used to analyze classified variables.

Age, gender, length of hospitalization, comorbidities (arterial hypertension, coronary heart disease, diabetes mellitus, chronic obstructive pulmonary disease), and laboratory features (leukocytes, lymphocytes, CRP, PCT, LDH, troponin I, D-dimer) as well as peripheral oxygen saturation were considered as relevant parameters. *P*-values below 0.05 were considered statistically significant. All analyses were performed with the SPSS program (Version 27.0) (IBM Corporation, Chicago, IL, USA).

CT image acquisition and image analysis

All patients underwent non-contrast CT of the chest in supine position with breath-holding after inspiration (GE CT Revolution HD/GSI; GE Healthcare, Chicago, IL, USA). The following scan parameters were used: tube voltage of 120 kV and dose modulation, reconstructed at 0.625 mm and 2.5 mm slice thickness, using both standard lung windows (1300 HU width; –500 HU center) and soft tissue window (360 HU width; 50 HU center). Scan coverage was from the apex of the lungs to the level of bilateral adrenals. Two chest radiologists evaluated the images on a picture archiving and communication system (PACS) workstation. An artificial intelligence(AI)-based automatic quantification of ground-glass opacities and consolidation was analyzed retrospectively, using the software application prototype CT-Pneumonia Analysis based on a Syngo.via VB40B workstation (Siemens Healthineers, Erlangen, Germany) and the standard (soft tissue) reconstruction with 0.625 mm slice thickness. Based on 3D segmentations of lesions, lungs, and lobes, the algorithm quantified the extent of overall abnormalities and the presence of high-opacity abnormalities, both globally and lobe-wise. The overall values used in this evaluation were: total opacity score: range between 0 and 20. To obtain this score, the opacity scores of the five lung lobes are summed up. Percentage of opacity: this value represents the percentage of opacity for the whole lung. The opacity score (range: 0–4) of each lung lobe is calculated as follows: ≤ 1% of opacity; score = 0; ≤ 25% of opacity; score = 1; ≤ 50% of opacity; score = 2; ≤ 75% of opacity; score = 3; > 75% of opacity; score = 4. This score was calculated for each lobe. For the left/right lung, the opacity score is the sum of the respective lobes and for the total opacity score, all lobe values are summed up (CT Pneumonia Analysis—Handbook, Siemens, Erlangen, Germany; 2020).

Results

Study population and patient characteristics

During the second wave of the pandemic, 260 COVID-19 patients were admitted to our hospital. The demographic and clinical characteristics of the patients are shown in Table 1. Patients had a mean age of 72 years (63–82 years interquartile range, IQR), and displayed a slight male predominance with 56.5%. The most frequent medical comorbidities of hospitalized COVID-19 patients were arterial hypertension (50.8%), diabetes mellitus (14.6%), coronary heart disease (10.4%), and chronic obstructive pulmonary disease (COPD) (5.0%) (Table 3). An AI-based automatic quantification of ground-glass opacities and consolidation in thin-section non-contrast chest CTs was performed on every patient on admission. One representative patient is shown (Fig. 1).

Length of hospital stay

The total length of hospitalization of COVID-19 patients was 6 days (3–11 days IQR) (Table 1). Patients with a severe/fatal disease course had a significantly longer length of hospital stay (11 days, 6–22 days IQR) as compared to patients with a mild (3 days, 2–5 days IQR) or moderate disease course (7 days, 4–11 days IQR) (Table 1). In addition, severely/critically ill patients were significantly older (76 years, 69–83 years IQR), as compared to mild (64 years, 54–80 years IQR)

Table 1 Clinical and demographic characteristics and of hospitalized COVID-19 patients ($n = 260$)

	Total ($n = 260$)	Mild ($n = 75$)	Moderate ($n = 126$)	Severe/fatal ($n = 59$)	*p*-Value	Kruskal-Wallis H
	Mean (25–75% IQR)	Mean (25–75% IQR)	Mean (25–75% IQR)	Mean (25–75% IQR)		
Age (years) (range)	72 (63–82)	64 (54–80)	74 (64–84)	76 (69–83)	< 0.001***	16.984
Female (*n*) (%)	113 (43.5%)	37 (49.3%)	60 (47.6%)	16 (27.1%)	–	–
Male (*n*) (%)	147 (56.5%)	38 (50.7%)	66 (52.4%)	43 (72.9%)	–	–
Length of hospitalization (days) (range)	6 (3–11)	3 (2–5)	7 (4–11)	11 (6–22)	< 0.001***	74.817
Mortality (*n*) (%)	38 (14.6%)	0	0	38 (64.4%)	–	–

IQR interquartile range
*$p < 0.05$, ***$p < 0.001$

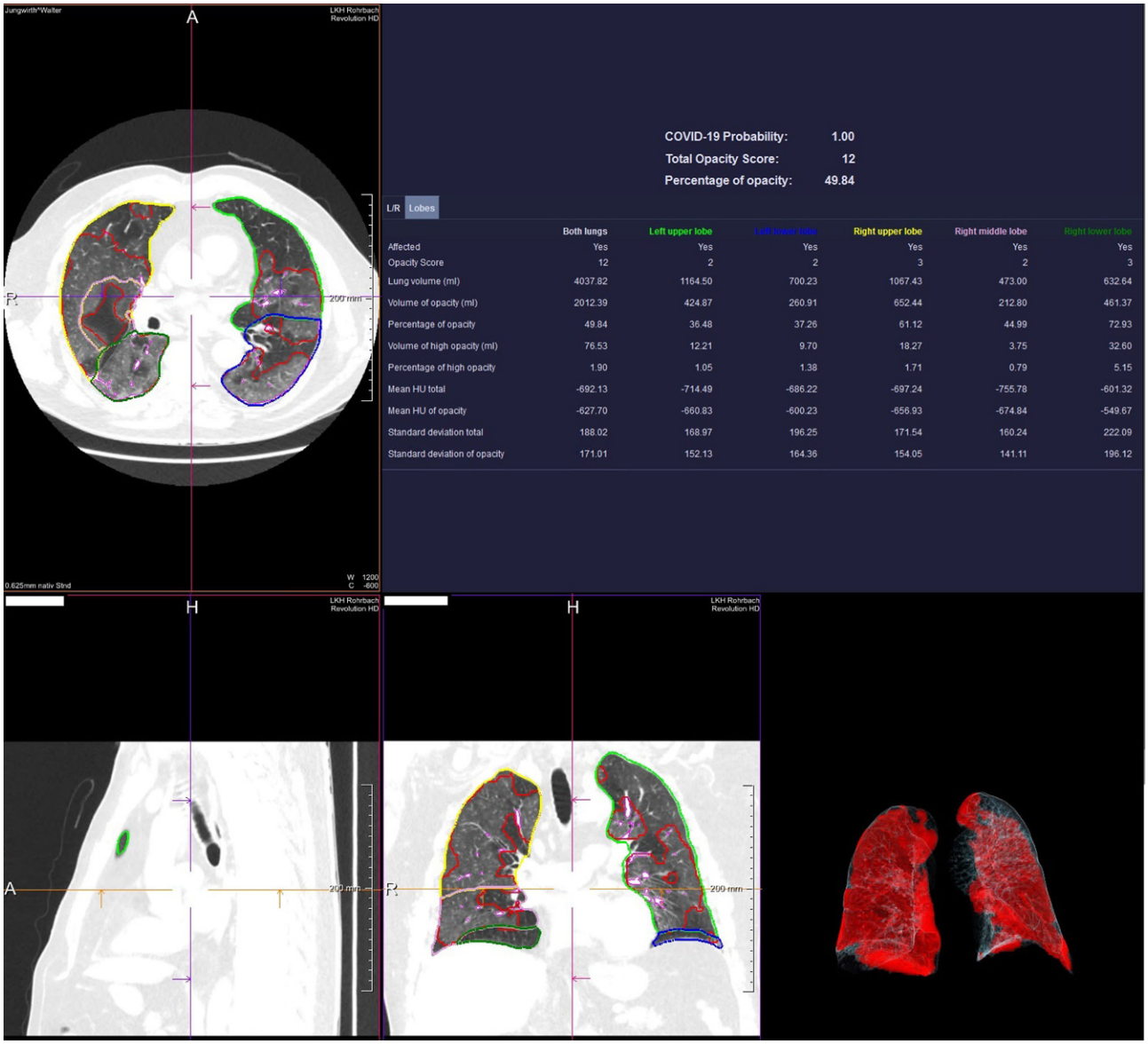

Fig. 1 Thin-section non-contrast chest CT of a representative COVID-19 patient with a severe disease course (patient 1). An AI-based automatic quantification of ground-glass opacities and consolidation was analyzed using the software application prototype "CT-Pneumonia Analysis" based on a Syngo.via VB40B workstation (Siemens Healthineers, Erlangen, Germany) and the standard (soft tissue) reconstruction with 0.625 mm slice thickness. Based on 3D segmentations of lesions, lungs, and lobes, the algorithm quantified the extent of overall abnormalities and the presence of high-opacity abnormalities, both globally and lobe-wise

or moderately ill patients (74 years, 64–84 years IQR) (Table 1).

Mortality

The overall mortality rate of patients was 14.6% (38 of 260 patients) (Table 1), 59 patients (22.7%) were classified as severely/critically ill, 13 patients (5%) were transferred to the intensive care unit (ICU), 7 patients died on the ICU, 6 patients survived ICU and were transferred back to the normal medical ward and could be discharged later on. Of the COVID-19 patients with a critical condition 31 died on the normal medical ward and were not transferred to ICU due to high age and/or severe underlying comorbidities, 126 patients (48.5%) had a moderate disease course requiring additional oxygen support, whereas 75 patients (28.8%) showed a mild disease course requiring no oxygen therapy (Table 1).

Laboratory findings and comorbidities of hospitalized COVID-19 patients

Patients with a severe/fatal disease course showed significantly higher numbers of leukocytes (mean 7.1 G/L, 5.3–9.7 G/L IQR) as compared to patients

Table 2 Laboratory features of hospitalized COVID-19 patients ($n = 260$)

	Total ($n = 260$)	Mild ($n = 75$)	Moderate ($n = 126$)	Severe/fatal ($n = 59$)	p-Value	Kruskal-Wallis H
	Mean (25–75% IQR)	Mean (25–75% IQR)	Mean (25–75% IQR)	Mean (25–75% IQR)		
Leucocytes (G/L) (4.0–10.0 G/L)	6.2 (4.8–8.2)	6.2 (4.6–7.7)	6.1 (4.5–8.5)	7.1 (5.3–9.7)	0.028*	7.148
Lymphocytes (G/L) (0.6–5.0 G/L)	0.8 (0.6–1.2)	1.0 (0.7–1.5)	0.8 (0.6–1.1)	0.7 (0.51–1.1)	0.001***	14.292
CRP (mg/L) (0.0–5.0 mg/L)	61.01 (23.44–118.08)	24.25 (6.6–62.3)	64.88 (31.03–118.34)	107.56 (61.34–176.23)	<0.001***	57.884
PCT (ng/mL) (0.0–0.5 ng/mL)	0.07 (0.04–0.19)	0.05 (0.03–0.08)	0.07 (0.04–0.15)	0.22 (0.07–0.67)	<0.001***	48.051
LDH (U/L) (125–220 U/L)	275 (208–348)	213 (184–272)	276 (213–325)	398 (288–552)	<0.001***	57.971
D-dimer (mg/L) (0.0–0.49 mg/L)	0.99 (0.55–2.17)	0.76 (0.41–3.22)	0.98 (0.59–1.91)	1.41 (0.72–3.34)	0.015*	8.461
Troponin I-HS (µg/L) (0.0–0.03 µg/L)	0.01 (0–0.03)	0.01 (0.0–0.01)	0.01 (0.01–0.03)	0.03 (0.01–0.07)	<0.001***	61.004
Peripheral oxygen saturation (SO2) (%)	92.8 (90–95)	95.0 (93.6–96.7)	92.0 (89.2–94.0)	90.0 (86.0–93.2)	<0.001***	67.126

IQR inter-quartile range, *CRP* C-reactive protein, *PCT* procalcitonin, *LDH* lactate dehydrogenase, *troponin I-HS* hypersensitive troponin I
*$p < 0.05$, ***$p < 0.001$

Table 3 Comorbidities of hospitalized COVID-19 patients ($n = 260$)

	Total ($n = 260$)	Mild ($n = 75$)	Moderate ($n = 126$)	Severe/lethal ($n = 59$)	p-Value	χ^2-test
	Mean (25–75% IQR)	Mean (25–75% IQR)	Mean (25–75% IQR)	Mean (25–75% IQR)		
Comorbidities (n) (%)[a]	158 (60.8%)	38 (50.7%)	83 (65.1%)	38 (64.4%)	0.104	4.520
Arterial hypertension (n) (%)	132 (50.8%)	35 (46.7%)	67 (53.35)	30 (50.8%)	0.671	0.797
Diabetes mellitus (n) (%)	38 (14.6%)	6 (8%)	21 (16.7%)	11 (18.6%)	0.148	3.822
Coronary heart disease (n) (%)	27 (10.4%)	3 (4%)	18 (14.3%)	6 (10.2%)	0.060	5.344
COPD (n) (%)	13 (5.0%)	2 (2.7%)	5 (4%)	6 (10.2%)	0.107	4.461

IQR interquartile range, *COPD* chronic obstructive pulmonary disease
*$p < 0.05$, ***$p < 0.001$
[a]Patients may have more than one comorbidity

with a mild (mean 6.2 G/L, 4.6–7.7 G/L IQR) or moderate disease course (mean 6.1 G/L, 4.5–8.5 G/L IQR) (Table 2). By contrast, patients with a severe/fatal disease course showed significantly lower numbers of lymphocytes (mean 0.7 G/L, 0.51–1.1 G/L IQR) as compared to patients with a mild (mean 1.0 G/L, 0.7–1.5 G/L IQR) or moderate disease course (mean 0.8 G/L, 0.6–1.1 G/L IQR) (Table 2). Patients with a severe/fatal disease course showed a significantly worse peripheral oxygen saturation on admission (mean 90.0%, 86.0–93.2% IQR) as compared to patients with a mild (mean 95.0%, 93.6–96.7% IQR) or moderate disease course (mean 92.0%, 89.2–94.0% IQR) (Table 2). In terms of laboratory findings on admission, patients with a severe/fatal disease course showed significantly higher levels of CRP, PCT, LDH, troponin I, and D-dimer, as compared to patients with a mild or moderate disease course (Table 2). We found no significant differences between the three COVID-19 patient groups regarding the frequency of medical comorbidities such as arterial hypertension, diabetes mellitus, coronary heart disease, or COPD. Overall, 60.8% of the patients had one or more of these comorbidities (Table 3).

Discussion

The district of Rohrbach, located in the northern part of Upper Austria, next to the border of Bavaria and the Czech Republic has a population of 56,545 people (November 2020). Rohrbach was reported to be the area with the highest 7-day incidence of SARS-CoV-2-positive cases worldwide during the second wave of the pandemic.

In this study we investigated all COVID-19 patients admitted to the Klinikum Rohrbach during the second wave of pandemic in a retrospective fashion. Overall, 260 patients were admitted, the mean age was 72 years, the overall mortality rate was 14.6% and 59 patients (22.7%) displayed a severe disease course with acute respiratory distress syndrome (ARDS) (Table 1). COVID-19 appeared mostly as typical viral pneumonia on thin-section chest CT, which was performed on every patient on admission. The disease was mainly distributed around the subpleural areas, predominantly in the lower lobes. Ground-glass opacities (GGO) were the most common imaging manifestation (Fig. 1).

In contrast to previously published reports, the mortality rate of COVID-19 patients transferred to our hospital was rather high. A significant proportion of fatal cases were not transferred to ICU due to high age and severe underlying comorbidities. Many of these old and vulnerable patients were transferred to the hospital from retirement/nursing homes and care facilities, in which COVID-19 clusters emerged during the second wave of the pandemic.

In terms of laboratory findings, we were able to show that hospitalized COVID-19 patients with a severe disease course had significantly higher levels of

CRP, PCT, LDH, troponin I, and D-dimer on admission as compared to mild or moderate cases. Similar findings have been published by Zhou et al., who postulated an 18-fold higher mortality for patients with D-dimer values greater than 1 µg/ml, as well as by Wang et al. who found significant higher values for leucocytes, D-dimer, LDH, GOT, GPT, and troponin I in ICU patients in comparison to non-ICU COVID-19 patients [19, 20].

Thus, such laboratory parameters in addition to measurement of the peripheral oxygen saturation in consideration of comorbidities might be of help to identify COVID-19 patients at risk of having a severe disease course, which is in accordance with previously published reports [21, 22].

The reasons why the district of Rohrbach displayed the highest 7-day incidence of SARS-CoV-2 positive cases worldwide in November 2020 during the peak of the second wave of the pandemic still remain unclear. One explanation for the high number of COVID-19 cases in this period of time might have been carelessness with respect to social distancing and a lack of adherence to lockdown sanctions.

Currently, there is still no specific drug for the treatment of patients with COVID-19. Some studies suggest positive therapeutic effects for remdesivir, when given at an early time point of infection. Overall, 19 of our patients (7.3%) received remdesivir. In these patients, onset of clinical symptoms was shorter than 10 days [23, 24].

Our study has several limitations. First, this was a retrospective analysis and data were obtained from patient medical records, therefore, our data cannot be generalized or extrapolated. Second, the time frame of our observation period was rather short (4 months). At present (September 2021), Austria is approaching the fourth wave of the pandemic and the district of Rohrbach shows a 7-day incidence of SARS-CoV-2 positive cases of around 160 cases/100,000 inhabitants. Vaccination against COVID-19 is currently ongoing and most of the inhabitants in retirement/nursing homes in the district have already been vaccinated successfully or presumably died during the second wave of the pandemic. On the other hand, several new and more aggressive virus mutations have emerged.

In conclusion, our study showed that hospitalized COVID-19 patients during the second wave of the pandemic in the district of Rohrbach had a rather high mortality rate. Patients with a severe disease course were significantly older and had significantly higher CRP, PCT, LDH, troponin I, and D-dimer levels as compared to mild or moderate cases. Whether these trends in hospitalized patients continue with the persistence of the pandemic, the emergence of novel virus mutations, and the availability of several different vaccines is presently unclear and remains to be determined.

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Declarations

Conflict of interest K. Rosenberger, F. Pöschl, S. Geschev, K. Steiner, S. Puig, J. Röper-Kelmayr and K.J. Aichberger declare that they have no competing interests.

Ethical standards The study was approved by the Institutional Review Committee and all data were collected retrospectively.

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