ORIGINAL ARTICLE

Comparison between COVID-19 outcomes in the first 3 waves of the pandemic: a reference hospital report

Monika Bociąga-Jasik[1,2], Wiktoria Wojciechowska[2,3], Michał Terlecki[2,3], Barbara Wizner[2,4], Marek Rajzer[2,3], Aleksander Garlicki[1,2], Krzysztof Sładek[2,5], Katarzyna Krzanowska[2,6], Jerzy Wordliczek[2,7], Marcin Krzanowski[2,6], Tomasz Grodzicki[2,4], Maciej T. Małecki[2,8]

1 Department of Infectious Diseases and Tropical Medicine, Jagiellonian University Medical College, Kraków, Poland
2 University Hospital, Kraków, Poland
3 Department of Cardiology, Interventional Electrocardiology and Arterial Hypertension, Jagiellonian University Medical College, Kraków, Poland
4 Department of Internal Diseases and Gerontology, Jagiellonian University Medical College, Kraków, Poland
5 Department of Pulmonology and Allergology, Jagiellonian University Medical College, Kraków, Poland
6 Department of Nephrology and Dialysis, Jagiellonian University Medical College, Kraków, Poland
7 Department of Interdisciplinary Intensive Care, Jagiellonian University Medical College, Kraków, Poland
8 Department of Metabolic Diseases, Jagiellonian University Medical College, Kraków, Poland

KEY WORDS

COVID-19, in-hospital death, pandemic waves, patients' characteristics, SARS-CoV-2

EDITORIAL

by Patrucco et al

ABSTRACT

INTRODUCTION The course of consecutive COVID-19 waves was influenced by medical and organizational factors.

OBJECTIVES We aimed to assess the outcomes of patients hospitalized for COVID-19 during the first 3 waves of the pandemic.

PATIENTS AND METHODS We performed a retrospective analysis of medical records of all COVID-19 patients admitted to the University Hospital in Kraków, Poland, a designated COVID-19 hospital in Małopolska province, between March 1, 2020 and May 31, 2021. The waves were defined as 1, 2, and 3, and covered the periods of March 2020 to July 2020, August 2020 to January 2021, and February 2021 to May 2021, respectively. Patients' characteristics and outcomes for waves 1 through 3 were compared.

RESULTS Data analyses included 5191 patients with COVID-19. We found differences in age (mean [SD], 60.2 [17.3] years vs 62.4 [16.8] years vs 61.9 [16.1] years, respectively, for waves 1, 2, and 3; $P = 0.003$), sex distribution (proportion of women, 51.4% vs 44.2% vs 43.6%; $P = 0.003$), as well as concentrations of inflammatory markers and oxygen saturation (the lowest and the highest for wave 1, respectively; $P < 0.001$). Hospital death rates in subsequent waves were 10.4%, 19.8%, and 20.3% ($P < 0.001$). Despite similarities in patients' characteristics, the length of hospital and intensive care unit stay was shorter for wave 3 than for wave 2. The risk factors for in-hospital death were: advanced age, male sex, cardiovascular or chronic kidney disease, higher C-reactive protein level, and hospitalization during the second or third wave.

CONCLUSIONS We identified differences in patients' clinical characteristics and outcomes between consecutive pandemic waves, which probably reflect changes in terms of COVID-19 isolation policy, hospitalization and treatment indications, and treatment strategies.

Correspondence to:
Maciej T. Małecki, MD, PhD, Department of Metabolic Diseases, Jagiellonian University Medical College, ul. Jakubowskiego 2, 30-688 Kraków, Poland, phone: +48 12 400 29 50, email: maciej.malecki@uj.edu.pl
Received: March 20, 2022.
Revision accepted: June 27, 2022.
Published online: July 4, 2022.
Pol Arch Intern Med. 2022; 132 (10): 16286
doi:10.20452/pamw.16286

INTRODUCTION The COVID-19 pandemic caused by SARS-CoV-2 was declared by the World Health Organization (WHO) a Public Health Emergency of International Concern at the end of January 2020.[1] The arising challenges concerning optimal preparation of the health care system to effectively respond to this new epidemiological threat required an immediate action. It comprised developing clinical recommendations, protocols for resuscitation in COVID-19 or use

WHAT'S NEW?

This study is the largest single-center retrospective report on hospitalized COVID-19 patients from Poland, and one of the largest ones in Europe published so far. It presents a comprehensive analysis of waves 1 through 3 of the COVID-19 pandemic from the perspective of the University Hospital in Kraków, Poland, a large regional coordinating center for patients with SARS-CoV-2 infection. The study identified substantial differences in patients' clinical characteristics and outcomes between consecutive COVID-19 waves. The potential medical and organizational causes of the identified differences were proposed. The results reported in this article may be useful for developing strategies to fight similar health crises in the future.

of personal protective equipment, establishing a collaboration model between administrative boards and medical staff, as well as acquiring and sharing knowledge about the management of patients with SARS-CoV-2 infection. Development and application of COVID-19 vaccines became crucial.[2,3] Another critical need from the very beginning of the pandemic was the preparation of effective strategies to secure the availability of a sufficiently-sized and well-trained health care workforce that would care for patients during the pandemic.[4,5] A major concern was the development of strategies to replenish the workforce supply as health care workers fell ill, were quarantined, and needed respite.[6,7] Hospital and emergency unit system reorganization became essential. Clinical and organizational experience, as well as scientific data on COVID-19, were initially gathered in the south of Europe—especially in Italy, which had faced critical health crisis as the first country in the continent.[8-11] This experience helped to deal with this new epidemiological challenge in Poland by means of discussing the optimal strategies of modifying hospital settings and educating health care professionals.[12-14]

The first case of SARS-CoV-2 infection in Poland was reported on March 4, 2020, while the University Hospital (UH) in Kraków began admitting patients with COVID-19 since March 17, 2020. The Polish public health care system, in response to the SARS-CoV-2 infection outbreak, was initially based on a network of hospitals designated exclusively for the treatment of patients diagnosed with COVID-19.[14] The UH in Kraków, with more than 900 beds and multiple outpatient clinics, had been transformed into such a hospital for Małopolska province, a region with a population of 3 361 000 inhabitants.

The aim of the present study was to assess and compare the characteristics and in-hospital outcomes of COVID-19 patients treated in a multidisciplinary UH, which was temporarily converted to an infectious medical center during the first 3 waves of the pandemic in Poland.

PATIENTS AND METHODS This retrospective analysis included medical records of 5191 COVID-19 patients who were admitted to the UH in Kraków between March 6, 2020 and May 31, 2021. Demographic and clinical data of the patients were extracted. The UH in Kraków is a tertiary reference hospital for adult patients (>17 years of age), with 900 beds, 33 hospital departments, 71 outpatient clinics, and an emergency department. Since March 2020, by a decision of the Polish government, it was temporarily converted into the regional center designated for the treatment of patients with COVID-19. The strategy of the Polish government was modified in October 2020—the Ministry of Health had then set up 16 coordinating hospitals that monitored a local network of smaller COVID-19 medical centers. During that period of time, the UH in Kraków coordinated the hospital care for patients with SARS-CoV-2 infection in Małopolska province, and it admitted particularly the patients who, except for the treatment of COVID-19, required specialized care, for example, due to myocardial infarction, stroke, pregnancy, or psychiatric disorders. During the entire analyzed period of the pandemic, the UH had between 200 and 500 beds dedicated for patients with COVID-19.

Most patients admitted to the UH came from Małopolska province and the neighboring regions. They were diagnosed with COVID-19 according to the WHO and Polish guidelines using the reverse transcriptase–polymerase chain reaction (RT-PCR) method.[15,16] The treatment algorithm for COVID-19 was based on constantly updated recommendations of the Polish Association of Epidemiologists and Infectiologists.[16] In TABLE 1, we summarized selected facts on the COVID-19–related governmental policies, medical recommendations, and the epidemiological situation in Poland between March 1, 2020 and May 31, 2021.

We gathered information on patients' age, sex, their clinical characteristics on admission (systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, oxygen saturation [SpO_2], as well as high-sensitivity C-reactive protein [hsCRP], D-dimer, and interleukin 6 [IL-6] levels). We also collected data regarding important clinical outcomes such as in-hospital death, noninvasive oxygen therapy, mechanical ventilation, admission to the intensive care unit (ICU), as well as the length of hospital and / or ICU stay.

Patients' characteristics and clinical outcomes for waves 1 through 3 were compared. The defined time intervals for the waves were as follows: wave 1, from March 1, 2020 to July 31, 2020; wave 2, August 1, 2021 to January 31, 2021; and wave 3, February 1, 2021 to May 31, 2021. Predictors of in-hospital mortality associated with COVID-19 during the whole analyzed period were assessed.

Statistical analysis The SPSS software, version 27 and SAS software, version 9.3 (SAS Institute Inc., Cary, North Carolina, United States)

TABLE 1 Selected data concerning COVID-19 governmental policies, medical recommendations, and the epidemiological situation in Poland between March 1, 2020 and May 31, 2021

Parameter	Wave 1	Wave 2	Wave 3
COVID-19 cases in Małopolska province[a], n	3535	113 908	104 626
COVID-19–related deaths in Małopolska province[a], n	63	2974	2691
Role of the UH in Kraków in the medical care system for COVID-19 in Poland	The regional reference center designated for the treatment of COVID-19 patients	The regional reference center designated for the treatment of COVID-19 patients (until September 2020) / a coordinating hospital for patients with COVID-19 (since October 2020)	A coordinating hospital for patients with COVID-19
Criteria for releasing COVID-19 patients from isolation	Clinical recovery (COVID-19 symptom–free) confirmed by 2 negative RT-PCR tests of sequential samples taken at least 24 hours apart	For symptomatic patients: 10 days after symptom onset plus at least 3 additional days without symptoms (including fever and respiratory tract symptoms). For asymptomatic cases: 10 days after a positive test for SARS-CoV-2	At least 10 days since the onset of symptoms and at least 24 hours since last fever without the use of antipyretic drugs and improvement in symptoms (eg, cough, shortness of breath)
Availability of vaccination against COVID-19	Not available	National Vaccination Program: Stage 0—since December 27, 2020 (risk groups including HCWs); Stage 1—since January 15, 2021 (persons aged >60 y)	National Vaccination Program: Stage 2—persons aged <60 y with chronic diseases; Stage 3—all persons aged >18 y
Recommended treatment	Symptomatic treatment	Antiviral: remdesivir (EMA recommendation as of July 25, 2020); anti-inflammatory: dexamethasone	Antiviral: remdesivir; anti--inflammatory: dexamethasone; tocilizumab
Virus variants	–	B.1.1.7 (Alfa) first detected in Poland in September 2020	B.1.1.7 (Alfa)—dominating in Poland
Selected, most important governmental policies regarding COVID-19	• March 12, 2020: announcement of the state of epidemiological threat –March 12, 2020: closing of schools, kindergartens, and nurseries –March 13, 2020: closing of restaurants, swimming pools, fitness clubs, cinemas, theaters, museums; reduced operation of shopping malls • March 24, 2020: introduction of the state of epidemic in Poland –Temporary restrictions on the functioning of specific institutions or workplaces –Banning of mass events and other public assemblies –Temporary prohibition of movement beyond the life and professional needs • March 31, 2020: additional restrictions –Limiting the number of customers in stores; shopping hours for seniors –Closing of hotels, hairdressing and beauty salons, parks, forests, and beaches –April 9, 2020: mandatory wearing of face masks • Announcement of a restriction withdrawal plan since April 16, 2020	• September 1, 2020: children coming back to schools (regular teaching) • October 17, 2020: announcement of new sanitary restrictions dividing the country into 2 zones (yellow and red) • October 23, 2020: the whole country announced a red zone with the following restrictions: –Grades 4–8 of primary schools—online teaching –From Monday to Friday, children under 16 years of age allowed to walk outside only under parents' supervision –Closing of restaurants • October 30, 2020: closing of cemeteries • November 9, 2020: –return to online teaching in primary schools (grades 1–3) and secondary schools –Closing of cultural institutions –Hotels opened only for persons travelling for business –Restrictions on the operation of shopping malls • November 21, 2020: a comprehensive action plan of defrosting economy announced • December 17, 2020: closing of ski slopes; sport centers open only for professional athletes	• February 28, 2021: introduction of new rules regarding sanitary restrictions –Opening of hotels, cultural institutions, ski slopes, swimming pools –Online teaching in primary and secondary schools • March 27, 2021: introduction of "hard lockdown"

a According to data published by Michał Rogalski (COVID-19 in Poland) based on reports of the Ministry of Health, Voivodship and District Sanitary--Epidemiological Station https://lifescience.pl/covid-19/aktualne-dane/

Abbreviations: EMA, European Medicines Agency; HCW, health care worker; RT-PCR, reverse transcriptase–polymerase chain reaction; UH, University Hospital

were used for database management and statistical analysis (license for Jagiellonian University Medical College). Continuous variables were presented as means and SDs or medians and interquartile ranges (IQRs), while categorical variables were shown as numbers and percentages.

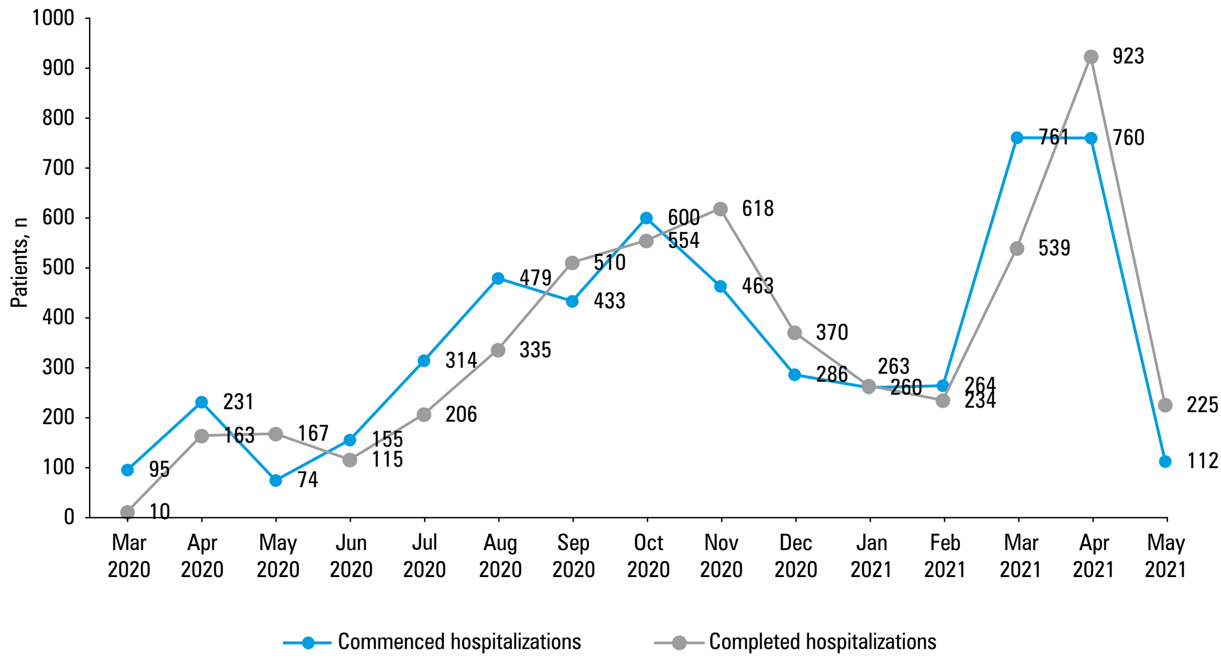

FIGURE 1 Number of hospitalized patients with COVID-19 between March 1, 2020 and May 31, 2021

The normality of distribution of continuous variables was assessed by the Shapiro–Wilk test.

The study population was divided into 3 groups according to the predefined waves of the pandemic. Differences between those groups were compared using 1-way analysis of variance for the normally distributed and the Kruskal–Wallis test for the nonnormally distributed continuous variables. Categorical variables were compared by the χ^2 test using the FREQ procedure. All post hoc analyses were performed using the Bonferroni adjustments. Multivariable logistic regression analysis was performed to assess the relation between in-hospital mortality and patients' age and sex, concomitant disorders (cardiovascular disease [CVD], chronic kidney disease [CKD]), inflammatory response (defined by the hsCRP level), and hospitalization during individual pandemic waves (1–3). Two-sided *P* values lower than 0.05 were considered significant.

RESULTS

Demographic data and patients' characteristics During the whole analyzed period, 5191 patients with COVID-19 were hospitalized in the UH in Kraków. The number of patients hospitalized monthly ranged from 95 in March 2020 to 761 in March 2021 and 760 in April 2021 (FIGURE 1). The highest number of admissions was observed during the second wave of the pandemic (n = 2545), and it was substantially greater than during the first (n = 875) and the third wave (n = 1771).

The majority of patients hospitalized for COVID-19 were over 60 years old (mean [SD] age, 61.9 [16.7] years; range, 17–101 years). The group of patients aged 60 to 79 years constituted 46.9% (n = 2432) of the entire cohort, those aged 80 to 99 years, 14.5% (n = 755), and there were also 3 centenarians. Among the remaining 38.6% (n = 2004) of the study patients, all were younger than 60 years, 11.9% (n = 616) were younger than 40 years, while only 0.2% (n = 13) were less than 20 years old (Supplementary material, *Figure S1*). Overall, the admitted patients were mostly male (54.8%; n = 2843). Differences in demographic data between the analyzed periods were identified for both age (mean [SD], 60.2 [17.3] years vs 62.4 [16.8] years vs 61.9 [16.1] years for waves 1, 2, and 3, respectively; *P* = 0.003) and sex distribution (women, 51.4% vs 44.2% vs 43.6%, respectively; *P* = 0.003). Patients' clinical characteristics on admission to the UH during the analyzed pandemic waves are presented in TABLE 2. In comparison with the first wave, the average SpO_2 was significantly lower during the second and third wave. Similarly, levels of biochemical markers of immune system activation (hsCRP, D-dimers, IL-6) were higher during waves 2 and 3 than during wave 1. During the third wave, the median (IQR) hsCRP level was significantly higher than during the second wave (62.1 [28.2–109.0] mg/l vs 53.0 [15.3–111.0] mg/l). Interestingly, D-dimer and IL-6 levels during the third wave were lower than during wave 2. The analysis of selected comorbidities showed that the patients hospitalized during waves 2 and 3 more frequently had concomitant CVDs and CKD (TABLE 2). There were no differences in the prevalence of diabetes mellitus, asthma, and chronic obstructive pulmonary disease between the analyzed waves.

Clinical outcomes We identified a significant difference in the length of hospital stay between the analyzed waves of the pandemic. Specifically, the median (IQR) length of hospitalization during wave 1 reached 18 (12–30) days, and was greater than during wave 2 (14 [10–22] days) and wave 3 (11 [8–16] days).

TABLE 2 Baseline characteristics of patients and hospital outcomes during individual COVID-19 pandemic waves

Characteristics	Wave 1	Wave 2	Wave 3	*P* value
Patients, n	875	2545	1771	–
Age, y	60.2 (17.3)	62.4 (16.8)[a]	61.9 (16.1)[a]	0.003
Female sex, %	51.4	44.2[a]	43.6[a]	0.003
Parameters on admission				
SBP[c], mm Hg	134.6 (20.6)	129.8 (23.3)[a]	129.7 (21.5)[a]	0.002
DBP[c], mm Hg	82.4 (15.0)	78.5 (14.5)[a]	78.1 (13.4)[a]	<0.001
Heart rate[c], bpm	83.8 (14.2)	85.9 (17.3)[a]	86.4 (16.2)[a]	0.002
Respiratory rate[c], n/min	14 (12–15)	16 (12–18)[a]	16 (12–18)[a]	<0.001
Oxygen saturation[c], %	96 (94–97)	95 (92–97)[a]	94 (91–97)[a]	<0.001
hsCRP[c], mg/l	18.8 (3.62–61.4)	53.0 (15.3–111.0)[a]	62.1 (28.2–109.0)[a,b]	<0.001
D-dimer[c], µg/ml	0.65 (0.38–1.29)	1.09 (0.57–2.47)[a]	0.94 (0.57–1.87)[a,b]	<0.001
IL-6[c], pg/ml	18.8 (1.5–59.4)	35.7 (15.3–87.3)[a]	33.3 (13.2–68.8)[a,b]	<0.001
Clinical course				
In-hospital death, %	10.4	19.8[a]	20.3[a]	<0.001
Noninvasive oxygen therapy, %	15.4	41.5[a]	25.3[a,b]	<0.001
Mechanical ventilation, %	8.6	11.6[a]	15.4[a,b]	<0.001
Admission to the ICU, %	11.4	12.5	12.2	0.71
Length of ICU stay, d	10 (4–21)	14 (8–27)[a]	9 (5–16)[b]	<0.001
ICU death, %	44	66.9	75.9	<0.001
Length of hospital stay, d	18 (12–30)	14 (10–22)[a]	11 (8–16)[a,b]	<0.001
Concomitant diseases				
Cardiovascular diseases[d], %	57.3	65.3[a]	64.1[a]	<0.001
Chronic kidney disease[e], %	3.2	12.5[a]	7.68[a,b]	<0.001
Diabetes mellitus, %	24.7	26.1	26.7	0.45
Asthma, %	6.5	5.9	6.1	0.82
COPD, %	5.0	5.6	5.1	0.71

Data are presented as mean (SD) or median (interquartile range) unless indicated otherwise.

P values for differences between individual pandemic waves

a Post hoc *P* <0.05 for difference vs wave 1

b Post hoc *P* <0.05 for difference vs wave 2

c Data available for: SBP/DBP for 4361 patients, heart rate: 4431 patients, respiratory rate: 3623 patients, oxygen saturation: 4128 patients, hsCRP: 5020 patients, D-dimer: 4572 patients, IL-6: 2991 patients

d Cardiovascular diseases group includes COVID-19 patients with one or more of the following conditions: arterial hypertension, coronary artery disease, heart failure, stroke, or atrial fibrillation

e Chronic kidney disease was diagnosed according to the classification recommended by the Kidney Disease Quality Outcome Initiative (K/DOQI) 2012[37]

Abbreviations: COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; hsCRP, high-sensitivity C-reactive protein; ICU, intensive care unit; IL-6, interleukin 6; SBP, systolic blood pressure

Mortality for the entire cohort of COVID-19 patients treated in the UH in Kraków was 18% (n = 953); however, it reached 22% in the group of patients aged 60 to 79 years (n = 537) and 39% among those aged 80 to 99 years (n = 294). Additionally, the death rate reached 60% (n = 61) in the group of patients aged 90 to 99 years. Interestingly, none of the 3 hospitalized centenarians died. In the group of patients younger than 60 years, the proportion of in-hospital death was 7.8% in individuals aged 40 to 59 years (n = 109). Mortality observed in the age group of 20 to 39 years was only 1.6% (n = 10), while in the group aged less than 20 years all the patients survived. During the whole analyzed period mortality was higher among men than women (20.3%; n = 576 vs 16.1%; n = 377; *P* = 0.001). The in-hospital death rate was 10.4% (n = 91), 19.8% (n = 503), and 20.3% (n = 359) for waves 1, 2, and 3, respectively (*P* <0.001).

Noninvasive oxygen therapy was necessary in 31.6% (n = 1641) patients overall; 15.4% (n = 135) during wave 1, 41.5% (n = 1057) during wave 2, and 25.3% (n = 449) during wave 3 (*P* <0.001). Among all patients with COVID-19 admitted to the UH, 12.2% (n = 634) required ICU treatment,

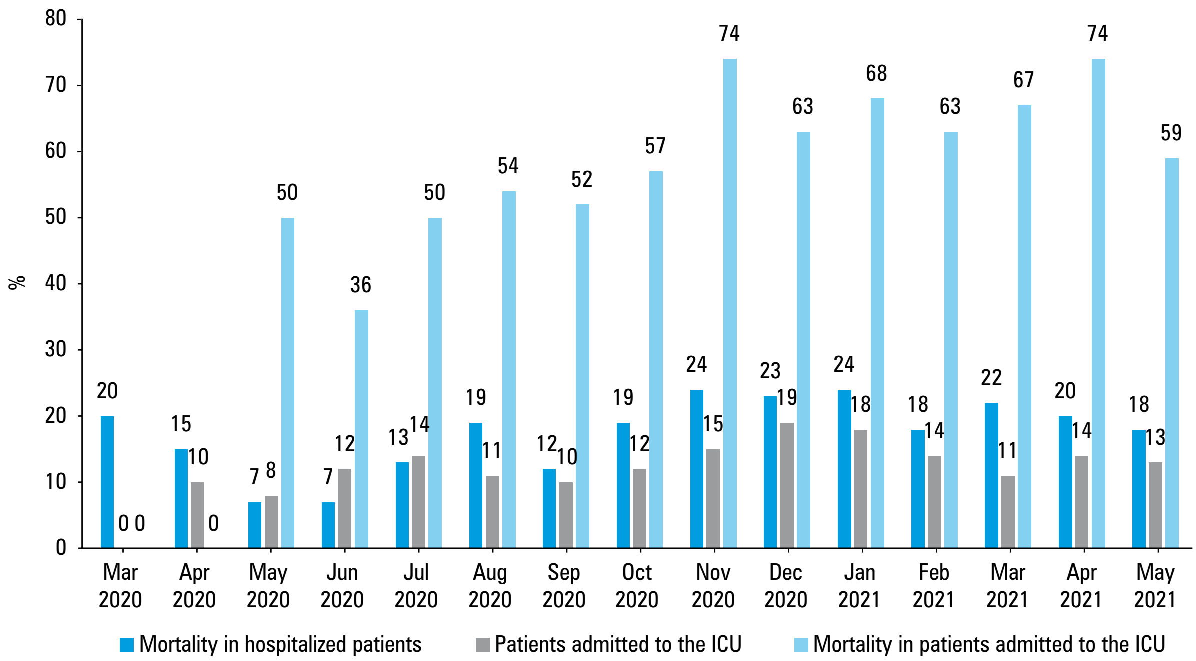

FIGURE 2 Overall and intensive care unit (ICU) mortality rates together with the rate of hospitalization in the ICU
Data are presented as the proportion of all hospitalized patients (for mortality in hospitalized patients and patients admitted to the ICU) or the proportion of patients admitted to the ICU (for mortality in patients admitted to the ICU)

mostly due to the progression of respiratory failure. This proportion was higher among men (64.5%; n = 409) than among women (35.5%; n = 225) (*P* <0.001). Overall, the ICU mortality rate during the whole analyzed period was very high and reached 66% (n = 421). Again, this proportion was higher among men than among women admitted to the ICU (69.9%; n = 286 vs 60.0%; n = 135; *P* <0.001). The proportion of COVID-19 patients hospitalized in the ICU was similar for all pandemic waves. Specifically, the percentage of patients admitted to the ICU during waves 1, 2, and 3 was 11.4% (n = 100), 12.4% (n = 318), and 12.2% (n = 216), respectively. The mortality rate of patients requiring ICU admission differed between the analyzed waves and reached 44% (n = 44), 66.9% (n = 213), and 75.9% (n = 164) during waves 1, 2, and 3, respectively (*P* <0.001).

The length of ICU stay differed between the waves and reached a median (IQR) of 10 (4–21) days, 14 (8–27) days, and 9 (5–16) days for waves 1, 2, and 3, respectively (*P* <0.001). Interestingly, the ICU stay was shorter during wave 3 than wave 2. Overall and ICU mortality rates together with the rate of hospitalization in the ICU are shown in FIGURE 2.

Risk factors for in-hospital death The independent predictors of in-hospital mortality are presented in FIGURE 3. In this multivariable logistic regression analysis, the risk factors for in-hospital death were advanced age, male sex, presence of CVD or CKD, higher hsCRP level, and hospitalization during wave 2 or 3 vs wave 1. Specifically, the risk for in-hospital death in patients aged 64 years or older (median age for the entire group) was 4-fold greater (odds ratio [OR], 4.31; 95% CI, 3.5–5.3) than in younger individuals. Male sex was also a predictor of in-hospital mortality (OR, 1.21; 95% CI, 1.03–1.4). Presence of chronic CVDs (OR, 1.25; 95% CI, 1.02–1.5) and CKDs (OR, 2.64; 95% CI, 2.1–3.3) increased the risk of death in patients with SARS-CoV-2 infection. Also, every increase in hsCRP by 10 units, reflecting the activation of the immune system during the disease course, positively correlated with the risk of death (OR, 1.09; 95% CI, 1.08–1.1). The odds of in-hospital death for waves 2 (OR, 1.44; 95% CI, 1.1–1.9) and 3 (OR, 1.63; 95% CI, 1.2–2.1) were higher than for wave 1.

DISCUSSION In the current report, we provide results of a large retrospective analysis of data from COVID-19 patients who required hospitalization and were admitted to the UH in Kraków during waves 1 through 3 of the COVID-19 pandemic in Poland. We found substantial differences in patients' clinical characteristics and outcomes between the 3 pandemic waves. Below, we discuss the scientific importance of these data and the potential causes of the identified differences.

This is one of the largest single-center reports presenting data on hospital care of patients with COVID-19 in Europe.[17-20] A retrospective analysis of hospital records of 5199 patients with COVID-19 was conducted in Poland before that study; however, the data were collected from 30 centers across the country and the final database for the study was very heterogeneous.[21]

First of all, similarly to earlier reports and according to the real-world data gathered in our study, this report illustrates a huge burden of

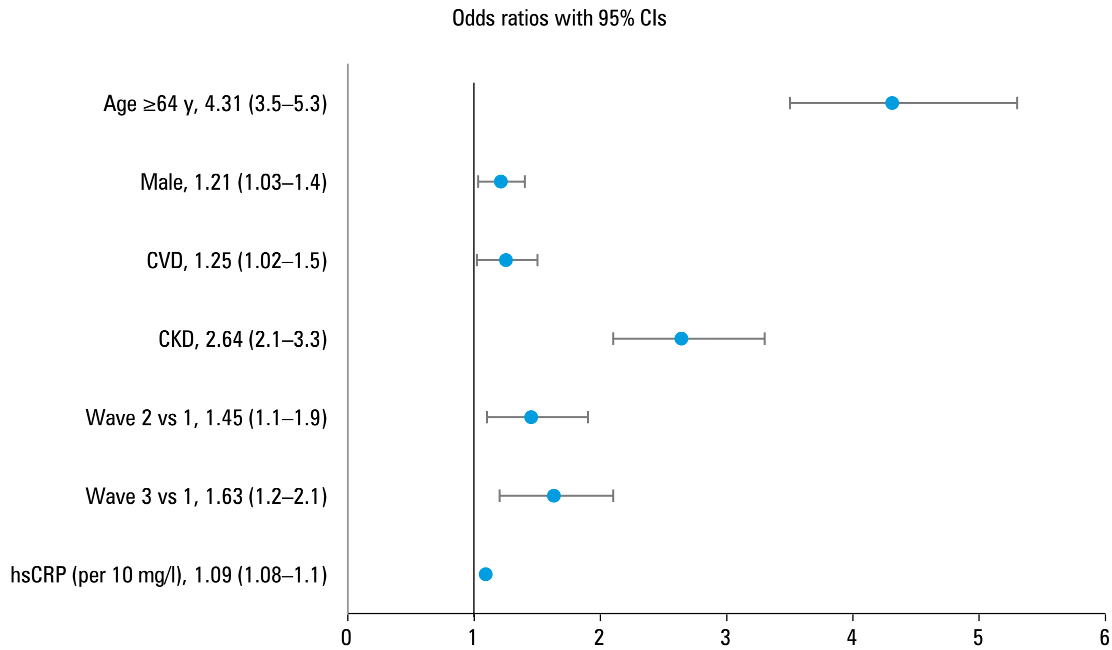

FIGURE 3 Multivariate logistic regression analysis for in-hospital mortality of hospitalized patients with COVID-19
Age = median of age, 64 years
Abbreviations: CKD, chronic kidney disease (as defined below TABLE 2); CVD, cardiovascular diseases (as defined below TABLE 2); others, see TABLE 2

the pandemic on the health care system, based on the example of the largest university hospital for adults in Małopolska province. During the first pandemic wave, university hospitals on the entire European continent played an important role in the struggle with COVID-19. Not only did they provide scientific knowledge and data but they also cooperated with other centers in an advisory capacity and developed recommendations for dealing with the new epidemiological situation.[17,18,20]

In Poland, early introduction of strong precautions in the initial phase of the pandemic significantly slowed down its beginning and minimized the scale of the first COVID-19 wave in 2020. However, due to the fact that all patients with SARS-CoV-2 infection were supervised by the epidemiological services and their hospitalization was mandatory, the number of hospital admissions was disproportionately high.[14,21] Owing to the lack of the medical staff and governmental experience combined with leaning on the WHO and European Center for Disease Prevention and Control regulations, many patients hospitalized during the first pandemic wave were admitted in a good general condition, a fact that is reflected in our data. These patients, in comparison with those hospitalized during the consecutive waves, were younger, mostly female, with a higher SpO_2 and lower levels of inflammatory markers on admission. In spite of this, the duration of hospitalization was longer, mainly because of the criteria for releasing COVID-19 patients from isolation, which required not only clinical recovery but also confirmation of convalescence in 2 negative RT-PCR tests of sequential samples taken at least 24 hours apart. However, as predicted by mathematical models, mitigating the preventive measures resulted in an increase in the number of new COVID-19 cases, with a peak in September 2020.[22] Data from other countries also proved that introduction of less strict anti-epidemic strategies was closely related to the number of new COVID-19 cases requiring hospitalization.[10,11,23]

The second and third waves were characterized by a much higher overall number of COVID-19 patients and, subsequently, a larger absolute number of cases with severe disease.[24] This fact is also consistent with our data. What is more, during waves 2 and 3 many affected people feared quarantine and tried to avoid medical assistance; consequently, many of them reported to the hospital at an advanced stage of the disease (second or third according to the National Institutes of Health).[25,26] During the second and third wave, the number of patients with COVID-19 admitted to the UH remained stable and high. It should be noted that since September 2020, by a decision of the local government, other hospitals in Małopolska province also became involved in the treatment of patients with COVID-19. In contrast to the beginning of the first wave, the COVID-19 patients admitted to the UH in Kraków since early fall of 2020 were preselected (included more severe cases or ones requiring specialized care).

In that period of time, the majority of COVID-19 patients admitted to the UH were older than 60 years, while people younger than 40 years rarely needed hospitalization—these data correspond with earlier reports.[27,28] Similarly to previous studies, the mortality rate in our report was closely related to age, reaching 60% in the group of the oldest patients. This phenomenon could probably be explained not only by the presence of many comorbidities in that group of patients, but also by mechanisms of aging contributing to the pathogenesis of severe COVID-19, including differences in the immune system, glycation, the epigenome, inflammasome activity, and biological age.[28] Our current results, as well as already published data from the UH database, support the existing evidence that male sex and comorbidities, in addition to advanced age, are major predictors of in-hospital mortality in patients with COVID-19.[11,18,28-31] It was hypothesized that worse prognosis among men affected by COVID-19 in comparison with women might be due to the presence of more comorbidities among the former sex group.[29] Other researchers proposed a theory that the differences between men and women in both innate and adaptive immune responses, partly related to sex-specific inflammatory responses resulting from X-chromosomal inheritance, could play an important role in the course of COVID-19.[31] Also, a low level of testosterone was linked to aging, obesity and some chronic diseases—all leading to systemic inflammation and endothelial dysfunction.[32]

The risk of death was very high among the patients with SARS-CoV-2 infection who required mechanical ventilation due to respiratory failure caused by COVID-19–related pneumonia. In our study, mortality rate among the patients requiring ICU admission exceeded 60% and was higher among men. A previous meta-analysis revealed that ICU mortality from COVID-19 was higher than the mortality usually seen in patients treated in the ICU for other viral pneumonias.[33] Such a high mortality rate in a modern, well-equipped ICU in the UH in Kraków might reflect, in addition to the virulence of SARS-CoV-2, shortcomings in terms of supervision of home isolation of patients with COVID-19 in Poland. We observed that a substantial number of patients reported to the hospital later than 10 days after the onset of symptoms, at a very advanced stage of the disease, with fully developed respiratory failure. However, it should be stressed that COVID-19 can cause silent hypoxemia, without corresponding features of respiratory failure.[34]

While the differences in mortality rates between the analyzed COVID-19 waves seem to be mainly related to the clinical characteristics of the admitted patients, they might also reflect a biology of different SARS-CoV-2 variants causing the infection. In a report on 8 super variants of SARS-CoV-2, some of them were linked to cilia dysfunctions, CVDs, thromboembolic diseases, and excessive stimulation of the innate immune system resulting in increased mortality.[35] Despite similar patients' characteristics for waves 2 and 3, the length of hospital and ICU stay was shorter during wave 3, which might be a result of more effective treatment strategies and growing clinical experience in consecutive COVID-19 waves.

This study has shortcomings typical of a retrospective observational analysis. Firstly, due to the nature of this study, no causal relationships could be proven. The results comprise observational data that were influenced not only by biological factors, such as mutations of SARS-CoV-2 or current clinical guidelines and available treatment, but also by the governmental strategies concerning social isolation, organization of COVID-19 medical care, recommendations on the duration of isolation, and other health care policy factors, and should be interpreted with full awareness of these aspects. We also did not take into consideration the changes in therapeutic strategies for COVID-19 and the use of specific treatments in the consecutive waves. This report is also lacking information on SARS-CoV-2 variants during individual waves of the pandemic. Additionally, mortality during the third wave could be slightly underestimated, as some patients hospitalized in the ICU at the end of May 2021 might have died after the analyzed period. However, we reported data from a large, comprehensive, homogenous database from a leading university medical center in Poland.

In summary, based on the data from a large UH in Poland, we identified substantial differences in patients' clinical characteristics and outcomes between the first 3 COVID-19 waves. They likely reflect a changing hospitalization policy as well as governmental and expert recommendations in Poland. However, some differences might result from more effective treatment and accumulation of clinical experience of the medical staff in consecutive waves. We believe that the results reported here may be useful for developing strategies to fight similar health crises in the future. Such strategies should certainly include a multispecialty approach that is currently investigated as part of the project named CRACoV-HHS (Model of multi-specialist hospital and non-hospital care for patients with SARS-CoV-2 infection), coordinated by the UH in Kraków.[36] Our results should also be useful with respect to a more accurate risk assessment for in-hospital mortality and guiding of therapeutic strategies.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

ACKNOWLEDGMENTS We would like to thank every medical staff member of the University Hospital in Kraków who provided care for patients and participated in gathering of data for this study. We acknowledge the tremendous work done by our colleagues who prepared the database of all patients hospitalized for COVID-19 in our hospital.

FUNDING This publication was supported by the National Center for Research and Development CRACoV-HHS project (Model of multi-specialist hospital and non-hospital care for patients with SARS-CoV-2 infection) through the initiative "Support for specialist hospitals in fighting the spread of SARSCoV-2 infection and in treating COVID-19" (SZPITALE-JEDNOIMIENNE/18/2020). The presented research was implemented by a consortium of the University Hospital in Kraków and the Jagiellonian University Medical College.

CONTRIBUTION STATEMENT Study conception and design: MBJ and MTM. Acquisition of data: all authors. Analysis and interpretation of data: WW, MT, MBJ, and MTM. Drafting of the manuscript: MBC and MTM. Critical revision: all authors. All authors have approved the final version of the manuscript.

CONFLICT OF INTEREST None declared.

HOW TO CITE Bociąga-Jasik M, Wojciechowska W, Terlecki M, et al. Comparison between COVID-19 outcomes in the first 3 waves of the pandemic: a reference hospital report. Pol Arch Intern Med. 2022; 132: 16286. doi:10.20452/pamw.16286

REFERENCES

1 Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020; 382: 727-733.

2 Blumenthal D, Fowler EJ, Abrams M, Collins SR. Covid-19 – implications for the health care system. N Engl J Med. 2020; 383: 1483-1488.

3 Leibner ES, Stokes S, Ahmad D, Legome E. Emergency department COVID management policies: one institution's experience and lessons learned. Emerg Med Pract. 2020; 22 (Suppl 5): 88-89.

4 Maxam M, Deronde KJ, Vega AD, et al. Development and implementation of a COVID-19 disease response protocol at a large academic medical center. Disaster Med Public Health Prep. 2020; 14: 792-795.

5 Metzl JM, Maybank A, de Maio F. Responding to the COVID-19 pandemic: the need for a structurally competent health care system. JAMA. 2020; 324: 231-232.

6 Firew T, Sano ED, Lee JW, et al. Protecting the front line: a cross-sectional survey analysis of the occupational factors contributing to healthcare workers' infection and psychological distress during the COVID-19 pandemic in the USA. BMJ Open. 2020; 10: e042752-e042762.

7 Htun HL, Lim DW, Kyaw WM, et al. Responding to the COVID-19 outbreak in Singapore: staff protection and staff temperature and sickness surveillance systems. Clin Infect Dis. 2020; 71: 1947-1952.

8 Comelli I, Scioscioli F, Cervellin G. Impact of the COVID-19 epidemic on census, organization and activity of a large urban emergency department. Acta Biomed. 2020; 91: 45-49.

9 Farcas A, Ko J, Chan J, et al. Use of incident command system for disaster preparedness: a model for an emergency department COVID-19 response. Disaster Med Public Health Prep. 2021; 15: e31-e36.

10 Ferrari R, Maggioni AP, Tavazzi L, Rapezzi C. The battle against COVID-19: mortality in Italy. Eur Heart J. 2020; 41: 2050-2052.

11 Chisci E, Masciello F, Michelagnoli S. The Italian USL Toscana Centro model of a vascular hub responding to the COVID-19 emergency. J Vasc Surg. 2020; 72: 8-11.

12 Kasiukiewicz A, Wojszel ZB. Assessment of referrals and hospitalizations in the hospital transformed into covid-19 facility in Poland during the "spring wave" of the epidemic in 2020 – a cross-sectional study. J Vasc Surg. 2020; 72: 8-11.

13 Sagan A, Bryndova L, Kowalska-Bobko I, et al. A reversal of fortune: comparison of health system responses to COVID-19 in the Visegrad group during the early phases of the pandemic. Health Policy. 2021; 20: S0168-S0185.

14 Pinkas J, Jankowski M, Szumowski L, el.al. Public health interventions to mitigate early spread of SARS-CoV-2 in Poland. Med Sci Monit. 2020; 26: e924730-e924737.

15 Jamshaid H, Zahid F, Din I, et al. Diagnostic and treatment strategies for COVID-19. AAPS PharmSciTech. 2020; 21: 222-236.

16 Flisiak R, Horban A, Jaroszewicz J, et al. Management of SARS-CoV-2 infection: recommendations of the Polish Association of Epidemiologists and Infectiologists as of April 26, 2021. Pol Arch Intern Med. 2021; 131: 487-496.

17 Carretta G, Contessa C, Boemo DG, et al. COVID-19 challenge: proactive management of a Tertiary University Hospital in Veneto Region, Italy. Pathog Glob Health. 2020; 114: 309-317.

18 Borobia AM, Carcas AJ, Arnalich F, et al. A cohort of patients with COVID-19 in a major teaching hospital in Europe. J Clin Med. 2020; 9: 1733-1743.

19 Giesen C, Diez-Izquierdo L, Saa-Requejo CM, et al. Epidemiological characteristics of the COVID-19 outbreak in a secondary hospital in Spain. Am J Infect Control. 2021; 49: 143-150.

20 Dommasch M, Zimmermann M, Kanz KG, et al. Role of university hospitals in Bavaria during the COVID-19 pandemic [in German]. Med Klin Intensivmed Notfmed. 2021; 117: 305-308.

21 Raciborski F, Pinkas J, Jankowski M, et al. Dynamics of the coronavirus disease 2019 outbreak in Poland: an epidemiological analysis of the first 2 months of the epidemic. Pol Arch Intern Med. 2020; 130: 615-621.

22 Orzechowska M, Bednarek AK. Forecasting COVID-19 pandemic in Poland according to government regulations and people behavior. medRxiv. Preprint posted online May 29, 2020.

23 He R, Zhang J, Mao Y, et al. Preparedness and responses faced during the Covid-19 pandemic in Belgium: an observational study and using the national open data. Int J Environ Res Public Health. 2020; 17: 7985-7999.

24 Flisiak R, Rzymski P, Zarębska-Michaluk D. Demographic and clinical overview of hospitalized COVID-19 patients during the first 17 months of the pandemic in Poland. J Clin Med. 2021; 11: 117-128.

25 COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Last update: May 31, 2022. https://www.covid19treatmentguidelines.nih.gov/. Accessed April 6, 2022.

26 Wytrychiewicz K, Pankowski D, Jasinski M, et al. Commentary on COVID-19 situation in Poland: practical and empirical evaluation of current state. Psychol Trauma. 2020; 12: 542-545.

27 Suleyman G, Fadel RA, Malette KM, et al. Clinical characteristics and morbidity associated with coronavirus disease 2019 in a series of patients in Metropolitan Detroit. JAMA Netw Open. 2020; 3: e2012270-e2012282.

28 Mueller AL, Mcnamara MS, Sinclair DA. Why does COVID-19 disproportionately affect older people? Aging (Albany NY). 2020; 12: 9959-9981.

29 Gujski M, Raciborski F, Jankowski M, et al. Epidemiological analysis of the first 1389 cases of COVID-19 in Poland: a preliminary report. Med Sci Monit. 2020; 26: e924702.

30 Terlecki M, Wojciechowska W, Klocek M, et al. Association between cardiovascular disease, cardiovascular drug therapy, and in-hospital outcomes in patients with COVID-19: data from a large single-center registry in Poland. Kardiol Pol. 2021; 79: 773-780.

31 Griffith DM, Sharma G, Holliday CS, et al. Men and COVID-19: a biopsychosocial approach to understanding sex differences in mortality and recommendations for practice and policy interventions. Prev Chronic Dis. 2020; 17: E63-E72.

32 Giagulli VA, Guastamacchia E, Magrone T, et al. Worse progression of COVID-19 in men: is testosterone a key factor? Andrology. 2021; 9: 53-64.

33 Armstrong RA, Kane AD, Cook TM. Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies. Anaesthesia. 2020; 75: 1340-1349.

34 Wilkerson RG, Adler JD, Shah NG, Brown R. Silent hypoxia: a harbinger of clinical deterioration in patients with COVID-19. Am J Emerg Med. 2020; 38: 2243.e5-2243.e6.

35 Hu J, Li C, Wang S, et al. Genetic variants are identified to increase risk of COVID-19 related mortality from UK Biobank data. Hum Genomics. 2021; 15: 10-20.

36 Sydor W, Wizner B, Strach M, et al. CRACoV-HHS: an interdisciplinary project for multi-specialist hospital and non-hospital care for patients with SARS-CoV-2 infection as well hospital staff assessment for infection exposure. Folia Med Cracov. 2021; 61: 5-44.

37 National Kidney Foundation. KDOQI clinical practice guideline for diabetes and CKD: 2012 update. Am J Kidney Dis. 2012; 60: 850-886.