RESEARCH LETTER

High postdischarge mortality in hospitalized COVID-19 patients with cardiovascular comorbidities

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Introduction The COVID-19 pandemic has affected more than 197 million people in more than 180 countries worldwide. Morbidity and mortality linked to this disease placed a significant burden on healthcare systems. COVID-19 has also been referred to as a thrombo-inflammatory disease with exuberant inflammatory responses (hyperinflammation, cytokine storm) further resulting in uncontrolled multiorgan failure, likely to be the leading cause of death.[1,2]

Cardiovascular disease (CVD) is a common comorbidity in patients with COVID-19, especially those with severe disease. More than 7% of patients experience myocardial injury from the infection (the rate is much higher, reaching 22%, in those critically ill individuals).[3,4] Studies demonstrated that COVID-19 in patients with underlying comorbidities had an increasingly rapid and severe course. Proportions of CVDs among patients with COVID-19 vary substantially: 17.1% (95% CI, 13.2%–20.9%) for hypertension; 4.5% (95% CI, 3.6%–5.5%) for other CVDs, and 8.5% (95% CI, 5.5%–11.4%) for diabetes mellitus.[5] Hospitalized COVID-19 patients with cardiovascular comorbidities have a poor prognosis, with in-hospital mortality rates as high as 36% in comparison with individuals without the history of CVD.[3-5] Notwithstanding, data on the outcomes of the disease in these patients following hospital discharge are scarce. In this study, we report on the short-term outcomes following hospital discharge in patients with COVID-19 and cardiovascular comorbidities.

Methods The study conforms to the Declaration of Helsinki. Informed consent for data analysis was obtained from all patients in accordance with the Polish law on patients' rights regarding data registration. Given the observational design of the study, approval for analyzing the recorded data was waived by the institutional review board on human research.

The analysis is based on data from the SILesian CARDiovascular (SILCARD) database. Detailed information on the database was published previously.[6] In summary, the database comprises records from all hospitals (n = 310) in the Silesian Province. The population of the region amounts to 4.5 million inhabitants, corresponding roughly to 12% of the general Polish population. The SILCARD database encompasses information on all consecutive adult patients hospitalized for any reason at the cardiology, cardiac surgery, vascular surgery, or diabetology departments as well as those hospitalized at the departments of internal medicine or intensive care units with the principal diagnosis of CVD. Cardiovascular disease was defined as any *I* code according to the *International Classification of Disease, Tenth Revision* (*ICD-10*). Information on hospitalizations due to COVID-19 and all-cause death was provided by the National Health Fund, which manages the entire health insurance system in Poland.

Overall, the study comprised records of 4277 patients from the SILCARD database hospitalized with COVID-19 between March and December 2020. The median (interquartile range [IQR]) follow-up was 72 (47–95) days. Based on the patient's status at the end of follow-up, the study population was divided into 2 groups: Group 1, survivors (n = 2483) and Group 2, deceased (n = 1794).

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Statistical analysis Statistical analysis was performed using the STATISTICA PL software, version 13.3 (TIBCO, Palo Alto, California, United States). Quantitative data were presented as means and standard deviations (SDs) or medians with IQRs. Qualitative data were presented as frequencies. The Shapiro–Wilk test was used to determine whether random samples followed a normal distribution. The χ^2 test was used to compare categorical variables. The unpaired *t* test was used to compare normally distributed continuous variables between the groups, whereas the Mann–Whitney test was used to compare continuous variables with a distribution other than normal. A Kaplan–Meier curve was created to visualize the estimated 6-month survival. A 2-sided *P* value of less than 0.05 was used to indicate statistical significance.

Results and discussion Overall, 1794 out of 4277 patients (41.9%) with COVID-19 and CVD died during the study period. Those who died were older than the survivors. Male sex, chronic coronary syndromes, heart failure, chronic kidney disease, and history of stroke were more prevalent among patients who died, as were other CVDs and non-CVDs (TABLE 1). The median (IQR) length of hospital stay for patients who were alive at the end of follow-up was 11 (4–21) days and was longer in comparison with 10 (4–20) days for those who died during hospitalization and 10 (5–18) days for those who died after hospital discharge ($P = 0.006$). However, the length of hospital stay was similar between patients who died during and after hospitalization ($P = 0.7$). The median time to death after discharge was 14 (7–30) days.

A total of 1289 out of 1794 deceased patients (71.8%)—corresponding to 30.1% of the entire study population—died during hospital stay. By contrast, 505 of 1794 deceased patients (28.2%; 11.8% of the entire cohort) died after hospital discharge. The estimated 6-month postdischarge mortality rate was 21% (Supplementary material, *Figure S1*).

Cardiovascular conditions are the most frequent comorbidities in patients hospitalized with COVID-19. The rate of CVD varies from 14% to 50%.[7-9] These rates go even as high as 60% in patients with disease complications and those in the critical phase of the disease.[7] The most frequent reported CVDs include, among others, hypertension (30%–56%), diabetes mellitus (15%–27%), coronary artery disease (8%–11%), and heart failure (7%–8%).[7,8] In our cohort of patients with CVD, the rates were substantially higher in comparison with the general population, namely, 69.5% for hypertension, 39.6% for heart failure, 37.7% for coronary artery disease, 29.6% for diabetes mellitus, and 15.9% for atrial fibrillation. These rates correspond well with the CVD frequencies seen among COVID-19 patients with myocardial injury.[8] There is a substantial heterogeneity among studies with respect to in-hospital mortality, which varies from 5% to 21%.[9] According to Guo et al,[8] in-hospital mortality rates were linked to CVD and myocardial injury. The authors reported mortality rates of 7.6% in patients with no underlying CVD and normal troponin T (TnT) levels, 13.3% in those with underlying CVD and normal TnT levels, 37.5% in those without underlying CVD but with elevated TnT levels, and 69.4% in those with underlying CVD and elevated levels of TnT.[8] In-hospital mortality rate in our cohort was 16.1% and was similar to that reported in other studies. Patients hospitalized with COVID-19 still experience extended effects of the disease after discharge. In addition, readmission is yet another crucial indicator of disease severity and healthcare system quality. Somani et al[10] reported that 3.6% of discharged patients returned for emergency care after a median of only 4.5 days. Respiratory distress was the most common cause for rehospitalization (50%). What is more, patients who were readmitted also had a shorter median length of stay during the index hospitalization (4.5 vs 6.7 days; $P = 0.006$).[10] Lavery et al[11] reported that the adjusted odds for readmission were higher for patients with specific comorbidities, which included chronic obstructive pulmonary disease (odds ratio [OR], 1.35; 95% CI, 1.28–1.42; $P < 0.001$), heart failure (OR, 1.58; 95% CI, 1.48–1.67; $P < 0.001$), diabetes mellitus (OR, 1.21; 95% CI, 1.14–1.28; $P < 0.001$), and chronic kidney disease (OR, 1.64; 95% CI, 1.55–1.74; $P < 0.001$). The risk of hospital readmission decreased with longer length of index hospital stay (OR, 0.99; 95% CI, 0.99–1.00; $P = 0.001$).[11] Chopra et al[12] examined 60-day outcomes among hospitalized patients with COVID-19. The authors demonstrated that 398 individuals (24.2%) died during hospitalization. By 60 days after discharge, additional 84 patients (17.4% of those who died; 5% of the entire study cohort) died. This resulted in an overall mortality rate for the cohort amounting to 29.2%.[12] We reported a much higher postdischarge mortality rate among patients with comorbid CVD, who accounted for roughly 28.2% of all deceased COVID-19 patients (11.8% of the entire study population). In our study, the median time to death after discharge was 14 (7–30) days. The overall mortality rate in our cohort of COVID-19 patients with CVDs reached 41.9%.

In light of the reported postdischarge readmission and mortality rates, there seems to be an urgent need for developing practice guidelines for safe discharge. Particular endeavors with regard to the acuity and location of care continuance should be undertaken for CVD patients, who might appear stable at discharge. Managed care plans designed for discharged patients with COVID-19 should include close monitoring (telemedicine), scheduled outpatient cardiology visits, and planned rehabilitation programs. Such actions might prevent hospital readmission and improve prognosis. These managed care strategies should be particularly intensive within 1 to 2 months of discharge.

TABLE 1 Baseline and clinical characteristics of the study population

Parameter	All patients (n = 4277)	Survivors (n = 2483)	Deceased (n = 1794)	*P* value
Age, y, mean (SD)	72 (12)	69 (13)	75 (10)	<0.001
Female sex	1851 (43.3)	1131 (45.5)	720 (40.1)	<0.001
Chronic coronary syndromes	1947 (45.5)	1075 (43.3)	872 (48.6)	0.001
History of myocardial infarction	483 (11.3)	259 (10.4)	224 (12.5)	0.04
Heart failure	1528 (35.7)	717 (28.9)	811 (45.2)	<0.001
Hypertension	3153 (73.7)	1798 (72.4)	1355 (75.5)	0.02
Diabetes mellitus	1629 (38.1)	867 (34.9)	762 (42.5)	<0.001
Atrial fibrillation	922 (21.6)	497 (20)	425 (23.7)	0.004
Arrhythmias (excluding atrial fibrillation)	881 (20.6)	520 (20.9)	361 (20.1)	0.53
History of stroke	740 (17.3)	384 (15.6)	356 (19.8)	<0.001
Prior PCI	456 (10.7)	243 (9.8)	213 (11.9)	0.03
Prior CABG	69 (1.6)	45 (1.8)	24 (1.3)	0.27
COPD	537 (12.6)	282 (11.4)	255 (14.2)	0.006
Asthma	460 (10.8)	269 (10.8)	191 (10.6)	0.88
CKD stage 3 or higher	669 (15.6)	309 (12.4)	360 (20.1)	<0.001
Renal replacement therapy	155 (3.6)	80 (3.2)	75 (4.2)	0.11
Cancer[a]	1276 (29.8)	723 (29.1)	553 (30.8)	0.18

Data are presented as number (percentage) unless otherwise indicated.

a History of or current cancer

Abbreviations: CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention

Study limitations The results of the study should be considered in light of its limitations. First, the SILCARD registry is based on the electronic database of a single national insurance company and is limited to core variables, such as demographic data, comorbidities, and in-hospital and follow-up events. In addition, the quality of data may be affected by the discordance between the quality of information reported by various centers. Finally, many of the discharges took place in the early period of the COVID-19 pandemic when there were no clear management recommendations.

SUPPLEMENTARY MATERIAL

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

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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