

# 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

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## ABSTRACT

**Background:** The coronavirus disease 19 (COVID-19) recently became one of the leading causes of death worldwide, similar to cardiovascular disease (CVD). Coexisting CVD may influence the prognosis of patients with COVID-19.

**Aims:** We analyzed the impact of CVD and the use of cardiovascular drugs on the in-hospital course and mortality of patients with COVID-19.

**Methods:** We retrospectively studied data for consecutive patients admitted to our hospital, with COVID-19 between March 6<sup>th</sup> and October 15<sup>th</sup>, 2020.

**Results:** 1729 patients (median interquartile range age 63 [50–75] years; women 48.8%) were included. Overall, in-hospital mortality was 12.9%. The most prevalent CVD was arterial hypertension (56.1%), followed by hyperlipidemia (27.4%), diabetes mellitus (DM) (25.7%), coronary artery disease (16.8%), heart failure (HF) (10.3%), atrial fibrillation (13.5%), and stroke (8%). Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ACEIs/ARBs) were used in 25.0% of patients, β-blockers in 40.7%, statins in 15.6%, and antiplatelet therapy in 19.9%. Age over 65 years (odds ratio [OR], 6.4; 95% CI, 4.3–9.6), male sex (OR, 1.4; 95% CI, 1.1–2.0), pre-existing DM (OR, 1.5; 95% CI, 1.1–2.1), and HF (OR, 2.3;

95% CI, 1.5–3.5) were independent predictors of in-hospital death, whereas treatment with ACEIs/ARBs (OR, 0.4; 95% CI, 0.3–0.6),  $\beta$ -blockers (OR, 0.6; 95% CI, 0.4–0.9), statins (OR, 0.5; 95% CI, 0.3–0.8), or antiplatelet therapy (OR, 0.6; 95% CI: 0.4–0.9) was associated with lower risk of death.

**Conclusions:** Among cardiovascular risk factors and diseases, HF and DM appeared to increase in-hospital COVID-19 mortality, whereas the use of cardiovascular drugs was associated with lower mortality.

**Key words:** COVID-19, cardiovascular disease, cardiovascular drugs, in-hospital mortality

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## INTRODUCTION

Since the WHO declared coronavirus disease 19 (COVID-19) a global pandemic in March 2020, more than 144 500 000 people worldwide (2 700 000 in Poland) have been affected, with approximately 3 000 000 fatal cases (64 000 in Poland) [1]. COVID-19 is currently one of the leading causes of mortality in many countries, with the number of deaths similar to those from cardiovascular disease (CVD) or cancer [1, 2].

The relation between the severity of the COVID-19 disease course and concomitant CVD is being studied worldwide; however, no large reports from Poland have yet been published. Many studies in other countries have confirmed that patients with pre-existing CVD or cardiovascular risk factors had worse COVID-19 outcomes [3–5]. The aforementioned data come mostly from non-European countries and meta-analyses of small observational studies with heterogeneous definitions of CVD. The frequency of cardiovascular risk factors and CVD among patients hospitalized due to COVID-19 is similar to that observed in the general population, but there is a disproportionately higher frequency of CVD among non-survivors of COVID-19 [3–6]. It is uncertain whether this finding is incidental or secondary to differences in age and sex distribution, or if there is an association between CVD and higher mortality in patients with COVID-19. Another problem is the lack of uniform standards for COVID-19 diagnosis, hospitalization, and therapy between countries. Therefore, differences in therapeutic models for COVID-19 may influence final outcomes, including the association between COVID-19 mortality and CVD. The impact of cardiovascular drugs on the clinical course of COVID-19 has also not yet been determined. At the beginning of the pandemic, the biggest controversies

involved angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (ACEIs/ARBs), as it has been hypothesized that these drugs may increase susceptibility to infection by SARS-CoV-2 and promote viral replication, subsequently worsening the disease course and outcomes [7, 8]. However, this hypothesis has not been confirmed in consecutive studies on mortality in COVID-19 [8–11]. Currently, there are limited data on prognosis for patients with COVID-19 being treated with other cardiovascular drugs such as  $\beta$ -blockers, statins, or antiplatelet therapy.

The purpose of this study was to analyze the impact of CVD and selected cardiovascular drugs on the course of hospitalisation and mortality of patients with COVID-19.

## METHODS

We retrospectively studied the medical records of all consecutive patients who were admitted to the University Hospital in Kraków (which was converted temporarily into an infectious disease hospital dedicated to COVID-19 treatment) between March 6, 2020, and October 15, 2020. Patients were admitted from the whole Małopolska Voivodship and neighboring regions. Thus, our study cohort may be assumed to be representative of the whole macro-region. Patients were diagnosed with COVID-19 according to WHO and Polish guidelines with the use of RT-PCR [12–14]. The treatment algorithm for COVID-19 was in accordance with the recommendations of the Polish Association of Epidemiologists and Infectiologists [13, 14]. Patient data were obtained from the Hospital Information System. Cardiovascular risk factors and CVD were identified based on a medical history of prehospital diagnosis and/or treatment and defined according to current European Society of Cardiology guidelines [15]. The analyzed endpoints in

## WHAT'S NEW?

We present results based on a large database of patients with COVID-19 treated in a single hospital according to the same standard. Our study cohort was representative of the population of the south-east macro-region of Poland. We analyzed the impact of cardiovascular disease and pharmacological treatment for cardiovascular disease on in-hospital outcomes in patients with COVID-19. The findings support existing evidence that advanced age, male sex, diabetes mellitus, and pre-existing heart failure are major predictors of poor outcomes in patients with COVID-19. We did not identify any potential harmful association between angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and unfavorable prognosis in patients with COVID-19, but we provided new evidence that the use of cardiovascular drugs (including ACEIs/ARBs,  $\beta$ -blockers, statins, and antiplatelet therapy) is associated with reduced mortality.

our study were: in-hospital mortality from any cause, need for treatment in the intensive care unit (ICU), non-invasive oxygen therapy, mechanical ventilation, length of hospital stay, and length of ICU stay. We also analyzed the use of cardiovascular drugs grouped into drug classes ( $\beta$ -blockers, ACEIs/ARBs, statins, and antiplatelet therapy). The study was approved by the Jagiellonian University Ethics Committee, decision number 1072.6120.278.2020.

### Statistical analysis

We used the SAS software, version 9.2 (SAS Institute, Cary, NC, USA), for database management and statistical analysis. The results were expressed as numerical values and percentages for categorical variables and mean values and standard deviation (SD) if parametric (assessed using the Kolmogorov-Smirnov test) or median and interquartile range (IQR) for continuous variables. To test the differences between survivors and non-survivors in means and proportions we applied the t-test and the chi-square statistic, respectively while in the case of nonparametric data, the Wilcoxon Signed Rank test were used. Using multivariable logistic regression, we searched for possible covariates of the likelihood of in-hospital death or the use of oxygen therapy. Then odds ratios (OR) and corresponding 95% confidence intervals (95% CI) were calculated for covariates influencing in-hospital death. To investigate factors determining prolonged hospitalisation (after log-transformation) the linear regression was implemented. We used Kaplan-Meier method to estimate survival curves among patients with established cardiovascular diseases, and the difference between survival curves for patients treated versus untreated with cardiovascular drugs during hospitalization were assessed with the log rank tests. In all analyses a *P*-value of 0.05 or less was considered statistically significant.

## RESULTS

### Study population

From March 6, 2020 to October 15, 2020, 1729 patients were admitted to the University Hospital in Kraków due to COVID-19 and completed their hospital course (i.e. from admission to discharge or death). Our study population included 843 women (median age [IQR], 64 [51–77] years) and 886 men (median age [IQR], 62 [50–74] years). In our sample, 950 (55%) patients were over 65 years of age.

The most prevalent cardiovascular risk factor was arterial hypertension (56.1%), followed by hyperlipidemia (27.4%) and diabetes mellitus (25.7%) (Table 1). The most common CVD were coronary artery disease (16.8% of patients), heart failure (10.3%), atrial fibrillation (13.5%), and a history of stroke (8%); 2.8% of patients had a previously implanted cardiac pacemaker or implantable cardioverter defibrillator (Table 1).

The median hospitalization length was 16 days (Table 2). Admission to the ICU was needed in 194 patients with a median length of ICU stay of 9 days. The overall in-hospital mortality was 12.9% (223 of 1729 patients), and 81% of non-survivors were older than 65 years (180 of 223 patients).

Of 1729 patients, 25.0% were treated with an ACEIs/ARBs, 40.7% with a  $\beta$ -blocker, 15.6% with a statin, and 19.9% with an antiplatelet drug (Table 2).

### Comparison of survivors with non-survivors

Tables 1 and 2 summarize the clinical characteristics of survivors and non-survivors, including risk factors and pre-existing diseases, use of medication, and results of medical tests at the time of admission. As compared to survivors, non-survivors were older, predominantly male, and had a higher prevalence of arterial hypertension, dia-

**Table 1.** Basic characteristic of participants

Characteristics	All (n = 1729)	Survivors (n = 1506)	Non-survivors (n = 223)	<i>P</i> -value <sup>a</sup>
Age, years, median (IQR)	63 (50–75)	61.0 (49–72)	78 (69–84)	<0.001
Female, n (%)	843 (48.8)	749 (49.7)	94 (42.1)	0.034
BMI <sup>b</sup> , kg/m <sup>2</sup> , mean (SD)	28.5 (5.04)	28.6 (4.86)	28.3 (6.15)	0.64
Pre-existing conditions, n (%)				
Arterial hypertension	970 (56.1)	813 (53.9)	157 (70.4)	<0.001
Hyperlipidemia	473 (27.4)	408 (27.1)	65 (29.1)	0.52
Diabetes mellitus	445 (25.7)	361 (24.0)	84 (37.7)	<0.001
Coronary artery disease	290 (16.8)	223 (14.8)	67 (30.0)	<0.001
Heart failure	179 (10.3)	121 (8.0)	58 (26.0)	<0.001
Atrial fibrillation	233 (13.5)	175 (11.6)	58 (26.0)	<0.001
Cardiac pacing <sup>c</sup>	49 (2.8)	36 (2.4)	13 (5.8)	0.004
Stroke	139 (8.0)	110 (7.3)	29 (13.0)	0.003
Asthma	106 (6.1)	97 (6.4)	9 (4.0)	0.16
COPD	89 (5.1)	72 (4.8)	17 (7.6)	0.07

Data are presented as mean (SD), median (interquartile range [IQR]) or number (%).

<sup>a</sup>For the difference between survivors and non-survivors. <sup>b</sup>Data available in 697 patients. <sup>c</sup>Cardiac pacing including any type of implantable device.

Abbreviations: BMI, body-mass index; COPD, chronic obstructive pulmonary disease; SD, standard deviation

**Table 2.** Clinical characteristics and drug therapy among survivors and non-survivors

Characteristics	All (n = 1729)	Survivors (n = 1506)	Non-survivors (n = 223)	P-value <sup>a</sup>
Parameters on admission				
SBP <sup>b</sup> , mm Hg, mean (SD)	132.3 (21.3)	133.5 (19.9)	124.4 (27.7)	<0.001
DBP <sup>b</sup> , mm Hg, mean (SD)	81.3 (14.1)	82.5 (13.1)	73.1 (16.6)	<0.001
Heart rate <sup>b</sup> /min, mean (SD)	83 (14.7)	83.3 (13.9)	86.9 (19.2)	0.003
Respiratory rate <sup>b</sup> /min, median (IQR)	14 (12–16)	14 (12–16)	16 (14–22)	<0.001
Oxygen saturation <sup>b</sup> , %, median (IQR)	96 (94–97)	96 (94–97)	94 (89–96)	<0.001
hsCRP <sup>c</sup> , mg/l, median (IQR)	36.9 (9.7–84.0)	30.1 (8.1–72.5)	93.7 (47.4–184.0)	<0.001
D-dimer <sup>b</sup> , mg/l, median (IQR)	0.77 (0.46–1.48)	0.70 (0.44–1.25)	1.59 (0.93–3.13)	<0.001
IL6, pg/ml <sup>b</sup> , median (IQR)	23.9 (6.4–63.2)	18.2 (4.7–46.4)	76.1 (36.2–166.8)	<0.001
NT-proBNP <sup>b</sup> , pg/ml, median (IQR)	594 (169–2199)	376 (133–1416)	3399 (1019–8147)	<0.001
hs cTn, ng/ml, median (IQR)	10.6 (5.2–32.9)	8.6 (4.7–20.9)	44.1 (17.6–165.7)	<0.001
Creatinine, µmol/l, median (IQR)	76.9 (63.4–96.9)	74.6 (62.4–91.2)	111.0 (80.9–173)	<0.001
Cardiovascular therapy, n (%)				
ACEI	315 (18.9)	281 (19.4)	34 (15.8)	0.21
ARB	124 (7.2)	119 (7.9)	5 (2.24)	0.002
ACEI/ARB	433 (25.0)	395 (26.2)	38 (17.0)	0.003
β-blocker	703 (40.7)	604 (40.1)	99 (44.4)	0.22
Antiplatelet therapy <sup>d</sup>	344 (19.9)	298 (19.8)	46 (20.6)	0.78
Statin	269 (15.6)	237 (15.7)	32 (14.3)	0.59
Clinical course				
Non-invasive oxygen therapy <sup>e</sup> , n (%)	465 (26.89)	332 (22.05)	133 (59.64)	<0.001
Mechanical ventilation, n (%)	154 (8.91)	48 (3.19)	106 (47.53)	<0.001
Admission to ICU, n (%)	194 (11.2)	86 (5.71)	108 (48.43)	<0.001
Length of ICU stay, days, median (IQR)	9 (5–16)	9.5 (5–18)	8 (4–14)	0.22
Length of hospital stay, days, median (IQR)	16 (11–25)	20.2 (13.1)	11 (6–17)	<0.001

Data are presented as mean (SD), median (IQR), or number (%).

<sup>a</sup>For the difference between survivors and non-survivors. <sup>b</sup>Data available in 1443 patients for SBP and DBP, 715 patients for NT-pro BNP, 1440 patients for D-dimer, 718 patients for IL6, 1397 patients for oxygen saturation, 1384 patients for heart rate, and 1231 patients for respiratory rate. <sup>c</sup>hsCRP mean (SD): all = 63.2 (75.7); survivors = 53.7 (65.9); non-survivors = 123.6 (101.9). <sup>d</sup>Antiplatelet therapy included those treated with low-dose aspirin or/and clopidogrel, ticagrelor, or prasugrel. <sup>e</sup>At least 5 l/min.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DBP, diastolic blood pressure; hsCRP, highly sensitive C-reactive protein; hs cTn, high-sensitivity cardiac troponin; ICU, intensive care unit; IL6, interleukin 6; NT-proBNP, N-terminal pro-brain natriuretic peptide; SBP, systolic blood pressure; SD, standard deviation

betes mellitus, coronary artery disease, heart failure, atrial fibrillation, stroke, and use of cardiac pacing.

The frequency of cardiovascular drug use did not differ between survivors and non-survivors, with the exception of ACEIs/ARBs, which were less commonly used by the latter group.

The median hospitalization length was shorter, and the need for ICU admission more common, in non-survivors than in survivors (Table 2). Compared to survivors, patients who died during hospitalization had significantly lower blood pressure and oxygen saturation values, higher heart and respiratory rates, and higher levels of immune-inflammatory and cardiac biomarkers on admission ( $P \leq 0.003$ ).

### Predictors of in-hospital death

Based on the multivariable logistic regression model, independent predictors of higher risk of in-hospital death from any cause were: age over 65 years, male sex, pre-existing diabetes mellitus, and a history of heart failure, whereas treatment with ACEIs/ARBs, β-blockers, statins, or antiplatelet therapy corresponded with a lower risk of death (Figure 1).

Based on Kaplan–Meier method the survival probability in patients with CVD was substantially higher among

those treated with ACEIs/ARBs, β-blockers, or statins (Figure 2).

Additional analysis was performed to assess predictors of in-hospital death in treated and not treated groups of patients. In 771 participants who were not treated during hospitalization with β-blockers, ACEIs, sartan, statin or antiplatelet drugs 94 (12.2%) died. In this group in multivariable logistic regression an older age (OR, 8.01; 95% CI, 4.58–13.33), male gender (OR, 2.58; 95% CI, 1.48–4.65), and history of hypertension (OR, 2.25; 95% CI, 1.26–3.98), heart failure (OR, 6.10; 95% CI, 2.06–19.83), or atrial fibrillation (OR 3.15, 95% CI, 1.18–8.47) were associated with higher risk of in-hospital death. Among participants treated with any of aforementioned class of cardiovascular drugs (n = 958), 829 (86.5%) survived. In analyses of in-hospital death, age above 65 years (OR, 3.72 95% CI, 2.22–6.53) and history of heart failure (OR, 1.94; 95% CI, 1.20–3.12) were associated with higher risk, while history of hypertension (OR, 0.48; 95% CI, 0.30–0.78) with lower risk of in-hospital death.

The analysis of the model in which cardiovascular drug were not taken into account an age above 65 years (OR, 5.3; 95% CI, 3.7–7.9), male sex (OR, 1.48; 95% CI, 1.09–2.00), and history of heart failure (OR, 2.14; 95% CI, 1.43–3.20) were associated with higher risk of in hospital mortality.

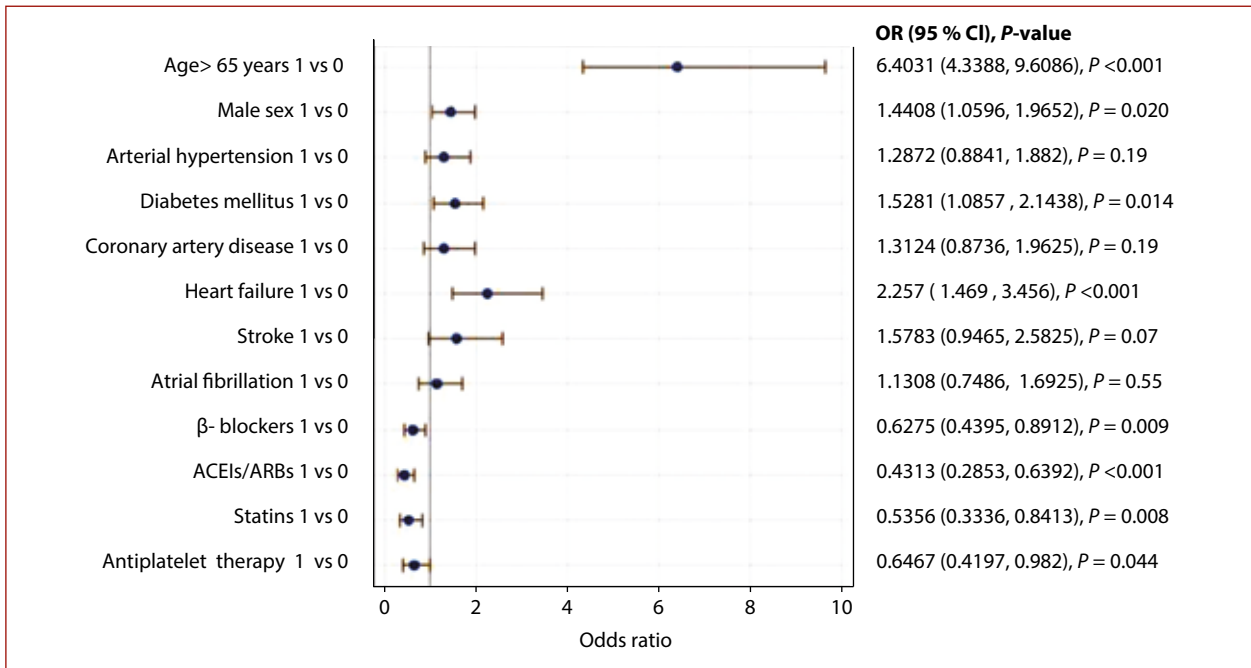


Figure 1. Multivariable logistic regression analysis

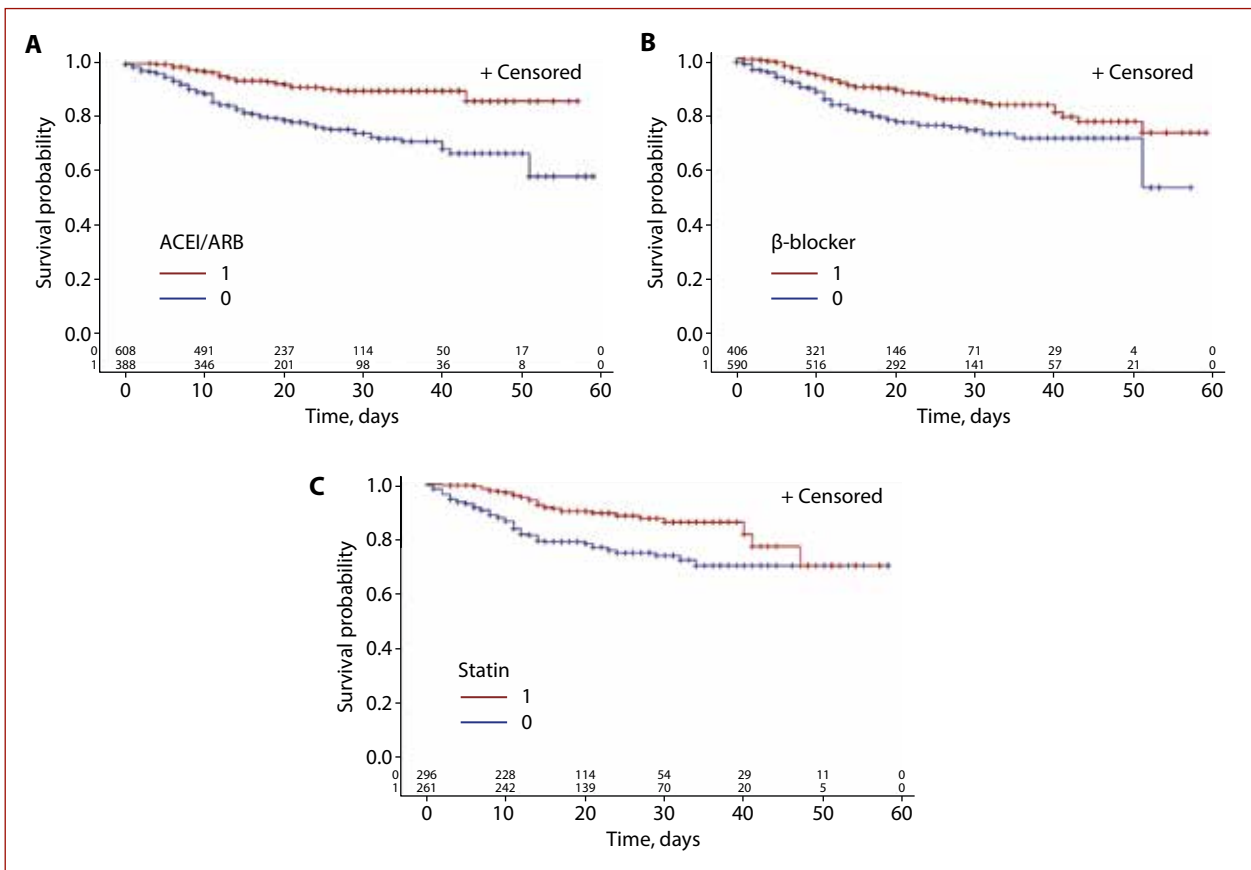


Figure 2. **A.** Survival probability among participants diagnosed with arterial hypertension, coronary artery disease, or heart failure by angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (ACEI/ARB) use. Red line indicates ACEI/ARB treatment; blue line indicates lack of ACEI/ARB treatment. TIME, days of in-hospital stay. Log rank  $P < 0.001$ . **B.** Survival probability among participants diagnosed with arterial hypertension, coronary artery disease, or heart failure by  $\beta$ -blocker use. Red line indicates  $\beta$ -blocker treatment; blue line indicates lack of  $\beta$ -blocker treatment. TIME, days of in-hospital stay. Log rank  $P < 0.001$ . **C.** Survival probability among participants diagnosed with coronary artery disease or hyperlipidemia by statin use. Red line indicates statin treatment; blue line indicates lack of statin treatment. TIME, days of in-hospital stay. Log rank  $P < 0.001$

**Table 3.** Other outcomes in survivors, analyzed using a linear regression model for length of hospitalization and a logistic regression model for oxygen therapy

Outcome	Risk factors	Model		
		R-square 0.14	P = 0.001	
		Parameter estimate	Standard error	P-value
Length of hospitalization	Age >65 years	0.12	0.02	<0.001
	Male sex	0.05	0.01	0.001
	Arterial hypertension	0.04	0.02	0.034
	Diabetes mellitus	0.05	0.02	0.004
	Coronary artery disease	–0.03	0.02	0.24
	Heart failure	0.02	0.03	0.34
	Atrial fibrillation	0.02	0.03	0.40
	Stroke	–0.01	0.02	0.52
	β-blocker	0.06	0.02	0.001
	ACEI/ARB	0.05	0.02	0.012
	Statin	0.02	0.02	0.38
	Antiplatelet therapy	0.02	0.02	0.28
Oxygen therapy	Age >65 years	1.73	1.29–2.32	
	Male sex	1.96	1.52–2.53	
	Arterial hypertension	1.26	0.92–1.74	
	Diabetes mellitus	1.13	0.83–1.52	
	Coronary artery disease	0.96	0.65–1.39	
	Heart failure	0.92	0.57–1.47	
	Atrial fibrillation	0.92	0.61–1.38	
	Stroke	1.20	0.75–1.88	
	β-blocker	1.21	0.89–1.63	
	ACEI/ARB	0.93	0.68–1.25	
	Statin	0.84	0.58–1.21	
	Antiplatelet therapy	1.01	0.70–1.45	

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CI, confidence interval; OR, odds ratio

### Other outcomes

Table 3 shows the results of the multivariable linear regression and multivariable logistic regression analysis. Older age, male sex, history of diabetes mellitus, arterial hypertension, and treatment with β-blockers or ACEIs/ARBs were independent predictors of longer length of hospital stay due to COVID-19. Age over 65 years and male sex were associated with a higher risk of requiring oxygen therapy.

## DISCUSSION

We present the data on the impact of CVD and cardiovascular drugs on in-hospital COVID-19 outcomes based on, to our knowledge, one of the largest single-center databases of COVID-19 patients in Poland [16, 17]. We confirm that pre-existing cardiovascular comorbidities and drug therapy have an impact on outcomes in patients hospitalized due to COVID-19. In our study, non-survivors were older, predominantly male, and had a higher prevalence of arterial hypertension, diabetes mellitus, coronary artery disease, heart failure, atrial fibrillation, and stroke than survivors. Moreover, we found that, beyond older age and male sex, diabetes mellitus and heart failure were independent predictors of in-hospital death from any cause. Importantly, we confirmed the beneficial effect of ACEIs/ARBs, β-block-

ers, statins, and antiplatelet therapy on survival in patients with indications for those drugs.

A higher percentage of men and individuals aged over 65 years among non-survivors in our cohort is consistent with previous reports, indicating that older age and male sex are independent risk factors for COVID-19 mortality [9, 16–18]. We have also found that, among survivors, male sex and older age were associated with requiring oxygen therapy and a longer hospital stay. The relationship between advanced age and worse prognosis in COVID-19 can be explained by a higher frequency of comorbidities, a hampered immune response with aging, and an increased susceptibility to secondary infection during hospitalization [18]. There are many hypotheses explaining sex differences in the clinical course of COVID-19, including: genetic, hormonal, immune, and behavioral factors, the distribution of cardiovascular risk factors, and differences in angiotensin-converting enzyme 2 (ACE2) expression on the cell surface [19].

Previous studies confirmed that CVD is an independent risk factor for death in patients with COVID-19 [6, 9, 20]. It is well known that the prevalence of CVD and metabolic diseases increases with age [21]. In our cohort, only heart failure and diabetes mellitus were independently associated with mortality in patients with COVID-19, which is



in accordance with the results of other studies [9, 16, 22]. Increased mortality in patients with COVID-19 with pre-existing heart failure is not surprising due to the well-known impact of chronic heart failure on reducing life expectancy [23]. Similarly to our observation, diabetes mellitus has been found to be independently associated with the severity of COVID-19 and increased COVID-19 mortality [22, 24]. Moreover, the presence of typical macrovascular complications (including heart failure and coronary artery disease) and microvascular complications (i.e. chronic kidney disease) of diabetes mellitus increases COVID-19 mortality [22, 24]. In agreement with our work, arterial hypertension was one of the most prevalent pre-existing CVD in patients with COVID-19 in previous studies [9, 20]. However, data about the relationship between arterial hypertension and COVID-19 mortality are inconclusive [9, 17]. We did not confirm the influence of arterial hypertension on in-hospital mortality.

In our study the prevalence of cardiovascular drug treatment did not differ between survivors and non-survivors, with the exception of ACEIs/ARBs, which were less commonly prescribed in non-survivors than in survivors. Moreover, we found that in-hospital use of ACEIs/ARBs is associated with a reduced probability of death (OR 0.42). It is an important observation that the aforementioned agents are not harmful, but may be fundamental for the protection of patients with CVD during the COVID-19 pandemic [8].

Our study also underlines the relationship between  $\beta$ -blocker use and mortality in COVID-19. Some previous studies showed that exposure to  $\beta$ -blockers reduced mortality in septic shock and improved outcomes in patients with respiratory failure [25, 26]. It has been hypothesized that in severely ill patients activation of the adrenergic system leads to activation of the renin-angiotensin-aldosterone system and over-expression of ACE2 receptors, which may facilitate entry of SARS-CoV-2 into host cells, leading to a more severe presentation of COVID-19 [27].  $\beta$ -blockers may therefore reduce host cell entry by the virus and reduce the catecholamine-dependent inflammatory over-response [27]. This hypothesis needs further research.

The third group of cardiovascular drugs that we found to be associated with altered COVID-19 mortality were statins. In a study of 8910 patients with COVID-19, Mehra et al. [9] noted that in-hospital statin use reduced mortality. In our registry, patients treated with statins also had a lower risk of in-hospital death (OR, 0.49).

In contrast to anticoagulant therapy, only a few observational studies have previously been reported regarding the protective or therapeutic effects of antiplatelet therapy in COVID-19, especially regarding aspirin use before and during hospitalization [28]. Due to the fact that SARS-CoV-2 infection leads to diffuse endothelial inflammation and dysfunction, which triggers platelet adhesion and aggregation [29], some authors claimed that there is a rationale to stabilize the endothelium and platelets during viral replication, with antiplatelet as well as anti-inflammatory

therapy [30]. The results we have obtained seem to support this point of view.

For all analyzed cardiovascular drugs, the key finding from our study is a positive influence on survival in patients with COVID-19. Hence, these drugs should not be withdrawn unless absolutely necessary.

The length of hospital stay in our cohort (median 16 days) confirms that COVID-19 is a serious illness requiring long treatment. Compared to survivors, patients who died had a worse clinical condition on admission and during their hospital stay. This is in accordance with other studies [3–6, 16, 17]. We therefore think that, in our cohort, the severity of clinical COVID-19 presentation on admission had a significant impact on the length of hospital stay.

Our study has several limitations and the results should be considered with caution. Firstly, the retrospective study design limits the ability to obtain complete data for patients' characteristics; however, we presented a large, comprehensive dataset of patients and checked the data carefully. Secondly, the retrospective nature of the study did not allow us to draw conclusion about cause-effect relationship.

## CONCLUSIONS

Our findings expand the previous evidence that advanced age, male sex, diabetes mellitus, and pre-existing heart failure are major predictors of poor outcomes in patients with COVID-19. The negative influence of pre-existing CVD on prognosis in patients with COVID-19 could be mitigated by in hospital use of cardiovascular drugs.

## Article information

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