ORIGINAL ARTICLE

Cardiac status and atherosclerotic cardiovascular risk of convalescents after COVID-19 in Poland

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KEY WORDS

atherosclerotic cardiovascular risk, COVID-19, prevention, risk assessment

ABSTRACT

INTRODUCTION The COVID-19 pandemic brought about cardiac complications and unfavorable lifestyle changes that may increase cardiovascular risk.

OBJECTIVES Our aim was to establish the cardiac status of convalescents several months after COVID-19, and the 10-year risk of fatal and nonfatal atherosclerotic cardiovascular disease (ASCVD) events, according to the Systemic Coronary Risk Estimation-2 (SCORE2) and SCORE2-Older Persons (OP) algorithms.

PATIENTS AND METHODS The study included 553 convalescents (mean [SD] age, 63.5 [10.26] years; 316 [57.1%] women), hospitalized at the Cardiac Rehabilitation Department, Ustroń Health Resort, Poland. The history of cardiac complications, exercise capacity, blood pressure control, echocardiography, 24-hour Holter electrocardiogram recording, and laboratory workup were assessed.

RESULTS A total of 20.7% of men and 17.7% of women ($P = 0.38$) had cardiac complications during acute COVID-19, most often heart failure (10.7%), pulmonary embolism (3.7%), and supraventricular arrhythmias (6.3%). On average, 4 months after COVID-19 diagnosis, echocardiographic abnormalities were found in 16.7% of men and 9.7% of women ($P = 0.1$), and benign arrhythmias in 45.3% of men and 44% of women ($P = 0.84$). Preexisting ASCVD was reported in 21.8% of men and 6.1% of women ($P < 0.001$). The median risk assessed by SCORE2/SCORE2-OP algorithms in apparently healthy people was high for the participants aged 40–49 years (3%; interquartile range [IQR], 2%–4%) and 50–69 years (8%; IQR, 5.3%–10%), and very high (20%; IQR, 15.5%–37%) for the participants aged 70 years and above. The SCORE2 risk in men aged over 70 years was higher than in women ($P < 0.001$).

CONCLUSIONS Data collected in the convalescents indicate a relatively small number of cardiac problems that could be associated with a history of COVID-19 in either sex, and a high risk of ASCVD, especially in men.

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INTRODUCTION The COVID-19 pandemic may lead to a potential increase in the number of patients with cardiovascular (CV) diseases and in the individual risk of atherosclerotic cardiovascular disease (ASCVD). This may be the result of complications due to the SARS-CoV-2 infection itself,[1] adverse lifestyle changes during the lockdowns and quarantine periods,[2-5] and

WHAT'S NEW?

The COVID-19 pandemic brought about cardiac complications, unfavorable lifestyle changes during the lockdowns, and limitations in preventive, diagnostic, and therapeutic procedures. We assessed the history of cardiac complications, exercise capacity, blood pressure control, echocardiography, 24-hour Holter electrocardiogram recording, and laboratory workup (cholesterol, fasting glucose, creatinine) of the convalescent group at an average of 4 months postinfection. In addition, we estimated the 10-year risk of fatal and nonfatal atherosclerotic cardiovascular disease events (ie, myocardial infarction and stroke) according to the Systemic Coronary Risk Estimation 2 algorithm. The data collected after several months of recovery indicate a relatively small number of cardiac problems that could be associated with a history of COVID-19 in both sexes, and a high underlying risk of atherosclerosis-related diseases, especially in men. Therefore, medical evaluation of COVID-19 convalescents should also include an assessment and correction of atherosclerosis risk factors.

limitations in the preventive, diagnostic, and therapeutic procedures due to changes in the organization of health care.[6,7]

COVID-19, both in the acute phasease and during recovery, is associated with an increased CV risk, including acute coronary events, pericarditis, myocarditis, arrhythmias, heart failure (HF), and pulmonary embolism (PE).[1,8-12] Up to 80% of COVID-19 convalescents experience worsening of exercise capacity, dyspnea, and chronic fatigue related to long COVID-19 syndrome.[13] Moreover, due to endothelial / glycocalyx damage and thrombus formation, SARS-CoV-2 infection can also accelerate the development of atherosclerosis and increase the risk of subsequent ASCVD events.[14,15]

However, the effects of the pandemic on the population health are not limited to the SARS-CoV-2 infection. The restrictive epidemiologic limitations and reorganization of health care contributed to a decline in the availability of outpatient and inpatient treatment, a reduction in the effectiveness of primary and secondary prevention of CV diseases, and an increase in CV mortality.[6,7] In addition, epidemiologic studies conducted on the Polish population indicated limited physical activity in 43% of people,[4] increased food and snacks consumption in 34%–43% and 52% of people,[4,5] respectively, and weight gain in 30% of the respondents,[5] which was secondary to the isolation during the pandemic. Similar effects of isolation on health-related behaviors were found worldwide.[2] These changes might translate into an increase in blood pressure (BP) and deterioration of the fat and carbohydrate balance, thus enhancing the populational risk of ASCVD.[4]

The Systemic Coronary Risk Estimation 2 (SCORE2) and the Systematic Coronary Risk Estimation 2-Older Persons (SCORE2-OP) algorithms help estimate an individual 10-year risk of CV disease (CVD) mortality and morbidity (fatal and nonfatal myocardial infarction [MI] and stroke) in apparently healthy people over 40 years old, with untreated or stable ASCVD risk factors.[16] A contact of COVID-19 convalescents with health care professionals gives the latter an opportunity to assess and correct ASCVD risk factors and improve the long-term prognosis.

The first aim of the study was to evaluate the cardiac status and the frequency of cardiac problems that could be associated with a history of COVID-19 several months after recovery in both sexes. The second aim was to assess ASCVD risk and establish the 10-year risk of fatal and nonfatal ASCVD events, according to the SCORE2 and SCORE2-OP algorithms, in the Polish COVID-19 convalescents.

PATIENTS AND METHODS The study group consisted of COVID-19 convalescents aged at least 18 years, who participated in the inpatient cardiopulmonary rehabilitation at the Cardiac Rehabilitation Department of the Ustroń Health Resort, Poland, up to 12 months after COVID-19 diagnosis. The diagnosis of COVID-19 was based on reverse transcription polymerase chain reaction testing or qualitative assessment of the presence of SARS-CoV-2 antigen in nasopharyngeal swabs.[17] Our analysis included all consecutive patients who completed the National Health Fund (NHF) cardiac rehabilitation (CR) program after COVID-19 from May 2021 (program implementation date in the Ustroń Health Resort) until the end of April 2022. The patients were admitted to the Ustroń Health Resort on schedule, from home, based on a referral from their family doctor. Eligibility criteria for the hospitalization and CR were fully consistent with the recommendations of the NHF.[18] They included: 1) complications of symptomatic SARS-CoV-2 infection in the respiratory, CV, nervous, or musculoskeletal system, or 2) decrease in muscle strength as assessed by the Medical Research Council (MRC) scale, or 3) persistent dyspnea with an intensity of 2–3 on the modified MRC (mMRC) dyspnea scale. Five patients who did not complete their hospital stay were excluded.

We retrospectively assessed the routinely available medical data listed below.

1 The medical history of CVDs, comorbidities, and treatment applied before COVID-19.

2 The course of COVID-19 and cardiac complications based on the medical history and diagnoses from hospitalization records from acute COVID-19 phase (if hospitalized). Based on these data, the severity of COVID-19 was determined as stages 1 to 4 (mild, moderate, severe, and critical, respectively), following the guidelines of the Polish Society of Epidemiologists and Infectiologists,[17] and briefly characterized in TABLE 1.

3 The cardiac symptoms present during convalescence based on medical history questionnaires.

4 The severity of dyspnea during daily activity on the 4-point mMRC dyspnea scale.[19]

5 The exercise capacity, measured as a distance in the 6-minute walk test (6MWT), in relation to the predicted distance calculated according to the formula: for men, 6MWT distance

TABLE 1 Severity of the acute phase of COVID-19

Variable	All (n = 542)	Men (n = 232)	Women (n = 310)	*P* value
Acute phase severity				
Stage 1 (asymptomatic or mildly symptomatic, SpO_2 ≥94% on room air)	262 (48.3)	97 (41.8)	165 (53.2)	<0.001
Stage 2 (fully symptomatic, SpO_2 90%–94% on room air)	172 (31.7)	76 (32.8)	96 (31)	0.13
Home oxygen therapy	51 (9.4)	27 (11.6)	24 (7.7)	0.12
Stage 3 (respiratory failure, SpO_2 <90% on room air/involvement ≥50% of the lung on CT/pulmonary embolism)	86 (15.9)	47 (20.3)	39 (12.6)	0.39
HFNO/NIV	58 (10.7)	28 (12.1)	30 (9.7)	0.37
Stage 4 (acute respiratory distress syndrome/septic shock/multiorgan failure/intensive care unit treatment)	22 (4.1)	12 (5.2)	10 (3.2)	0.67
Invasive ventilation	16 (3)	9 (3.9)	7 (2.3)	0.27
Cardiac complications during the acute phase of the disease				
Acute HF/exacerbation of chronic HF	58 (10.7)	32 (13.8)	26 (8.4)	0.04
Pulmonary embolism	20 (3.7)	9 (3.9)	11 (3.5)	0.84
Myocarditis	2 (0.4)	0	2 (0.4)	0.22
Acute coronary syndrome/cardiogenic shock	1 (0.2)	1 (0.2)	0	0.25
Ventricular arrhythmia	1 (0.2)	1 (0.2)	0	0.39
Supraventricular arrhythmia/AF	34 (6.3)	10 (4.3)	24 (7.7)	0.1
Pericardial effusion	10 (1.8)	4 (1.7)	6 (1.9)	0.86

Data are presented as number (percentage).

Abbreviations: AF, atrial fibrillation; CT, computed tomography; HF, heart failure; HFNO, high-flow nasal oxygen therapy; NIV, noninvasive ventilation

[m] = (7.57 × height [cm])–(5.02 × age [years])–(1.76 × weight [kg])–309; for women, 6MWT distance [m] = (2.11 × height [cm])–(2.29 × weight [kg])–(5.78 × age [years])+667.[20]

6 The exercise tolerance with the assessment of fatigue and dyspnea during the 6MWT on the 10-point Borg scale.[21]

7 The arterial oxygen saturation (SpO_2), measured by pulse oximetry at rest and after the 6MWT.

8 The systolic blood pressure (SBP) and diastolic blood pressure (DBP) in a series of measurements. Hypertension was defined as SBP equal to or above 140 mm Hg and DBP equal to or above 90 mm Hg, or the use of antihypertensive drugs.

In the patients who gave their written consent to additional examinations, a comprehensive cardiologic assessment was performed, and the collected laboratory data are listed below.

1 Transthoracic 2-dimensional echocardiography (TTE) using a ClearVue 550 ultrasound device (Koninklijke Philips N.V, Eindhoven, the Netherlands), following the recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging[22-24] with the assessment of:

a left ventricular (LV) end-diastolic volume index, LV end-systolic volume index, and LV ejection fraction by the biplane disk summation method;

b LV diastolic function based on the mitral peak E-wave and A-wave velocities, mitral E/A ratio and change in the mitral E velocity and the E/A ratio during the Valsalva maneuver, left atrial surface area, and the continuous wave Doppler tricuspid regurgitation systolic jet velocity;

c right ventricular (RV) basal dimension, proximal RV outflow diameter, and tricuspid annular longitudinal excursion in M-mode;

d systolic pulmonary artery pressure and the risk of pulmonary hypertension estimated based on the continuous wave Doppler tricuspid regurgitation systolic jet velocity, the inferior vena cava size and collapsibility, pulmonary velocity acceleration time, and right atrial surface area;

e the presence of pericardial effusion of at least 5 mm.

2 Twenty-four-hour electrocardiogram (24h-ECG) Holter recording conducted as per the 2017 International Society for Holter and Non-Invasive Electrocardiology and Heart Rhythm Society expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry[25] with the assessment of:

a the average, maximum, and minimum heart rate (HR);

b the number, type, and complexity of conduction disturbances;

c the number, type, and complexity of arrhythmias.

3 Laboratory blood tests:

a total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density

lipoprotein cholesterol (LDL-C), and triglycerides by the direct method; non–HDL-C calculated as follows: TC – HDL-C = non–HDL-C.[17] Hypercholesterolemia was diagnosed when the TC was at least 190 mg/dl or more, LDL-C was at least 115 mg/dl, or the participant was on lipid-lowering medications.[26-28]

b Fasting blood glucose. Impaired fasting glycemia was defined as a fasting plasma glucose concentration between 100 and 125 mg/dl.[29]

c Serum creatinine concentration and creatinine clearance (CrCl) were calculated according to the Cockcroft–Gault formula.[30]

d Plasma D-dimer concentration. The cutoff values for D-dimer were adjusted for age and assumed as normal if they were below 0.5 mg/l for people younger than 50 years, and normal below (age × 0.01) mg/l for people aged 50 years and older.[31]

4 The individual risk of ASCVD events was evaluated using the SCORE2 and SCORE2-OP algorithms in apparently healthy participants, that is those without preexisting ASCVD, diabetes, or chronic kidney disease with CrCl below 45 ml/min.[16] The 10-year risk of fatal and nonfatal CV events, such as MI or stroke, in the participants aged 40–69 years was assessed according to the SCORE2 algorithm. The SCORE2-OP algorithm was used to estimate this risk for the participants aged 70 years and older. In both algorithms, age, sex, smoking status, SBP, and non–HDL-C were considered.

Statistical analysis The results were analyzed using MedCalc software version 20.106 (MedCalc Software Ltd. Ostend, Belgium). The values of quantitative parameters were characterized using the arithmetic mean and SD or median and interquartile range (IQR), depending on the normality of the distribution assessed with the Kolmogorov–Smirnov test. Qualitative data were described using the percentage of cases. The results obtained for the age groups (44–49 vs 50–69 vs 70 years and older) and for the men vs women groups were compared using 1) the *t* test for independent variables with or without the Welch adjustment or the Mann–Whitney test; 2) one-way analysis of variance with the Tukey–Kramer post hoc test, or the Kruskal–Wallis test with the Conover post hoc test; or 3) the χ^2 test or the Fisher exact test, as required. In the tests, the *P* value below 0.05 was adopted as the limit of statistical significance.

Ethical considerations The study was approved by the Bioethical Committee of the Medical University of Silesia in Katowice, Poland (PCN/CBN/0022/KB1/68/21 of May 15, 2021, and PCN/CBN/0052/KB1/68/I/21/22 of March 29, 2022).

RESULTS

The study enrolled 553 consecutive patients, at the mean (SD) age of 63.5 (10.26) years, of whom 316 (57.1%) were women. The median time from COVID-19 diagnosis to the study enrollment was 23.1 weeks (IQR, 16.25–29).

In the acute phase of the disease, 237 patients (43.7%) required hospitalization; of those 86 (15.9% of all study patients) had severe COVID-19 (stage 3) with hypoxemic respiratory failure, and 22 (4.1% of all study patients) required intensive care unit treatment (stage 4) (TABLE 1). The remaining patients had mild to moderate infection (stage 1 or 2). The percentage of participants who had asymptomatic or mildly symptomatic COVID-19 (stage 1) was higher in women than in men (P <0.001). A total of 105 convalescents (19%) had acute cardiac complications; the most commonly diagnosed were HF exacerbation, supraventricular arrhythmias, and PE (TABLE 1). Only in the case of HF the percentage of men and women differed and was higher in men (P = 0.04).

On average 4 months after being diagnosed with COVID-19, most convalescents continued to experience symptoms that adversely affected their quality of life and exercise capacity, including symptoms that could suggest significant cardiac problems, such as dyspnea, chest pain, palpitations, or insufficient BP control (TABLE 2). The baseline exercise capacity of the convalescents was reduced to 74% (66.9%–80.6%) of the predicted value in men and 80.5% (69.1%–90.5%) in women (P <0.001); however, SpO_2 at rest and postexercise remained within the normal range (TABLE 2). Of the examined convalescents, 295 (53.3%) were diagnosed with hypertension, including 146 men (61.6%) and 149 women (47.2%) (P <0.001) (TABLE 3). Of those, 85 (15.4%) had grade 2 or 3 hypertension and required urgent modification of pharmacotherapy.

TTE was performed in 252 patients. In 18 men (16.7%) and 14 women (9.7%) (P = 0.1), it revealed at least 1 abnormality that could result from post–COVID-19 complications, such as myocarditis, pericarditis, acute coronary syndrome, unstable BP, or PE. The detected abnormalities included: impaired LV systolic function in 12 patients (4.8%), impaired RV systolic function in 3 patients (1.2%), grade 2 LV diastolic dysfunction in 5 patients (2%), and moderately increased systolic pulmonary artery pressure in 11 patients (4.4%) (TABLE 4). The proportion of patients with left or right ventricular dysfunction was higher in men than in women (P = 0.02 and 0.04, respectively).

Of 247 patients with a 24h-ECG, 110 (44.5%) showed at least 1 non–life-threatening abnormality, most often an increased number of premature ventricular or supraventricular contractions (TABLE 5). Arrhythmias occurred with a similar frequency in both sexes, except for episodes of nonsustained ventricular tachycardia (NSVT), which occurred only in men (P = 0.006). The NSVT occurred more often in the participants with LVEF below 50% than in the others (3 patients [25%] vs 3 patients [1.3%], respectively; P <0.001). Five out of 6 patients with NSVT (83.3%) had a prior diagnosis of coronary artery disease (CAD) (P <0.001).

TABLE 2 Cardiac symptoms of post-COVID/long COVID-19 syndrome and cardiac parameters during convalescence at an average of 4 months after COVID-19

Variable	All (n = 542)	Men (n = 232)	Women (n = 310)	*P* value
Cardiac symptoms of post-COVID/long COVID syndrome				
Weakness/fatigue	540 (99.6)	231 (99.6)	309 (99.7)	0.84
Exercise dyspnea	533 (98.3)	229 (98.7)	304 (98.1)	0.56
Chronic cough	56 (10.3)	21 (9.1)	35 (11.3)	0.4
Chest pain	33 (6.1)	14 (6)	19 (6.1)	0.96
Palpitations/tachycardia	75 (13.8)	17 (7.3)	58 (18.7)	<0.001
Increased blood pressure	20 (3.7)	3 (1.3)	17 (5.5)	0.01
Cardiac parameters				
Dyspnea (mMRC scale)	2 (2–2)	2 (2–2)	2 (2–2)	0.33
Degree of fatigue (Borg scale)	5 (3–6)	5 (3–5)	5 (4–6)	<0.001
Degree of dyspnea (Borg scale)	4 (1–5)	3 (0–5)	4 (1–6)	0.03
6MWT distance, m	390 (330–420)	405 (360–450)	360 (310–420)	<0.001
6MWT, %pred	76.9 (67.6–86.4)	74 (66.9–80.6)	80.5 (69.1–90.5)	<0.001
SpO_2 at rest, %, mean (SD)	96.71 (1.23)	96.72 (1.17)	96.70 (1.27)	0.83
SpO_2 post-exercise, %, mean (SD)	97.34 (0.85)	97.31 (0.78)	97.37 (0.89)	0.43

Data are presented as number (percentage) or median (interquartile range) unless indicated otherwise.

Abbreviations: mMRC, modified Medical Research Council dyspnea scale; 6MWT, the 6-minute walk test; %pred, percentage of predicted value

TABLE 3 Blood pressure control and hypertension grades during convalescence at an average of 4 months after COVID-19

Blood pressure control with hypertension grades	All (n = 553)	Men (n = 237)	Women (n = 316)	*P* value
SBP at rest, mm Hg	132 (119–147)	138 (124–149)	129 (118–142)	0.003
DBP at rest, mm Hg	80 (74–86)	83 (75–90)	78 (72–82)	<0.001
SBP postexercise, mm Hg	133 (121–148)	137 (127–150)	131 (118–135)	0.008
DBP postexercise, mm Hg	79 (83–87)	83 (74–90)	76.5 (70–82)	<0.001
Optimal BP (SBP <120 mm Hg and DBP <80 mm Hg)	61 (11)	16 (6.8)	45 (14.2)	<0.001
Normal BP (SBP 120–129 mm Hg or DBP 80–84 mm Hg)	132 (23.9)	53 (22.4)	79 (25)	0.02
High normal BP (SBP 130–139 mm Hg or DBP 85–89 mm Hg)	65 (11.8)	22 (9.3)	43 (13.6)	0.009
Grade 1 HA (SBP 140–159 mm Hg or DBP 90–99 mm Hg)	159 (28.8)	87 (36.7)	72 (22.8)	0.23
Grade 2 HA (SBP 160–179 mm Hg or DBP 100–109 mm Hg)	75 (13.6)	35 (14.8)	40 (12.7)	0.56
Grade 3 HA (SBP ≥180 mm Hg or DBP ≥110 mm Hg)	10 (1.8)	6 (2.5)	4 (1.3)	0.53
Isolated systolic HA (SBP ≥140 mm Hg and DBP <90 mm Hg)	51 (9.2)	18 (7.6)	33 (10.4)	0.04

Data are presented as number (percentage) or median (interquartile range).

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; HA, hypertension; SBP, systolic blood pressure

The results of laboratory workup are shown in TABLE 6. Hypercholesterolemia was diagnosed in 72 men (72.7%) and 103 women (78.6%) (*P* = 0.21). Of 231 patients, non–HDL-C level below 150 mg/dl was found in 89 patients (38.5%), between 150 and 199 mg/dl in 87 patients (37.7%), between 200 and 249 mg/dl in 43 patients (18.6%), and 250 mg/dl or higher in 12 patients (5.2%). The non–HDL-C level above 150 mg/dl was found in 64.6% of men and 59.1% of women (*P* = 0.39). Impaired fasting glycemia was found in 13 men (18.1%) and 6 women (5.7%) without previously diagnosed diabetes (*P* = 0.009). Increased values of D-dimers were found in 32 men (34.4%) and 52 women (40.9%) (*P* = 0.33); including 5 patients (50%)

TABLE 4 Echocardiographic parameters during convalescence at an average of 4 months after COVID-19

Echocardiographic parameters		All (n = 252)	Men (n =108)	Women (n = 144)	*P* value
LVEDVi, ml/m^2		65.78 (13.88)	72.2 (15.66)	60.88 (9.91)	<0.001
LVESVi, ml/m^2		28.04 (9.15)	32.06 (11.17)	24.98 (5.59)	<0.001
LVEF, %		57.45 (6.01)	56.01 (6.77)	58.53 (5.23)	0.001
LA area, cm^2		19.6 (3.87)	21.45 (4.29)	18.22 (2.83)	<0.001
Patients with LV systolic dysfunction	HFmrEF	9 (3.6)	6 (5.7)	3 (2.1)	0.13
	HFrEF	3 (1.2)	3 (2.8)	0	0.04
Patients with LV diastolic dysfunction	Grade 1	83 (33.6)	50 (47.2)	33 (23.4)	<0.001
	Grade 2	5 (2)	4 (3.8)	1 (0.7)	
	Grade 3	0	0	0	
RVD1, mm		37.28 (4.4)	40.25 (3.42)	35.06 (3.69)	<0.001
RVOT prox, mm		27.72 (4.32)	30.06 (4.5)	25.97 (3.21)	<0.001
RA area, cm^2		15.64 (3.3)	17.27 (3.24)	14.45 (2.81)	<0.001
TAPSE, mm		23.79 (4.24)	23.69 (4.69)	23.85 (3.88)	0.77
Patients with RV systolic dysfunction (TAPSE <16 mm)		3 (1.2)	3 (2.8)	0	0.04
TR Vmax, m/s		1.88 (0.29)	1.8 (0.28)	1.93 (0.29)	0.02
TRPG, mm Hg		14.64 (4.63)	13.62 (4.45)	15.24 (4.66)	0.049
SPAP, mm Hg		17.78 (4.88)	16.77 (4.75)	18.36 (4.89)	0.07
AcT, ms		126.47 (26.29)	122.4 (25.30)	129.49 (26.68)	0.03
Patients at risk of pulmonary hypertension	Low	241 (95.6)	102 (94.4)	139 (96.5)	0.42
	Intermediate	11 (4.4)	6 (5.6)	5 (3.5)	
	High	0	0	0	
Patients with pericardial effusion		4 (1.9)	1 (1.1)	3 (2.4)	0.49

Data are presented as mean (SD) or number (percentage).

Abbreviations: AcT, pulmonary velocity acceleration time; HFmrEF, heart failure with mid-range ejection fraction; HFrEF, heart failure with reduced ejection fraction; LA, left atrium; LV, left ventricle; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume index; RA, right atrium; RVD1, basal right ventricular linear dimension; RVOT prox, proximal right ventricular outflow diameter; SPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular longitudinal excursion by M-mode; TRPG, peak systolic tricuspid pressure gradient; TR Vmax, tricuspid regurgitation systolic jet velocity

with an increased risk of pulmonary hypertension assessed on TTE.

Of 553 patients included in the study, 22 men (21.8%) and 8 women (6.1%) (P <0.001) had a history of ASCVD; approximately half had comorbidities increasing the risk of atherosclerosis, such as diabetes, chronic kidney disease, hypercholesterolemia, and obesity (TABLE 7). Current smokers accounted for 10.3% (24 participants) of those with known smoking status, but up to 25.8% of individuals aged 40–50 years. The history of smoking was more common in men than in women (P <0.001).

In 233 apparently healthy (in terms of ASCVD) participants aged 40 years or older, the obtained data allowed for assessing the 10-year risk of fatal and nonfatal atherosclerotic CV events (TABLE 8). Of those, 89 (38.2%) had high, and 31 (13.3%) very high ASCVD risk, and these were more often men (P <0.001). The median risk assessed with the SCORE2/SCORE2-OP algorithms in apparently healthy people was high for the participants aged 40–49 years (3%; IQR, 2%–4%) and 50–69 years (8%; IQR, 5.3%–10%), and very high (20%; IQR, 15.5%–37%) for the participants aged 70 years and more (TABLE 8). The SCORE2 risk in the participants below the age of 70 was higher in men than in women (P <0.001).

DISCUSSION The present study assessed the cardiac status and the risk of cardiac problems that could be associated with a history of COVID-19

TABLE 5 24-hour Holter electrocardiography parameters during convalescence at an average of 4 months after COVID-19

24-hour Holter ECG parameters		All (n = 247)	Men (n = 106)	Women (n = 141)	*P* value
Average HR, bpm		73.55 (8.8)	73.58 (9.4)	73.52 (8.34)	0.95
HR <40 bpm at night	Patients	10 (4)	7 (6.6)	3 (2.1)	0.1
	Events	3.5 (2–5)	0	0	0.14
HR <50 bpm during the day	Patients	65 (26.3)	27 (25.5)	38 (27)	0.79
	Events	2 (1–5)	0	0	0.86
2nd degree AV block Mobitz 1	Patients	0	0	0	–
2nd degree AV block Mobitz 2	Patients	3 (1.2)	2 (1.9)	1 (0.7)	0.58
	Events	1 (1–1)	2 (2–2)	2 (2–2)	0.41
3rd degree AV block	Patients	0	0	0	–
Premature supraventricular beats (>200/day)	Patients	37 (15)	13 (12.3)	24 (17)	0.3
	Events	390 (272.5–654)	578 (271.8–1250.3)	350 (272.5–537)	0.24
AF	Patients	8 (3.2)	2 (1.9)	6 (4.3)	0.3
Premature ventricular beats (>100/day)	Patients	37 (15)	20 (18.9)	17 (12.1)	0.14
	Events	533 (235–1205.3)	565.5 (278.5–1562.5)	430 (221.3–970.5)	0.48
Ventricular tachycardia	Nonsustained	6 (2.4)	6 (5.7)	0	0.006
	Sustained	0	0	0	–

Data are presented as median (interquartile range) or number (percentage).

Abbreviations: AV block, atrioventricular block; ECG, electrocardiogram; HR, heart rate; others, see **TABLE 1**

TABLE 6 Laboratory parameters during convalescence at an average of 4 months after COVID-19

Laboratory parameter	All (n = 231)	Men (n = 99)	Women (n = 132)	*P* value
Total cholesterol, mg/dl	225 (188.35–276.2)	219.6 (183.5–255.2)	235.9 (197.35–280.65)	0.02
HDL-C, mg/dl	64.1 (48.78–84.43)	53.6 (41.03–69.95)	70.45 (57.5–91.4)	<0.001
LDL-C, mg/dl	139.55 (115.8–170.9)	129.8 (111.78–158.48)	146.4 (119.45–171.08)	0.03
Triglycerides, mg/dl	165.5 (122.83–224.93)	184.4 (121.25–270.38)	155.5 (123.7–205)	0.06
Non–HDL-C, mg/dl	164.2 (130.53–195.25)	164.3 (135.38–191.55)	162.05 (128.35–202.4)	0.93
Fasting glucose, mg/dl	88.05 (80.4–97.1)	90.4 (81.6–100.2)	85.3 (78.95–94.05)	0.006
Creatinine, mg/dl	0.93 (0.85–1.02)	0.98 (0.92–1.13)	0.88 (0.82–0.95)	<0.001
CrCl, ml/min	90.63 (73.1–108.04)	101.33 (85.41–119.08)	81.66 (68.71–98.29)	<0.001
D-Dimer, mg/l	0.45 (0.27–0.81)	0.39 (0.25–0.77)	0.5 (0.31–0.83)	0.052

Data are presented as median (interquartile range).

SI conversion factors: to convert total cholesterol, HDL-C, and LDL-C to mmol/l, multiply by 0.0259; triglycerides to mmol/l, by 0.0113; glucose to mmol/l, by 0.055; serum creatinine to μmol/l, by 88.4.

Abbreviations: CrCl, creatinine clearance; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

at an average time of 4 months after recovery, taking into account sex differences. Altogether, 19% of the patients had a history of CV complications related to the acute phase of COVID-19, most often HF (10.7%, more often in men), PE (3.7%), and supraventricular arrhythmias (6.3%). After several months, over 90% of the convalescents continued to have dyspnea and reduced exercise tolerance. However, their resting and exercise SpO_2 was normal, and some echocardiographic abnormalities that could result from complications of COVID-19 were found in only 12.7% of the patients, with a similar frequency in men and women. Additionally, in 44.5% of the convalescents of both sexes, non–life-threatening arrhythmias were recorded on 24h-ECG, most often an increased number of premature ventricular or supraventricular contractions. The study evaluated the underlying ASCVD risk in the COVID-19 convalescents and calculated the 10-year risk of fatal and nonfatal ASCVD according to the SCORE2/SCORE2-OP algorithms. Of the respondents, 21.8% of men and 6.1% of women had a history of ASCVD (equivalent to

TABLE 7 Medical history of cardiovascular diseases, comorbidities, and treatment administered

Cardiovascular diseases, comorbidities, and treatment applied		All (n = 553)	Men (n = 237)	Women (n = 316)	*P* value
Coronary artery disease		96 (17.6)	52 (21.9)	44 (13.9)	0.01
History of myocardial infarction		28 (5.1)	25 (10.5)	3 (0.9)	<0.001
Previous coronary revascularization		46 (8.3)	37 (15.7)	9 (2.8)	<0.001
Stroke		15 (2.7)	8 (3.4)	7 (2.2)	0.44
Hypertension		404 (73.1)	186 (78.5)	218 (69)	0.01
Chronic heart failure		43 (7.8)	24 (10.1)	19 (6)	0.07
Atrial fibrillation		45 (8.1)	18 (7.6)	27 (8.5)	0.69
Venous thromboembolism or pulmonary embolism[a]		21 (3.8)	9 (3.8)	12 (3.8)	>0.99
Diabetes		151 (27.3)	71 (30)	80 (25.3)	0.23
Chronic kidney disease (CrCl <60 ml/min)[b]		21 (7.5)	4 (3.2)	17 (11)	0.02
Hypercholesterolemia		247 (44.7)	120 (50.6)	127 (40.2)	0.01
Overweight and obesity	BMI 25–29.9 kg/m^2	88 (28.6)	34 (6.2)	54 (9.8)	0.07
	BMI ≥30 kg/m^2	245 (44.3)	93 (39.2)	152 (48.1)	0.04
Smoking status	Current	24 (4.3)	16 (15)	8 (5.7)	<0.001
	Former	88 (15.9)	48 (44.9)	40 (28.6)	
	Never	135 (24.4)	43 (40.2)	92 (65.7)	
	Unknown	306 (55.3)	–	–	
β-Blockers		231 (52)	90 (47.4)	141 (55.5)	0.09
Antiarrhythmic drugs		9 (2)	5 (2.6)	4 (1.6)	0.51
ACE-I/ARB		199 (44.5)	96 (50.3)	103 (40.4)	0.04
MRA		26 (5.9)	16 (8.5)	10 (3.9)	0.045
Loop diuretics		43 (9.7)	16 (8.5)	27 (10.7)	0.44
Insulin (percentage of patients diagnosed with diabetes)		31 (26.7)	13 (23.6)	18 (29.5)	0.48
Acetylsalicylic acid		105 (23.6)	55 (29.1)	50 (19.6)	0.02
Anticoagulants		58 (12.9)	27 (14)	31 (12.2)	0.57

Data are presented as number (percentage).

a Not related to COVID-19

b According to the National Kidney Foundation[50]

Abbreviations: ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; BMI, body mass index; CrCl, creatinine clearance calculated from the Cockcroft-Gault formula; MRA, mineralocorticoid receptor antagonists

a very high ASCVD risk). Current smokers accounted for 10.3% of those with known smoking status (more common in men); non–HDL-C of at least 150 mg/dl was found in 61.5% of the patients, and half of the participants had elevated BP values (more commonly men). Consequently, the risk of ASCVD, according to the SCORE2/SCORE2-OP, was high or very high in 63.5% of men and 42.4% of women, even without a history of ASCVD. These data indicate an urgent need to analyze and correct the ASCVD risk factors in this population.

Hypertension, diabetes, and CAD are common in patients hospitalized for COVID-19, especially in men,[1] which our study also confirmed. A possible association has been proven between CVDs and CV risk factors and a more severe course of COVID-19 (relative risk of 5 for CVDs, 2.5 for hypertension, and 3.2 for diabetes),[32-34] and an increase in the risk of death (crude fatality ratio of 13.2% for individuals with CVDs and 9.2% for diabetic patients vs 1.4% for patients with no comorbid conditions).[1,33-36]

The epidemiologic data suggest a sex-related difference in the severity of COVID-19, with a more favorable outcome in women than in men.[37,38] On the other hand, women more often experience the symptoms of long COVID-19.[13] The sex-related differences are nowadays explained by sex-specific expression patterns of a protein mediating the virus binding and some differences in response of the immune, coagulation, and endocrine systems to infection and stress.[37,38] In our group, the percentage of women with asymptomatic or mildly symptomatic infection was also higher than of men, although women more often experienced some cardiac symptoms of long COVID-19, such as palpitations / tachycardia and unstable BP during the recovery period.

Cardiac complications of COVID-19 are a significant clinical problem mainly in the acute

TABLE 8 The 10-year risk of fatal and nonfatal atherosclerotic cardiovascular events according to the Systematic Coronary Risk Estimation 2 and the Systematic Coronary Risk Estimation 2-Older Persons algorithms by age and sex

ASCVD	All (n = 233)	Men (n = 101)	Women (n = 132)	*P* value
Age 40–49 years: 31 patients (13.3%)				
Primary prevention	31 (100)	16 (51.6)	15 (48.4)	0.86
Secondary prevention	0	0	0	
Low risk	11 (35.5)	1 (6.2)	10 (66.7)	0.002
Moderate risk	15 (48.4)	12 (75)	3 (20)	
High risk	5 (16.1)	3 (18.8)	2 (13.3)	
Very high risk	0	0	0	
SCORE2 risk[a], %	3 (2–4)	4 (3–6.3)	2 (1–3)	<0.001
Age 50–69 years: 184 patients (79%)				
Primary prevention	159 (86.4)	60 (77.9)	99 (92.5)	0.005
Secondary prevention	25 (13.6)	17 (22.1)	8 (7.5)	
Low risk	19 (10.3)	3 (3.9)	16 (15)	0.001
Moderate risk	66 (35.9)	21 (27.3)	45 (42.1)	
High risk	73 (39.7)	36 (46.8)	37 (34.6)	
Very high risk	26 (14.1)	17 (22.1)	9 (8.4)	
SCORE2 risk[a], %	8 (5.3–10)	9 (7.5–11)	7 (5–10)	<0.001
Age ≥70 years: 18 patients (7.7%)				
Primary prevention	13 (72.2)	3 (37.5)	10 (100)	0.006
Secondary prevention	5 (27.8)	5 (62.5)	0	
Low risk	0	0	0	0.01
Moderate risk	2 (11.1)	0	2 (20)	
High risk	11 (61.1)	3 (37.5)	8 (80)	
Very high risk	5 (27.8)	5 (62.5)	0	
SCORE2-OP risk[a], %	20 (15.5–37)	17 (17–21.5)	36 (12–41.5)	0.65

Data are presented as median (interquartile range) or number (percentage).

a Only patients without preexisting atherosclerotic cardiovascular diseases, diabetes, or chronic kidney disease with CrCl <45 ml/min

Abbreviations: ASCVD, atherosclerotic cardiovascular diseases; SCORE2, Systemic Coronary Risk Estimation 2 algorithm; SCORE2-OP, Systematic Coronary Risk Estimation 2-Older Persons

phase of the disease and the early recovery period, however, they can also impact short- and long-term outcomes.[8] In a meta-analysis of 220 studies by Pellicori et al,[1] as in our group, the most frequent acute complications were supraventricular arrhythmias / atrial fibrillation (8.5%; range, 0%–24.7%), venous thromboembolism (6.1%; range, 0%–46.2%), PE (4.3%; range, 0%–23.8%), and HF (6.8%; range, 0%–24%). Renda et al[9] reported that age, female sex, in-hospital acute HF, and atrial fibrillation during the acute COVID-19 were predictors of mortality and major adverse CV and cerebrovascular events among 6-month COVID-19 convalescents.

Rezel-Potts et al[10] investigated a group of 428 650 convalescents and found that the incidence of new-onset diabetes and CVDs also increased (adjusted rate ratio, 5.82; 95% CI, 4.82–7.03 for CVD, and 1.81; 95% CI, 1.51–2.19 for diabetes) in the first 4 weeks after COVID-19, and then dropped to values equal to the control group between 13 and 52 weeks after COVID-19 onset. Xie et al,[11] in their study of 153 760 patients from the national databases of the United States Department of Veterans Affairs, provided evidence that increased CV risk (atherosclerotic and nonatherosclerotic complications) persists for up to a year and is independent of age, sex, and major ASCVD risk factors. In our cardiac assessment carried out on average 4 months after COVID-19, the frequency of ventricular and supraventricular arrhythmias also remained higher than that reported for the general population,[39] while the proportion of patients with LV systolic and diastolic dysfunction was similar in our study and the general population.[40] The echocardiographic abnormalities and cardiac arrhythmias were found with a similar frequency in men and women. The exercise capacity of the convalescents was reduced, especially in men, who were less likely to experience the mildly symptomatic acute phase of COVID-19. However, the pathogenesis of low

cardiorespiratory fitness, chronic dyspnea, and fatigue after COVID-19 is more complex, and symptoms do not directly depend on the severity of acute SARS-CoV-2 infection or the dysfunction of the heart and lungs.[41-43]

ASCVDs are the leading cause of death in both sexes, although epidemiologic observations indicate that women are less likely to suffer from CV complications than men of the same age.[44] These sex-related differences in atherogenesis are associated with, among others, differential regulation of glycemia, insulin sensitivity, lipid metabolism, and adipose tissue homeostasis controlled, for example, by sex hormones.[45,46] In our analysis, the preexisting ASCVD, and some factors increasing the risk of atherosclerosis, that is, smoking, hypertension, and impaired fasting glycemia were more frequent in men than in women. Consequently, the risk of ASCVD according to the SCORE2/SCORE2-OP algorithms was higher in men than in women aged below 70 years.

Studies conducted in the Polish population before the COVID-19 pandemic[26-28,47] indicated an equally high level of main ASCVD risk factors as in the described group of COVID-19 convalescents. Lu et al[47] analyzed the data from the HAPIEE (Health, Alcohol and Psychosocial Factors in Eastern Europe) study, covering 30 882 adults aged 45–69 years from the Czech Republic, Russia, Poland, and Lithuania, collected from 2002 to 2008. In this group, which matched the age of the participants in our study, the prevalence of hypertension and hypercholesterolemia was over 60% and 75% in men and 55% and 80% in women, respectively. The mean (SD) BP was assessed as SBP 138.38 (21.29) mm Hg, DBP 86.33 (11.83) mm Hg, and the mean (SD) TC level was 226 (43) mg/dl. These results are very close to our findings in the COVID-19 convalescents, also in terms of higher prevalence of hypertension in men and hypercholesterolemia in women. Unfortunately, the authors did not estimate CV risk according to the SCORE algorithm.

In the Polish multicenter nationwide health study WOBASZ II (2013–2014),[26] the prevalence of hypertension and hypercholesterolemia in the older subgroup aged 50–79 years was 46.7%–60.4% and 71.3%–79.9%, respectively. In that study, 18.6% of the participants with hypertension and hypercholesterolemia had a high SCORE risk. It is worth noting that the percentage of patients with hypercholesterolemia in the Polish population has not changed since the 2003–2005 WOBASZ study.[27] Similarly, in the subgroup of patients aged 40–79 years from the NATPOL study (2011),[28] mean LDL-C concentrations were as high as the values found in the COVID-19 convalescents, and high TC of at least 190 mg/dl was found in 54.3% of the participants. It is worth remembering that according to the 2021[16] and earlier guidelines of the European Society of Cardiology on CVD prevention in clinical practice, the Polish population has been classified as one at a high risk of ASCVD, and high values of ASCVD risk factors found in the COVID-19 convalescents probably only reflected this status.

The percentage of patients in primary prevention with high ASCVD risk in the post–COVID-19 group was significantly higher (38.4% vs 3.5%) than in the general population participating in the Program of Prevention and Early Detection of Cardiovascular Disease of the NHF conducted in 2017 and 2018 by Liput-Sikora et al.[48] The most crucial factor contributing to the low-risk value in the above study was probably low mean (SD) age of the participants (43.4 [7] years for men and 43.2 [6.9] years for women), which in turn affected the age-related BP and lipid values.[49]

Limitations The obtained retrospective data did not allow for unequivocal determination of the etiology of abnormalities found in additional tests as resulting from COVID-19 or being a consequence of a chronic disease. Moreover, the percentage of patients with acute coronary syndrome secondary to COVID-19 is most likely underestimated due to the participation of these patients in an NHF care program intended for patients with MI (KOS-ZAWAŁ).

Patients with CVDs and diabetes have a higher risk of developing COVID-19 and cardiac complications. In addition, there has been an increase in the number of newly diagnosed cases of CVDs and diabetes in the first several months after COVID-19 diagnosis. That may result in higher values of the parameters determining the ASCVD risk in the convalescents than in the general population.

As the method for ASCVD risk assessment changed in 2021 (SCORE algorithm assessing the 10-year risk of death due to ASCVD was replaced with new SCORE2/SCORE2-OP algorithms estimating the 10-year risk of fatal and nonfatal ASCVD events), comparisons of the risk level in the populations assessed according to different algorithms are of limited usefulness.

The tissue Doppler imaging was unavailable in the on-site echocardiography facility, and an assessment of the LV diastolic function using this method was not performed.

Conclusions Despite reports of cardiac complications in 19% of the participants in the acute phase of the disease, a relatively small number of cardiac problems that could be associated with a history of COVID-19 are present in both sexes after an average of 4 months of recovery. On the other hand, our data indicated a high prevalence of ASCVD risk factors in the COVID-19 convalescents, especially in men. The high ASCVD risk is an unjustifiably overlooked background for the increased CV risk associated with SARS-CoV-2 infection, which may contribute to the deterioration of the long-term prognosis of the convalescents.

ARTICLE INFORMATION

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