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COVID-19 as additional cardiovascular risk factor in young and middle-aged patients

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Objective. This study aimed to determine the prevalence and risk factors of new cases of coronary heart disease (CHD), arterial hypertension (AH) and diabetes mellitus in patients with new coronavirus infection (COVID-19).
Methods. This open comparative, prospective study included 658 patients: 111 (16.8%) men and 547 (83.2%) women aged from 25 to 44 years — 432 (65.6%), from 45 to 59 years — 226 (34.4%) subjects. Depending on the history of COVID-19 infection (between March 2020 and June 2021) patients were divided into two groups. The main group included 416 patients (63.2%) aged 40 (33; 47) years who had history of COVID-19 (343 (82.5%) with mild, 56 (13.5%) with moderate-to-severe course, 17 (4%) with severe course); the comparison group included 242 (36.8%) patients aged 41 (32.8; 47) years who did not have COVID-19.
Results. There was a statistically significant increase of systolic blood pressure (SBP) (from 127 to 129 mm Hg, p = 0,006), number of hypercholesterolemic (from 6,7% to 48,3%, p < 0.001) and overweight patients (from 40.1% to 75.9%, p < 0.001). During the observation period, one in four (23.3%) young and middle-aged subjects developed: 8.6% hypertension, 6.3% diabetes mellitus (DM), and 5.5% CHD. The estimated risk of premature cardiovascular events after COVID-19 was 74% higher than in the comparison group. In the group of patients who developed new cases of AH, CHD and DM, moderately severe (p < 0.001) and severe course (p = 0.002) of COVID-19 with subsequent admission to hospital were registered more frequently. In the group of patients who did not develop new cases of studied events mild disease course (p < 0.001) of COVID-19 was more prevalent.
Conclusions. One in four patients aged 18 to 59 years may develop cardiovascular event as the long term COVID-19 complication. The risk of premature cardiovascular events after COVID-19 infection was 74% higher than in

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a group of people of similar age and sex. Smoking, hypercholesterolemia, excess body weight, three or more cardiovascular risk factors may be considered as factors for timely stratification of patients due to the risk of developing CHD or DM.

Keywords: COVID-19, risk factors, cardiovascular diseases, age.

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Introduction

COVID-19 (the new coronavirus infection, COrona-VIrus Disease 2019) has posed certain challenges to both healthcare system and individual person's health. In addition large prevalence and direct socio-economic losses, the potential impact of COVID-19 on cardiovascular morbidity and mortality is of particular concern since there is an evidence of a more severe course of the disease in both patients with cardiovascular disease (CVD) risk factors (RFs) and established CVDs. The results of numerous studies indicate the mutual aggravation of the COVID-19 course and cardiovascular pathology. It has been shown that from15 % to 70 % of deaths are registered in patients with cardiovascular pathology accompanying the COVID-19. The pathogenesis of cardiovascular damage in the background of inflammation are complex and include the effects of hypoxia, systemic proinflammatory effects, direct myocardial and vascular endothelial damage [1]. Currently, more and more data are being collected on the consequences of this infection — specifically, that the acute phase of COVID-19 is the beginning of the continuum on the way to recovery. According to a study by O'Hearn M. et al., most admissions due to new coronavirus infection occur in patients with concomitant cardiometabolic disease [2]. The authors estimate that among 906,849 admissions, 30 % occurred in patients with obesity, 26 % with arterial hypertension (AH), 20 % with diabetes mellitus (DM) and 12 % with heart failure. The mean age of admitted patients was 63 (51–74) years, including 1678 (61.2 %) males and 1063 (38.8 %) females.

The meta-analysis of 56 studies included 159,698 patients with COVID-19 and showed that acute cardiac injury (odds ratio (OR) 13.29, 95 % CI 7.35–24.03), arterial hypertension (AH) (OR 2.60, 95 % CI 2.11–3.19), heart failure (OR 6, 72, 95 % CI 3.34–13.52), cardiac arrhythmias (OR 2.75, 95 % CI 1.43–5.25), cardiac heart disease (CHD) (OR 3.78, 95 % CI 2.42–5.90), and cardiovascular diseases (CVD) (OR 2.61, 95 % CI 1.89–3.62) were significantly associated with mortality [3]. Cardiac arrhythmias (OR 7.03, 95 % CI 2.79–17.69), acute cardiac injury (OR 15.58, 95 % CI 5.15–47.12), CHD (OR 2.61, 95 % CI 1.09–6.26), CVD (OR 3.11, 95 % CI 1.59–6.09) and AH (OR 1.95, 95 % CI 1.41–2.68) were also significantly associated with the admission to intensive care unit in patients with COVID-19.

Data from the ACTIV international registry both involved outpatients (n = 1057, men 41.91 %, women 58.09 %) and inpatients (n = 4751, men 46.39 %, women 53.61 %) of the Eurasian region with COVID-19 showed more severe clinical couse in patients with comorbidities in admitted patients who were older than outpatients. The median age was higher in those with the more severe course of COVID-19 (lower and upper quartiles: Q1-Q3) 59.0 (50–69) and 49.9 (38–60) years, respectively]. Moreover, females tended to have the severe course of COVID-19 more often than males (53.6 %). Obesity (OR 1.079, 95 % CI (0.829–1.404, $p = 0.57$) and AH (OR 3.123, 95 % CI 2.946–4.852, $p < 0.01$), along with DM, chronic kidney disease, chronic obstructive pulmonary disease and cancer substantially affected the prognosis. The unfavorable cluster of 4 diseases in terms of prognosis can be determined: AH, CHD, heart failure, DM [4].

Given the available literature data on the prevalence of cardiovascular complications and its association with the history of infection, as well as the contribution of COVID-19 to the development of cardiovascular risk (CVR), we can assume that the number of patients with the above-mentioned complications will increase. In this regard, young and middle-aged patients (both with and without cardiovascular risk

factors) should be monitored on the subject of premature cardiovascular morbidity development in the after COVID-19.

Due to of the role of carbohydrate metabolism disorders in the development of atherosclerosis, high cardiovascular morbidity and mortality, the registration of the new cases of type 2 DM, is also important for the prediction of the disease course. The literature data on COVID-19 as risk factor for CVD in young and middle-aged individuals are currently scarce and contradictory due to different methodological approaches and inclusion criteria, which led to the conduction of this study.

The aim of the study was to determine the prevalence and risk factors of new cases of CHD, AH, and diabetes mellitus in patients who underwent COVID-19.

Material and Methods

A total of 658 patients were included in an open comparative prospective study: 111 (16.8 %) men and 547 (83.2 %) women who underwent medical examination by a general practitioner. There were 432 (65.6 %) patients aged 25–44 years and 226 (34.4 %) patients aged 45–59 years. The SCORE score on the relative risk scale (RR) was 2.47 ± 2.5 % for people aged 40 years and older; 1.05 ± 0.4 for people under 40 years old. Low CVR was found in 202 (30.6 %), moderate in 389 (59.1 %), high in 48 (7.2 %), and very high in 19 (3.1 %) patients.

Inclusion criteria: men and women aged 25 to 59 years; compliance with all study procedures; signed written consent to participate in the study.

Exclusion criteria: mental disorder; alcohol dependence; participation in another study.

Patients were divided into two groups based on whether they had COVID-19 infection (between March 2020 and June 2021): the main group included 416 (63.2 %) patients aged 40 (33; 47) years after COVID-19; the comparison group included 242 (36.8 %) patients aged 41 (32.8; 47) years without COVID-19 history.The groups were comparable by age (p = 0.324) and gender: the main group had 361 (86.8 %) women and 55 (13.2 %) men, the comparison group had 197 (81.4 %) women and 45 (18.6 %) men, p = 0.083. The diagnosis of COVID-19 was confirmed by the positive oral and nasopharyngeal smear polymerase chain reaction test for SARS-CoV-2 and/or typical pattern according to chest computed tomography.Data on the history of infection and the severity of the disease were obtained from the patients' medical records.

At the first visit, all patients were assessed for demographic characteristics, the presence of risk factors (smoking, obesity, hypercholesterolemia), concomitant CVDs (AH, CHD, myocardial infarction history, DM), and laboratory data (total cholesterol, glucose). At the second visit, which took place one year after, in addition to the assessment of the above-mentioned indicators, new cases of AH, CHD, and DM diagnosed according to the existing guidelines were registered [5, 6]. The presence of CHD was performed by the history of myocardial infarction, revascularization or confirmed coronary atherosclerosis by coronary angiography (CAG).

All patients with new cases were advised to limit salt intake (less than 5 g/day), alcohol, to quit smoking if present, to control body weight, to exercise regularly (at least 30 minutes of moderate-intensity dynamic activity for 5–7 days a week) and to receive appropriate medication therapy.

The period from recovery after COVID-19 to the development of outcomes lasted from 1 to 7 months [median: 3 months, interquartile range 25–75 %: 2–4 months].

Patients with body mass index (BMI) value of 25–29.9 kg/m² were considered overweight and obese — with BMI over 30 kg/m². CVR was calculated using Systematic Coronary Risk Estimation (SCORE) scale at the age of 40 years and over, and under 40 years — using OR scale [7].

The study was performed at the Internal Medicine Outpatient Department of the Faculty of Medicine of the Pirogov Russian State Medical University and the Outpatient Department of the City Clinical Hospital № 13. The study protocol was approved by the local Ethics committee of the Pirogov Russian State Medical University. The study was performed in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Data were presented as medians with interquartile range for quantitative variables that significantly deviated from normal distribution. Mann-Whitney U-test was used to analyze the differences between the groups; Spearman correlation analysis was used to study the relationship between the studied parameters. To assess the risk factors for cardiovascular events we used

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logistic regression model thatincluded: sex, age, body mass index (BMI), systolic and diastolic blood pressure (BP) (SBP and DBP) levels, absolute and relative CVR according to SCORE scale, presence or absence of AH, CHD, DM, COVID-19. Differences were considered statistically significant at $p < 0.05$.

Results

In total, 343 (82.5%) patients had a mild course of COVID-19, 56 (13.5%) had a moderate-to-severe course, and 17 (4.0%) had severe course followed by hospital admission. Characteristics of patients before and after COVID-19 are shown in Table 1.

Table 1. **Characteristics of study participants before and after COVID-19**

Parameter	Before COVID-19, n = 416	After COVID -19, n = 416	p
SBP, mmHg	127 (110;148)	129 (125;136)	0,006
DBP, mmHg	85 (81;93)	85 (75;87)	0,866
HR, bpm	76 (68;93)	77 (75;85)	0,001
Smoking, n (%)	102 (24,5)	48 (11,5)	< 0,001
Hypercholestero-lemia, n (%)	28 (6,7)	201 (48,3)	< 0,001
Cholesterol, mmol/l	5 (5;5)	5 (5;6)	< 0,001
Glucose, mmol/l	5 (3;8)	4 (4;6)	0,038
Hyperglycemia, n (%)	21 (5)	33 (7,9)	0,121
BMI, kg/m^2	23 (23;32)	25 (22;34)	0,003
Excessive body weight, n (%)	167 (40,1)	316 (75,9)	< 0,001
Obesity, n (%)	18 (4,3)	13 (3,1)	0,464
CHD, n (%)	9 (2,1)	23 (5,5)	0,019
DM, (%)	9 (2,1)	26 (6,25)	0,005
AH, n (%)	36 (8,6)	73 (17,5)	< 0,001
SCORE CVR, %	1 (1;13)	6 (1;13)	0,086
CVR low, n (%)	145 (34,8)	62 (14,9)	< 0,001
CVR moderate, n (%)	230 (52,2)	256 (61,5)	0,078
CVR high, n (%)	31 (6)	35(8,4)	0,700
CVR very high, n (%)	10 (7)	63 (15,2)	< 0,001
CVR relative, score	1 (1;7)	2 (1;7)	0,606

Study outcomes developed in 97 (23,3%) people after COVID-19; 40 (16,5%) — in comparison group, $p = 0,050$. New cases of confirmed AH in the comparison group were registered in 29 (11.9%) patients, DM — in 9 (3.7%) patients, CHD — in 9 (3.7%) patients (5 patients had acute coronary syndrome, coronary atherosclerosis was confirmed in 4 patients according to CAG). In the main group 36 patients (8.6%) had new cases of AH, 26 (6.3%) — DM, 23 (5.5%) — CHD (15 patients had myocardial infarction, 8 — percutaneous coronary intervention, i.e. stent placement) (Table 2).

Table 2. **Characteristics of patients afterCOVID-19 with (group 1) and without(group 1) (group 2) the development of the new cases of AH, CHD and DM**

Parameter	Group 1, n = 97	Group 2, n = 319	p
Age, years	44 (42;46)	39 (39;41)	0,000
Aged 18–44 years, n (%)	49 (50,5)	217 (68)	0,002
Aged 45–59 years, n (%)	48 (49,4)	102 (31,9)	0,002
Males, n (%)	17 (17,5)	38 (11,9)	0,116
Mild course of COVID-19, n (%)	52 (53,6%)	291 (91,2%)	< 0,001
Moderately severe course of COVID-19, n (%)	35 (36,1%)	21 (6,6%)	< 0,001
Severe course of COVID-19, n (%)	10 (10,3%)	7 (2,2%)	0,002
SBP, mmHg	127 (130;134)	127 (128;131)	0,090
DBP, mmHg	76 (86;87)	75 (85;86)	0,035
HR, bpm	76 (75;77)	75 (75;77)	0,985
Smoking, n (%)	16 (16,4)	32 (10)	0,479
Hypercholesterolemia, n (%)	31 (31,9)	170 (53,2)	0,000
Cholesterol, mmol/l	5 (5,1;5,3)	5 (5,02;5,08)	0,000
Glucose, mmol/l	5 (5,0;5,3)	5 (5,0;5,1)	0,102
Hyperglycemia, n (%)	3 (3)	30 (9,4)	0,004
BMI, kg/m^2	27 (25,5;26,5)	23 (24,4;24,9)	0,000
Excessive body weight, n (%)	83 (85,5)	248 (77,7)	0,126
Obesity, n (%)	1 (1)	13 (4)	0,256
CHD, n (%)	21 (21,6)	2 (0,6)	0,000
DM, (%)	26 (26,8)	0	0,000
AH, n (%)	73 (75,2)	0	0,000
SCORE CVR, %	2,7 (2,5;3,9)	2,0 (2,1;2,6)	0,004
CVR low, n (%)	8 (8,2)	54 (16,9)	0,052
CVR moderate, n (%)	23 (23,7)	233 (73)	0,000
CVR high, n (%)	3 (3)	32 (10)	0,051
CVR very high, n (%)	63 (64,9)	0	0,000
CVR relative, score	1 (0,89;1,29)	1 (0,96;1,11)	0,526

The data of correlation analysis between new cases of AH, CHD, and studied parameters are presented in Table 3.

The above-mentioned data were used for a more detailed assessment by logistic regression analysis (Table 4).

Discussion

In most cases, COVID-19 manifests with respiratory and general symptoms, which persist for a certain period after recovery that is named "postcovid period/syndrome" in the literature. However, some patients of any age can develop changes in the cardiovascular system (vascular thrombosis, acute myocardial damage, acute coronary syndrome, new cases of CVD etc.), including in the long-term [8, 9].

While evaluating patients' characteristics after COVID-19, we paid attention to statistically signifi-

Table 3. **The data of the correlation analysis between new cases of AH, CHD, and studied parameters**

Parameter	r	p
New cases of AH, CHD, DM		
Smoking	0,20	< 0,001
Sleep disorder	0,15	< 0,001
Three or more RFs	0,16	< 0,001
SBP	0,15	< 0,001
DBP	0,17	< 0,001
Moderate CVR	0,19	< 0,001
High CVR	0,45	< 0,001
COVID-19	0,25	< 0,001
Development of AH		
High CVR	0,35	< 0,001
Aged 45–59	0,16	< 0,001
Hypercholesterolemia	0,14	< 0,001
DM	0,15	< 0,001
Development of CHD		
DM	0,53	< 0,001
Smoking	0,16	< 0,001
Hypercholesterolemia	0,37	< 0,001
Excessive body weight	0,17	< 0,001
High CVR	0,28	< 0,001
Three or more RFs	0,28	< 0,001
Development of DM		
Smoking	0,16	< 0,001
Hypercholesterolemia	0,37	< 0,001
Excessive body weight	0,22	< 0,001
Three or more RFs	0,29	< 0,001

Table 4. **Factors, associated with the development of cardiovascular events after COVID-19. The results of logistic regression analysis**

Parameter	OR	(95% CI)	p
Any cardiovascular events			
Sleep disorder	2,48	1,51–4,07	< 0,001
Smoking	3,09	1,89–5,06	< 0,001
Three or more RFs	11,01	6,54–18,55	< 0,001
COVID-19	1,74	1,14–2,65	0,010
High CVR	42,7	12,6–144,6	0,001
Development of AH			
High CVR	11,3	5,99–21,04	0,001
Aged 45–59	3,16	1,88–5,31	< 0,001
Hypercholesterolemia	3,59	2,01–6,41	< 0,001
Development of CHD			
DM	14,33	5,19–39,51	0,001
Three or more RFs	13,03	4,33–39,18	< 0,001
Smoking	3,67	1,56–8,60	0,003
Hypercholesterolemia	8,63	4,36–17,06	< 0,001
Excessive body weight	3,67	1,47–9,11	0,005
Development of DM			
Smoking	4,75	2,11–10,72	< 0,001
Hypercholesterolemia	6,04	3,121–11,38	< 0,001
Excessive body weight	7,02	2,59–19,02	< 0,001
Three or more RFs	11,70	4,30–31,84	< 0,001

cant increase of BP level (from 127 to 129 mm Hg, p = 0.006); increase of patients with hypercholesterolemia (from 6.7% to 48.3%, p < 0.001); overweight (from 40.1% to 75.9%, p < 0.001); very high CVR (from 7 to 15.2%, p < 0.001) and, correspondingly, decrease of patients with low CVR (from 34.8% to 14.9%, p < 0.001).

The fact of decrease of the number of smokers should be highlighted: from 24,5% to 11,5%, p < 0,001. It should be noted that patients included in the above study who suffered from COVID-19 had a median age of 40 (33; 47) years, predominately females (86,8%), and every fourth person (24,5%) smoked. Excessive body weight was present in 40,1% of patients. Mean score by the SCORE scale was 2.62 ± 2.6%, relative SCORE was 1.04 ± 0.48. Only 34.8% of patients from low-risk group, 52.2%, from moderate risk group, 6% from high-risk group and 7% of patients from very high-risk group had a low score by the SCORE scale

The registration of new cases of AH and CHD after COVID-19 can be mainly explained by the morbidity of elderly people, especially of those with initial cardiovascular pathology. Prediction of the consequences of this infection based on the degree of CVR in order to prevent the development of adverse outcomes at younger age is also relevant, since the delayed development of cardiovascular complications is considered to be one of the features of COVID-19 [10–12]. In this regard, prevention of life-threatening cardiovascular events by reducing the risk of CVD and identifying associated risk factors is the highest priority [13].

Between 1st and 7th months [median 3 (2; 4)] after COVID-19, one in four (23.3%) young and middle-aged subjects developed the study endpoints: 8.6% had AH, 6.3% had DM, and 5.5% had CHD. The estimated risk of premature cardiovascular events after COVID-19 was 74% higher than in the population of similar age and sex represented by the comparison group. In the group of patients who developed new cases of AH, CHD and DM, a moderately severe (p < 0.001) and severe course (p = 0.002) of COVID-19 followed by admission was registered more frequently; in the group of patients who did not develop CV events — a mild course (p < 0.001) of COVID-19.

Our findings are similar to those of other researchers. The study by Stefan N. et al. showed that comorbidities also increased the risk of COVID-19-related death among young adults (n = 3163). These findings come from the March 2020 Lean European Open Survey on SARS-CoV-2 (LEOSS) aimed to examine the prevalence and clinical course of SARS-CoV-2 in-

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fection. It revealed an additional influence of obesity, DM and AH on the increased risk of adverse outcomes in young and middle-aged patients. Compared to patients aged 18 to 55 years without obesity, DM and AH (n = 593), the adjusted risk of death (OR 7.42, 95% CI 1.55–27.3) in similar age group of patients with these pathologies was comparable with mortality risk in patients aged 56–75 years but without obesity, DM and AH (OR 8.21, 95% CI 4.10–18.3) [14].

The results of the retrospective study also confirmed that excess weight and AH contribute to the development of adverse outcomes of COVID-19 in young and middle-aged individuals [15].

While analyzing the group of patients who developed study outcomes, we noted that the age of these patients was higher compared with those without remote events. Patients in the main group were more likely to have CHD, AH and DM; baseline CVR, BP and BMI were higher than in the comparison group, which is consistent with data from other studies [16].

A systematic review by Harrison S et al. that included data from 84 clinical trials conducted between January 1, 2020, and November 5, 2020 showed that chronic kidney disease (OR 3.07, 95% CI 2.43–3.88), DM (OR 2.09, 95% CI 1.80–2.42) were the RF of fatal outcome and severe COVID-19. AH (OR 2.50, 95% CI 2.02–3.11), smoking history (OR 1.26, 95% CI 1.20–1.32), cerebrovascular disease (OR 2.75, 95% CI 1.54–4.89), and CVD (OR 2.65, 95% CI 1.86–3.78) contributed to more severe outcomes. Liver disease was associated with higher odds of death (OR 2.81, 95% CI 1.31–6.01), but not with the severe course of COVID-19. Smoking was associated with a higher risk of severe COVID-19 (OR 1.80, 95% CI 1.14–2.85), but not with mortality. Obesity was associated with a higher risk of death (OR 2.18, 95% CI 1.10–4.34), but there was no evidence of the association with more severe COVID-19 course. Patients admitted with COVID-19 were diagnosed acute heart failure (2%), myocardial infarction (4%), deep vein thrombosis (7%), myocardial damage (10%), angina pectoris (10%), cardiac arrhythmias (18%), pulmonary embolism (19%) and venous thromboembolism (25%) [17].

It is pivotal for the practicing physician, especially in the outpatient setting, to identify the group of patients who need earlier additional examination in order to prescribe rational preventive therapy. According to the results of our study, the presence of factors such as sleep disturbance (OR 2.48), smoking (OR 3.09), three or more of any CVD RF (OR 11.01), high CVR (OR 42.7), the very fact of COVID-19 was associated with higher probability of cardiovascular events and could be considered as possible risk factors in clinical practice.

The likelihood of developing AH increased by 11.3-fold those with high CVR, 3.59-fold in hypercholesterolemic patients, and 3.16-fold in middle-aged patients. DM (OR 14.33), three or more CHD RF (OR 13.03), smoking (OR 3.67), hypercholesterolemia (OR 8.63), and excess body weight (OR 3.67) were significantly associated with the development of CHD after COVID-19. The development of DM in young and middle-aged patients was associated with smoking (OR 4.75), hypercholesterolemia (OR 6.04), excess body weight (OR 7.02) and the presence of three or more RFs (OR 11.70). All of the above-mentioned parameters are proven components of high CVR, are easily identified in routine practice, and are modifiable [18].

Our results highlighted the effect of COVID-19 pandemic on human health and allow to consider a new coronavirus infection as a possible cardiovascular RF. This fact confirms the necessity of following the principles of prevention of non-infectious diseases as a priority of the health care system, starting at young age [20].

In the Russian Federation databases of COVID-19 patients were created, one of which named TARGET-VIP, studying clinical and medical history parameters, multimorbidity structure, treatment outcomes at hospital and outpatient setting in patients aged 58.0 ± 14.8 years, of 51.3% which are males. It was shown that higher mortality was observed during the first months after the disease (31.4%), especially in persons with severe course, indicating the need to improve the continuity between different health care units, as well as long-term complex, including outpatient follow-up of such patients [21].

This study allowed to identify risk factors associated with the development of AH, CHD and DM after the infection, which could be used for the development of multifactorial approach for timely detection and correction of cardiometabolic risk in young and middle-aged individuals that shouldinclude the healthy lifestyle principles.

Study limitations

The young and middle-aged patients included into the study underwent annual prophylactic examina-

tions, which defined set of necessary tests that limit the extrapolation of the results obtained. Due to the course of COVID-19, it is not possible to completely exclude the fact that some of the study participants in the comparison group did not have this infection asymptomatically. Therefore, it is difficult to argue that the new cases of AH, CHD, and DM are the direct consequence of the infection and are not due to the risk factors and concomitant pathology that existed before COVID-19.

Conclusion

One in four people aged from 18 to 59 years may develop a cardiovascular event after COVID-19, with a 74% higher risk those without the history of COVID-19. This probability was associated with initial high CVR, the presence of 3 or more of any CVD RFs, smoking, and sleep disorders. High CVR and hypercholesterolemia may be useful to identify the most vulnerable group of patients to develop AH, especially those aged 45–59 years; smoking, hypercholesterolemia, excess body weight, and three or more CVD RFs may be used to stratify patients for the risk of CHD or DM. Further inveatigation of factors associated with adverse cardiometabolic events and the formation of the phenotype of the most vulnerable young and middle-aged patient is necessary.

Conflict of interest. None declared.

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