CORRESPONDENCE

Research Letter

Risk Factors for a Severe Course of COVID-19 in Persons Aged 18 to 61

Information on the risk factors for a severe course of COVID-19 in persons of working age is incomplete. DKMS, a charitable organization, registers volunteers between 18 and 61 years of age for potential stem cell donation. The aim of the study was to identify risk factors for severe COVID-19 in this population. The institutional review board of TU Dresden (IRB00001473) approved the study. All participants provided their consent.

Methods

A health questionnaire was used to collect information on virus testing, risk factors (obesity, smoking, arterial hypertension, diabetes mellitus), symptoms, and treatment for COVID-19. Severe respiratory tract infections were defined by the following combinations of symptoms: fever and cough, dyspnea and cough, dyspnea and fever, or dyspnea and myalgia. Hospitalization due to respiratory tract symptoms was defined by the need for supplemental oxygen with or without ventilation. To define the risk factors for severe COVID-19, multivariable logistic regression models were calculated with information on the factors age, sex, body mass index (BMI), diabetes mellitus, arterial hypertension, smoking status, and month of infection for the endpoints severe respiratory tract infection and hospitalization. The test results should be regarded as exploratory. The p-values were not adjusted for multiple testing. Further details of the study are available at https://doi.org/10.1101/2020.11.05.20226100.

Results

In total, 4 440 895 registered volunteers were contacted and 924 557 consented to study participation. Among them, 157 544 participants had been swab-tested for SARS-CoV-2; 7948 reported positive tests. The median age was 35 years. More women (70%) than men (30%) took part. Altogether, 15% of participants reported that their BMI was ≥ 30 kg/m^2, 21% had been active smokers in 2019, 2% were on medication for diabetes mellitus, and 8% for arterial hypertension. The most commonly reported symptom was anosmia (65%), followed by myalgia (58%), cough (54%), sore throat (42%), fever (41%), and dyspnea (27%). Among the participants who tested positive for SARS-CoV-2, 947 (11.9%) reported an asymptomatic course; 5014 (63.1%), reported mild/moderate symptoms; and 1,987 (25%), severe respiratory tract infections. Of the last-named group, 286 (3.6%) patients were hospitalized for respiratory tract infections, 161 (2.0%) needed supplemental oxygen, and 22 participants (0.28%) required mechanical ventilation.

In multivariable analyses the risk of hospitalization due to respiratory symptoms was 5.3 times higher for participants aged 55 to 61 years than for the group of 18- to 24-year-olds *(Table)*. Nevertheless, the absolute risk (9%) of hospitalization was no more than moderate even in the group of 55- to 61-year-olds *(Figure)*. Participants with a BMI of 35–40 kg/m^2 had a 2.1 times higher risk of hospitalization than those of normal weight. No interactions were found among sex, age, and BMI. Details on the impact of age and BMI are shown in *Table 1*. Diabetes mellitus requiring medication (OR 1.59, p = 0.012), but not arterial hypertension (OR 0.98, p = 0.857), increased the risk of severe respiratory tract symptoms.

TABLE

Multivariable risk factor analysis

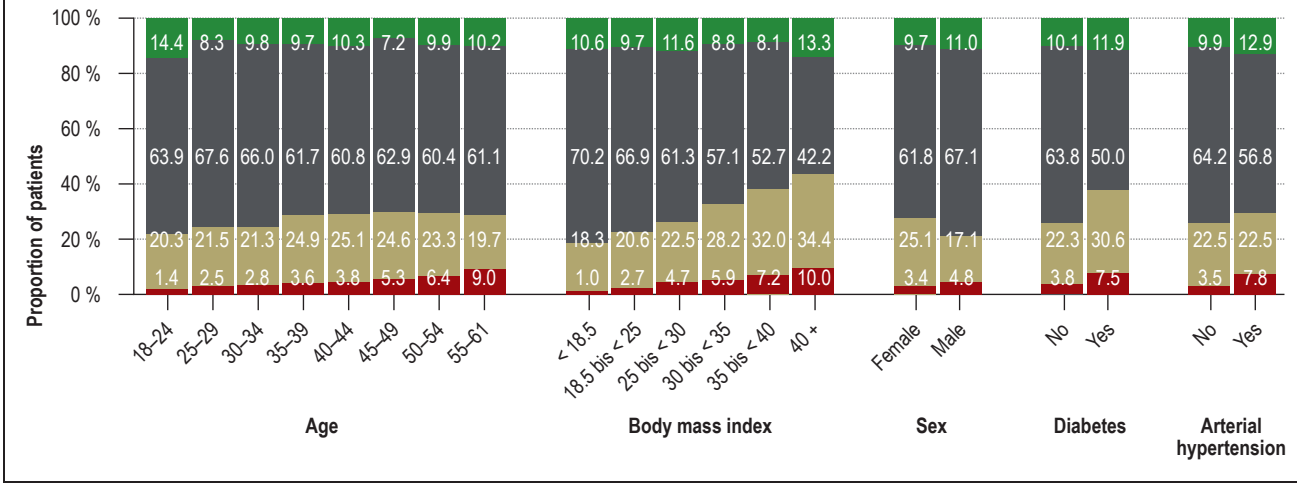
	Total number of participants	Severe respiratory tract symptoms	Hospitalization
	157 544 (%)	OR [95% CI]	OR [95% CI]
Age group			
18–24	25 404 (16)	1	1
25–29	23 802 (15)	1.13 [0.93; 1.38]	1.75 [0.94; 3.25]
30–34	26 835 (17)	1.15 [0.94; 1.40]	1.84 [1.00; 3.40]
35–39	24 408 (15)	1.36 [1.11; 1.68]	2.28 [1.23; 4.20]
40–44	19 388 (12)	1.36 [1.09; 1.69]	2.24 [1.18; 4.23]
45–49	14 763 (9)	1.42 [1.14; 1.78]	3.16 [1.72; 5.80]
50–54	13 650 (9)	1.45 [1.16; 1.82]	3.84 [2.12; 6.94]
55–61	9294 (6)	1.39 [1.08; 1.78]	5.33 [2.92; 9.70]
BMI (kg/m²)			
< 18.5	2760 (2)	0.78 [0.47; 1.28]	0.43 [0.06; 3.14]
18.5 to < 25	85 185 (54)	1	1
25 to < 30	45 344 (29)	1.27 [1.12; 1.45]	1.35 [1.00; 1.83]
30 to < 35	16 766 (11)	1.66 [1.40; 1.98]	1.66 [1.14; 2.41]
35 to < 40	5614 (4)	2.02 [1.51; 2.68]	2.10 [1.20; 3.69]
≥ 40	1875 (1)	2.46 [1.60; 3.78]	3.24 [1.56; 6.74]
Arterial hypertension			
No	144 697 (92)	1	1
Yes	12 847 (8)	0.98 [0.80; 1.20]	1.26 [0.87; 1.81]
Diabetes mellitus			
No	154 440 (98)	1	1
Yes	3104 (2)	1.59 [1.10; 2.28]	1.62 [0.82; 3.20]

OR, Odds ratio; CI, confidence interval; BMI, body mass index

Discussion

This study on registered stem cell donors aged between 18 and 61 years enables exploration of risk factors for a severe course of COVID-19 in persons of working age with relatively few health impairments. The participants reported lower prevalence of diabetes mellitus, arterial hypertension, and nicotine abuse than in the general population (1). Precisely for this group, the information on risk factors for COVID-19 remains incomplete to date. Age was even more closely associated with the occurrence of severe respiratory infections and hospitalization than has been

FIGURE



Severity of COVID-19 course by age, BMI, and diabetes mellitus or arterial hypertension treated with drugs. The size of the bars represents the distribution of the severity of disease. Red, Hospitalizations; beige, severe respiratory tract symptoms; gray, mild clinical courses; green, asymptomatic courses.

described for other respiratory viral infections, e.g., influenza; in contrast, the impact of obesity was comparable (2–3). Age, obesity, and diabetes are well-established risk factors for the occurrence of respiratory failure and death due to COVID-19 in the elderly (4–5).

The results presented here have several limitations. First, the analysis is based on self-reported data with no external assessment, and there is no guarantee that the sample was representative. Group-specific response behavior may therefore have affected the results of this study. Second, by virtue of the study design, persons who could not take part in the survey due to the health consequences of SARS-CoV-2 infection—at the least, those who died of the infection—were automatically not represented in the study population. According to data from the Robert Koch Institute, this group is small, with a case fatality rate of 0.11% for persons of this age group and sex distribution, but is systematically not documented. Third, the questionnaire focused solely on acute respiratory problems. Severe complications without concomitant respiratory failure or long-term sequelae were not systematically captured.

In conclusion, the study shows that for relatively healthy persons between 18 and 61 years old, age, BMI, and diabetes mellitus are major risk factors. The impact of these factors is clinically meaningful, in contrast to the ABO blood group, the relevance of which for the severity of COVID-19 has not yet been clearly established. This information may be useful for individual counseling of members of this group with regard to vaccination against SARS-CoV-2 or to motivate them to adhere to measures to prevent infection.

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Conflict of interest statement
Prof. Dalpke has received an honorarium from Amgen for giving a lecture.
The remaining authors declare that no conflict of interest exists.

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