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Association of BMI with general health, working capacity recovered, and post-acute sequelae of COVID-19

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Abstract

Objective: The aim of this study was to determine the risk of post-acute sequelae of COVID-19 associated with the continuous spectrum of BMI.

Methods: Epidemiology of Long COVID (EPILOC) is a population-based study conducted in Baden-Württemberg (Germany), including subjects aged 18 to 65 years who tested positive for SARS-CoV-2 between October 2020 and April 2021. Eligible subjects answered a standardized questionnaire, including sociodemographic characteristics, lifestyle factors, and the presence of specific symptoms. Participants assessed their current general health recovery and working capacity compared with the pre-infection situation and provided their body height and weight. Generalized additive models were used to assess the association of BMI with general health recovered, working capacity recovered, and prevalence of fatigue, cognitive impairment, and chest symptoms.

Results: The analyses included 11,296 individuals (41% male), with a mean age of 44.0 (SD 13.7) years. Best general health recovery was observed at BMI of 22.1 (95% CI: 21.0-27.0) kg/m^2 in men and BMI of 21.6 (95% CI: 20.3-23.1) kg/m^2 in women. In addition, we found that increasing BMI was consistently associated with post-COVID fatigue, neurocognitive impairment, and chest symptoms.

Conclusions: High BMI contributes to impaired recovery after SARS-CoV-2 infection; however, a low BMI is associated with impaired recovery as well.

INTRODUCTION

Post-acute health problems and other sequelae affecting a significant proportion of COVID-19 survivors and lasting for up to 12 months have been reported [1–3]. Body mass index (BMI) ≥ 30 kg/m^2 is an established risk factor for severe acute COVID-19 [4–6], and it also has been associated with post-acute sequelae of COVID-19 [7–9].

Post-acute COVID-19 sequelae are manifold [10]. However, most of the burden, in terms of impaired general health recovery and lost working capacity, is attributable to symptoms of fatigue, cognitive impairment, and chest symptoms (shortness of breath, chest pain, wheezing) [1].

U- or J-shaped associations of BMI with acute complications of COVID-19 have been observed [11, 12]. Therefore, BMI ≥ 30 kg/m^2 but also a low BMI might be associated with post-acute sequelae of COVID-19. However, the risk of post-acute sequelae of COVID-19 associated with the continuous spectrum of BMI has not yet been determined.

Therefore, we investigated the associations of BMI with self-reported general health recovered, working capacity recovered, and common symptom clusters such as fatigue, cognitive impairment, and chest symptoms in COVID-19 survivors. In addition, we considered possible effect modification by important covariates.

Study Importance

What is already known?

- BMI ≥ 30 kg/m^2 is an established risk factor for severe acute COVID-19.
- Some studies found BMI ≥ 30 kg/m^2 also to be associated with post-acute sequelae of COVID-19.

What does this study add?

- This study describes health recovery over the continuous spectrum of BMI.
- There is an optimal BMI range in which general health recovery is best; recovery is worse with a higher or lower BMI.

How might these results change the direction of research or the focus of clinical practice?

- Future studies should shed light on the biological pathways underlying this association.
- Prevention policies for obesity should be considered as a component of future pandemic preparedness strategies.

METHODS

Study design

Epidemiology of Long COVID (EPILOC) is a population-based study conducted in the Federal State of Baden-Württemberg in southwestern Germany [1]. The study included subjects aged 18 to 65 years who tested positive for SARS-CoV-2 by polymerase chain reaction (PCR) between October 1, 2020, and April 1, 2021, and whose infection was notified to the local public health authorities.

Eligible subjects were invited to return a standardized questionnaire including sociodemographic characteristics, and lifestyle factors. It evaluated the presence of 30 specific symptoms before and during the acute infection phase and when filling out the questionnaire (i.e., 6 to 12 months after acute infection). For symptoms present at the time of the survey, we also asked whether and to which grade each symptom impaired daily life activities (none, light, moderate, or strong). Clusters of strongly correlated current symptoms were previously identified [1]. The present work focuses on the three most common symptom clusters fatigue (including rapid physical exhaustion or chronic fatigue), cognitive impairment (including concentration difficulties, memory disturbance, and confusion), and chest symptoms (including shortness of breath, chest pain, and wheezing). A cluster was counted as present if at least one included symptom was reported at the time of the survey but was not prevalent before the SARS-CoV-2 infection.

In addition, participants assessed their current general health recovery and working capacity compared with the situation before the acute SARS-CoV-2 infection (in 10% steps from 0% to 100%). The question was, "What percentage of your original work capacity (before your positive corona test) have you regained today?" The use of this single question has shown similar relations to sick leave and health-related quality of life in occupational studies [13]. Similarly, the current general health condition compared with the situation before the acute SARS-CoV-2 infection was assessed. In addition, participants were asked to provide their current body height (in cm) and weight (in kg, without shoes and light clothing only).

Ethical approval was obtained from the respective ethical review boards of the study centers in Freiburg (21/1484) and Ulm (337/21).

Statistical analysis

We used generalized additive models (GAM) to assess the association of BMI with general health recovered, working capacity recovered, and post-COVID prevalence of fatigue, cognitive impairment, and chest symptoms. BMI was entered as a smooth term. An identity link and Gaussian error term were used for general health and working capacity recovered as outcomes and a logit link and binomial error term for prevalence outcomes.

All models were fitted for men and women separately and were adjusted for age (continuous), education (university entrance qualification yes/no), smoking status (current or past vs. regular cigarette smoker), and severity of the initial COVID-19 illness (medically treated yes/no).

Fitted curves for average covariate values with corresponding 95% pointwise confidence intervals (CIs) were plotted by BMI from 15 to 45 kg/m^2. For prevalence outcomes, the linear predictor was backtransformed to probabilities using the logistic function. Finally,

TABLE 1 Characteristics of the study population

	Men		Women	
	N	Mean proportion	*N*	Mean or proportion
Age (y), mean (SD)	4674	45.0 (13.7)	6622	43.3 (13.6)
Age class (y), *N* (%)	4674		6622	
<30		893 (19.1)		1516 (22.9)
30–<40		861 (18.4)		1233 (18.6)
40–<50		819 (17.5)		1183 (17.9)
50–<60		1359 (29.1)		1939 (29.3)
≥60		742 (15.9)		751 (11.3)
University entrance qualification, *N* (%)	4674	2510 (53.7)	6622	3439 (51.9)
Ever smoker, *N* (%)	4674	1846 (39.5)	6622	2078 (31.4)
BMI (kg/m^2), mean (SD)	4674	27.0 (4.8)	6622	25.4 (5.6)
BMI class, *N* (%)	4674		6622	
<18.5 kg/m^2		30 (0.6)		188 (2.8)
≥18.5–<25 kg/m^2		1706 (36.5)		3620 (54.7)
≥25–<30 kg/m^2		1989 (42.6)		1658 (25.0)
≥30 kg/m^2		949 (20.3)		1156 (17.5)
Medical treatment of acute SARS-CoV-2 infection, *N* (%)	4674	984 (21.1)	6622	1567 (23.7)
Percent general health recovered, mean (SD)	4604	90 (14)	6497	88 (15)
Percent general health recovered, *N* (%)	4604		6497	
100% recovery		2262 (49.1)		2692 (41.4)
90% recovery		1091 (23.7)		1688 (26.0)
≤80% recovery		1251 (27.2)		2117 (32.6)
Percent working capacity, mean (SD)	4630	90 (16)	6535	89 (17)
Percent working capacity, *N* (%)	4630		6535	
100% recovery		2616 (56.5)		3294 (50.4)
90% recovery		899 (19.4)		1400 (21.4)
≤80% recovery		1115 (24.1)		1841 (28.2)
Newly developed symptom clusters,[a] *N* (%)				
Any symptom (any grade)	4674	2655 (56.8)	6622	4544 (68.6)
Any symptom (moderate to strong)		1591 (34.0)		3090 (46.7)
Fatigue (any grade)	4586	1464 (31.9)	6489	2666 (41.1)
Fatigue (moderate to strong)		828 (18.1)		1720 (26.5)
Neurocognitive impairment (any grade)	4600	1187 (25.8)	6523	2291 (35.1)
Neurocognitive impairment (moderate to strong)		526 (11.4)		1175 (18.0)
Chest symptoms (any grade)	4617	1204 (26.1)	6548	2168 (33.1)
Chest symptoms (moderate to strong)		553 (12.0)		1029 (15.7)

[a]The symptom clusters fatigue (including rapid physical exhaustion or chronic fatigue), cognitive impairment (including concentration difficulties, memory disturbance, and confusion), and chest symptoms (including shortness of breath, chest pain, and wheezing) were counted as present if at least one included symptom was reported at the time of the survey but was not present before the SARS-CoV-2 infection.

optima for general health recovered and working capacity recovered were derived numerically, and model-based 95% CIs using posterior resampling.

We used spline-factor interaction terms (for discrete factors) and tensor product interactions (for age) to investigate possible effect modification. All analyses have been performed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Of 50,457 subjects invited to participate, 12,053 (24%) responded, and 11,296 with available data on BMI and covariates (41% male, mean age 44.0 years) were included in the analysis. Men were more frequently "ever smokers" than women (39.5 vs. 31.4%) and had a higher BMI (27.0 vs. 25.4 kg/m^2) on average (Table 1). The average

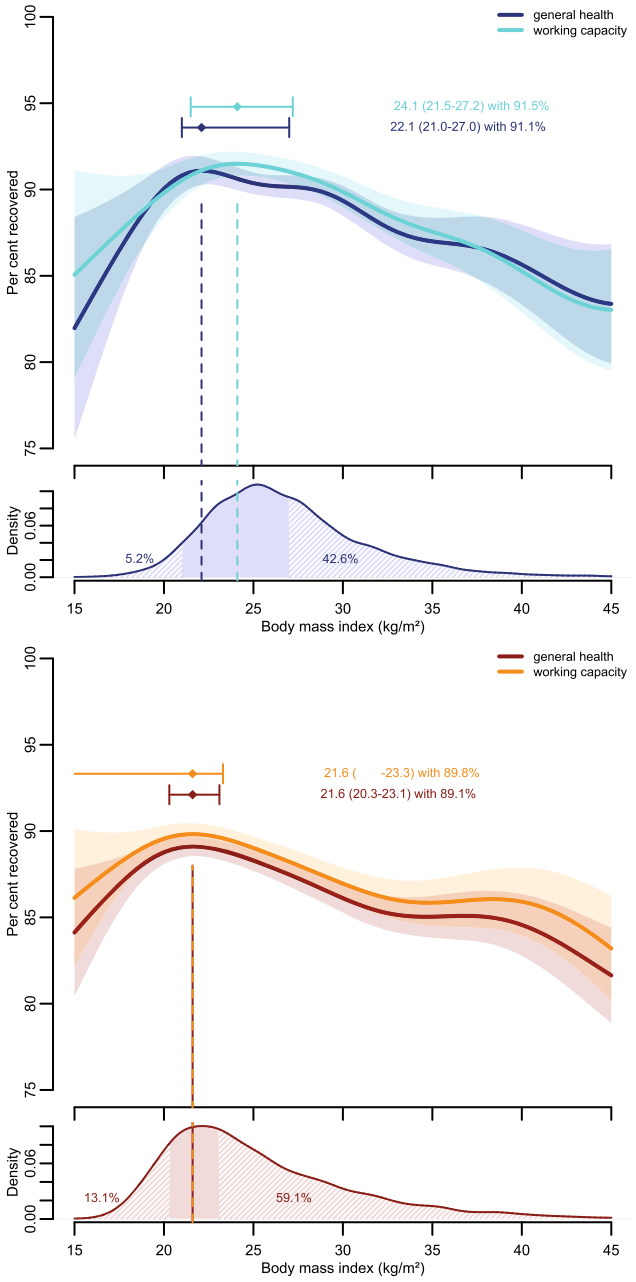

FIGURE 1 Percent general health and working capacity recovered by body mass index (BMI) in men (top panel, blue colors) and women (bottom panel, red colors), along with the BMI distribution in men and women. The dots with whiskers represent the BMI associated with maximum general health (working capacity) recovered with its corresponding 95% CI. The associations are adjusted for age, education, smoking status, and treatment of acute SARS-CoV-2 infection. Shaded areas indicate parts of the BMI distribution where general health recovery was statistically significantly impaired either because of lower or higher than optimal BMI values

general health recovery was 90% in men and 88% in women. The average working capacity recovery was also 90% in men and 89% in women. Persistent new symptom clusters (not already present before infection) of fatigue, neurocognitive impairment, and chest symptoms were less prevalent in men than in women.

Low and high BMI were associated with both impaired general health and working recovery (Figure 1) in men and women. Best general health recovery was observed in men at BMI of 22.1 (95% CI: 21.0-27.0) kg/m^2, and best working capacity recovered at 24.1 (95% CI: 21.4-27.1) kg/m^2. In women, the best general health recovery was observed at BMI of 21.6 (95% CI: 20.3-23.1) kg/m^2, and the best working capacity recovered at 21.6 (95% CI: NA-23.3) kg/m^2.

General health and working capacity recovered were lower in participants requiring medical treatment during acute infection (i.e., higher severity of the acute COVID disease) (Supporting Information Figure S1). However, the association of BMI with general health and working capacity recovery looked similar in medical treated and not treated subjects. Regarding smoking status, curves also looked similarly in never and ever smokers (Supporting Information Figure S2).

In contrast, age modified the associations of BMI with general health and working capacity recovered (p values < 0.01; Supporting Information Figure S3). A high BMI was less strongly associated with impaired recovery in younger than older men and women.

Regarding symptom clusters, we found that increasing BMI was consistently associated with fatigue, neurocognitive impairment, and chest symptoms in men and women (Figure 2), irrespective of the grade of impairment (any grade, or moderate to strong). There was also a tendency for increased risk at low BMI (< 20 kg/m^2) for some symptoms (fatigue in men, neurocognitive impairment of any grade in women, and chest symptoms of grade moderate to strong in women). However, statistical power was rather low at the lower end of the BMI distribution.

DISCUSSION

We found a clear association between increasing BMI and impaired general health and working capacity recovery. In men, general health recovery was statistically significantly compromised above 27.0 kg/m^2 and in women above BMI of 23.1 kg/m^2. In addition, a low BMI was associated with statistically significantly impaired recovery in men below BMI of 21.0 kg/m^2 and in women below BMI of 20.3 kg/m^2.

BMI ≥ 30 kg/m^2 being a risk factor for post-acute sequelae of COVID-19 is in line with other studies [7, 8]. However, a negative association between a low BMI and health outcomes after COVID-19 has not yet been reported. From a public health perspective, a high BMI is the more relevant issue, as only 5% of men and 13% of women in our cohort had BMI below 21.0 and 20.3 kg/m^2, respectively. In contrast, 43% of men and 59% of women had a BMI above 27.0 and 23.1 kg/m^2, respectively, and thereby a statistically significant impaired general health recovery.

Interestingly, age had little effect on general health recovery at an optimal or lower BMI: the average general health recovery at BMI of 22.1 kg/m^2 was only 0.8% lower in 55-year-old compared with 25-year-old men, whereas at BMI of 35.0 kg/m^2, average general health recovery was 4.1% lower in 55-year-old than 25-year-old men.

Loosen et al. found hypertension and lipid metabolism disorder, in addition to obesity, to be associated with a Long COVID syndrome

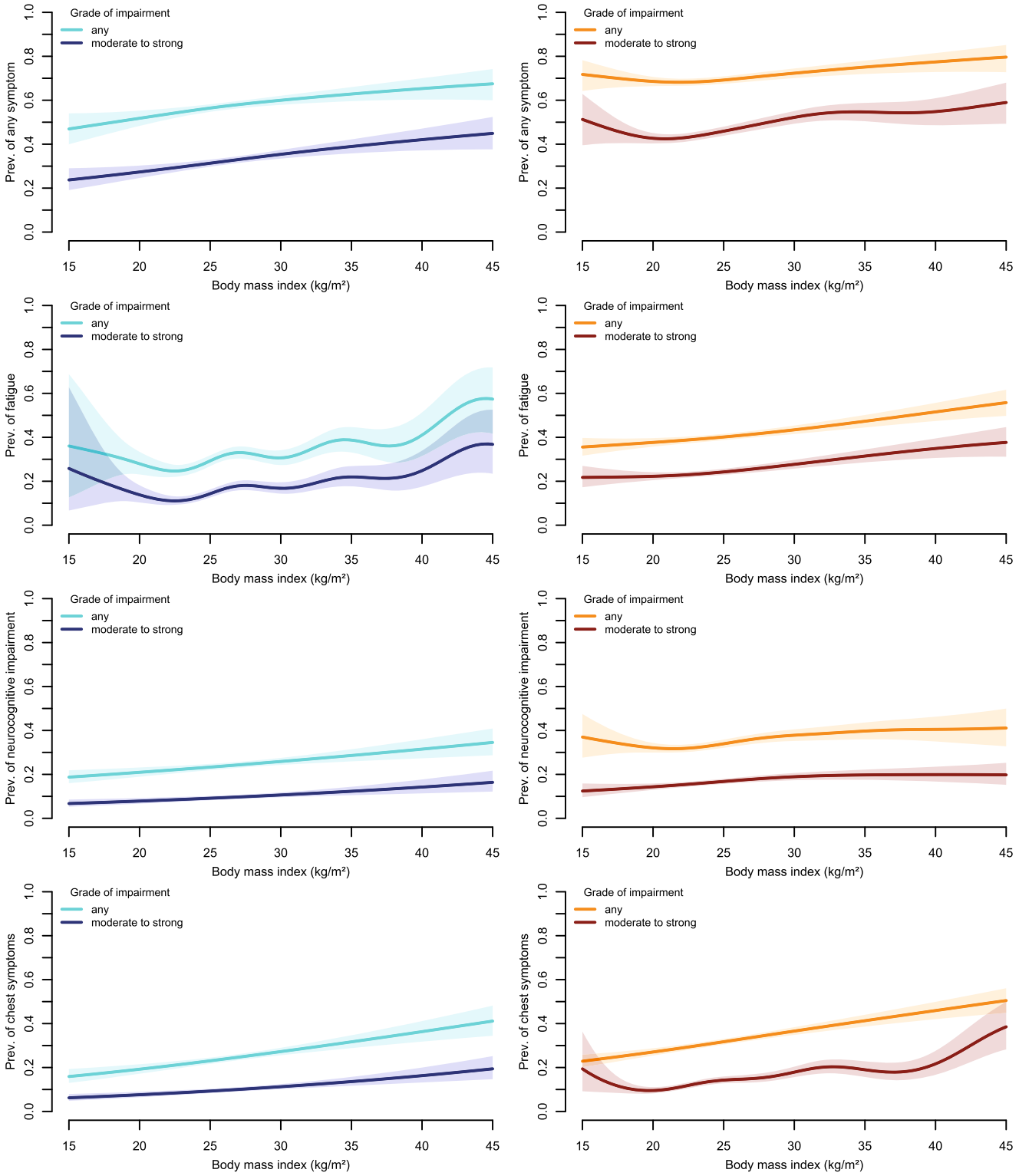

FIGURE 2 Prevalence of different symptom clusters (not present before infection) by body mass index (BMI) in men (left panels, blue colors) and women (right panels, red colors), by grade of impairment. The associations are adjusted for age, education, smoking status, and treatment of acute SARS-CoV-2 infection

diagnosis by a general practitioner [8]. These obesity-associated metabolic comorbidities accompanied by subclinical inflammation might explain the stronger association in older than younger participants, as these comorbidities develop over time.

The strengths of the present work are the large sample size and the population-based approach, including many participants who had a mild (or even asymptomatic) infection. In addition, we used a flexible modeling approach instead of relying on predefined BMI categories.

The main limitation of this work is its reliance on self-reported weight and height and a limited response rate of 24%. In addition, we used BMI at the time of the survey, and body weight might have already been affected by the acute COVID-19 disease or its sequelae and pandemic-related influences. Furthermore, a low BMI might result from (known or unknown) health problems already present before infection, and impaired recovery may not necessarily result from a low BMI per se.

Despite these limitations, we show evidence that a high BMI contributes to impaired general health, working capacity recovery, and the presence of post-COVID sequelae after SARS-CoV-2 infection.O

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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