



Applied nutritional investigation

Nutritional status of patients with COVID-19 1-y post-ICU stay: A prospective observational study



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ABSTRACT

Objectives: Patients discharged from the intensive care unit (ICU) often experience physical complaints and poor nutritional intake, which negatively affect their nutritional status (NS). The aim of this study was to describe the NS of patients with COVID-19 1-y post-ICU stay.

Methods: This was an observational study of adult patients with COVID-19 1-y post-ICU stay. NS assessment (nutrient balance, body composition, and physical status) was performed. We examined nutritional intake and nutrition-related complaints. Nutritional requirements were determined with indirect calorimetry and body composition with bioelectrical impedance. Fat-free mass index (FFMI) and fat mass index (FMI) were calculated. Physical status was determined using handgrip strength, the 6-min walk test, and the 1-min sit-to-stand test. Descriptive statistics and paired sample *t* tests were used for analysis.

Results: We included 48 patients (73% men; median age 60 y [IQR 52;65]). Median weight loss during the ICU stay was 13%. One-y post-ICU stay, 12% of weight was regained. Median body mass index was 26 kg/m² and 23% of the patients were obese (body mass index >30 kg/m² and high FMI). Of the patients, 50% had high FMI and 19% had low FFMI. Median reported nutritional intake was 90% of measured resting energy expenditure. Nutrition-related complaints were seen in 16%. Percentages of normal values reached in physical tests were 92% of handgrip strength, 95% of 6-min walking distance, and 79% of 1-min sit-to-stand test.

Conclusions: Despite almost fully regained weight and good physical recovery in adult patients 1-y post-ICU stay, NS remained impaired because of elevated FMI, even though reported nutritional intake was below the estimated requirements.

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Introduction

Malnutrition and weight loss are frequently observed in critically ill patients with COVID-19 [1,2] most likely due to the

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concomitant hypermetabolic and catabolic state [3]. It is well known that muscle mass rapidly decreases during intensive care unit (ICU) stay and is associated with impaired muscle function, a longer hospital length of stay (LOS), and higher mortality [4]. One of the factors contributing to this is inadequate protein and energy intake. Inadequate protein and energy supply is associated with risk for mortality [5]. Approximately 60% of critically ill patients with COVID-19 survive [6] and return home [7].

After ICU discharge, these patients often continue to experience physical impairment (e.g., decreased muscle and lung function), fatigue, nutrition-related complaints (e.g., dysphagia), and reduced cognitive function and quality of life as main problems [8,9]. These aspects are also known as post-intensive care syndrome (PICS) [10]. It has been shown that 60% to 80% of ICU survivors remain functionally impaired 12 to 18 mo after their stay in the ICU [9,11]

and that the majority of (hospitalized) patients with COVID-19 is diagnosed with PICS [12–14]. Many patients do not return to work in the first year after hospital admission, thus placing a great burden on the patients, their family, the health care system, and society. Nutritional support strategies may decrease the burden of critical illness [15,16]. Therefore, it is recommended that the nutritional status (NS) of patients with COVID-19 post-ICU stay be carefully monitored to reduce complications [17].

Nutritional assessment (NA) is the quantitative evaluation of NS. This assessment involves interpretation of the following domains:

- Nutrient balance (i.e., nutritional intake, requirements, and nutrient losses);
- Body composition;
- Physical status (including muscle strength and functionality); and
- Biochemical status [18].

Based on limited short-term follow-up data, overall NS is not restored in post-COVID-19 patients. It has been shown that patients with COVID-19 were able to achieve an adequate reported nutritional intake 3 to 5 mo after ICU admission [19] despite frequently observed nutrition-related problems such as decreased appetite and feelings of being full [2,20]. Most of these patients (almost) fully regained their unintended weight loss 3 to 5 mo post-ICU stay [2,19]. Concerning body composition, normal fat-free mass index (FFMI) [21] and high fat mass [22] were observed in most patients 3 mo after recovery from acute COVID-19. Physical status was impaired 3 to 6 mo after ICU stay in most patients with COVID-19 [12,23].

So far no further (long-term) follow-up data of complete NA is available on patients with COVID-19 post-ICU stay [24]. Therefore, our aim was to investigate NS, specifically measured resting energy expenditure (REE), body composition, and physical status in patients with COVID-19 1 y after ICU discharge. We hypothesized that NS is still impaired 1-y post-ICU stay.

Material and methods

Study population and design

This prospective observational study was conducted from March 2021 through July 2021 in the Erasmus Medical Centre (MC) or at home if this was more convenient for the patient, with approval from the institutional review board of the [Blinded for peer review]. Patients with COVID-19 (> 18 y of age) post-ICU stay were included. Some of these patients were involved in the ongoing 3-y prospective multicenter cohort study, CO-FLOW (COVID-19 Follow-up care paths and Long-term Outcomes Within the Dutch health care system) [25]. Patients with a metabolic disease requiring a specific diet (e.g., phenylketonuria) or (home) parenteral nutrition starting >7 d before admission unrelated to COVID-19, were excluded [3]. All patients were admitted to the ICU for invasive ventilation and in accordance with international guidelines, patients were generally discharged from the ICU when vital signs were stable without support and continuous monitoring and or when treatment was no longer required. Data on patient characteristics and NA were collected 1 y after ICU discharge. Written informed consent was obtained before data collection. Data management was performed using Castor Electronic Data Capture, version 2021.1 (Castor EDC, the Netherlands).

Patient characteristics

Patient characteristics included age, weight, height, sex, body mass index (BMI), ICU LOS, duration of mechanical ventilation and continuous renal replacement therapy (CRRT) during ICU stay, mortality risk (APACHE IV) upon ICU admission, rehabilitation trajectory after discharge (y/n), and comorbidities. Current weight (kg) 1 y after ICU stay was measured on a calibrated scale to the nearest 0.1 kg. For comparison reasons, body weight history before, during (ICU) admission, and after hospitalization was assessed from medical charts and checked with the patient.

Nutritional status assessment

A trained dietitian performed NA including nutrient balance, body composition, and physical status.

Nutrient balance

During ICU stay, all patients were fed according to our nutrition protocol, which is based on the guidelines of the European Society for Clinical Nutrition and Metabolism (ESPEN) [4]. Nutritional intake 1-y post-ICU was obtained by using a 24-h diet recall and a global diet history. Nutrition-related complaints (i.e., taste, smell, and/or swallowing problems, and losses) were examined by interviews. Appetite degree was evaluated on a numeric rating scale (0–10). Data on gastrointestinal (GI) symptoms and feeding intolerance included vomiting (y/n), abdominal distension (y/n), and diarrhea (Bristol stool scale ≥ 6) [26]. Optimal nutritional requirements were determined individually. The calculated energy requirement corresponded with the measured REE (mREE) using indirect calorimetry (Q-NRG+, Cosmed, Italy) during resting state according to the guidelines [27,28]. The total energy requirement was determined individually based on influential factors such as physical activity levels [29] and ranged from 10% to 50% (minimum of 10% in case of sedentary lifestyle to maximum of 50% in case of vigorously active lifestyle). Comparison of mREE and predicted REE (pREE) with formulas (mREE / pREE \times 100%) was performed to explore hypometabolism (<90%) and hypermetabolism (>110%) [30]. Furthermore, if available mREE during ICU admission was compared with mREE 1-y post-ICU stay. One-y post-ICU stay protein requirement ranged from 0.8 to 1.2 g/kg, with an average norm of 1 g/kg [4,31]. Actual body weight (kg) was used to determine requirements, unless there was fluid overload, estimated dry body weight was used [3].

Body composition

Body composition was measured with a multifrequency bioelectrical impedance analysis (InbodyS10, Inbody Co. Ltd., Seoul, Korea) with patients in a supine position. Based on segmental impedance and reactance whole body and segmental fat-free mass (FFM), fat mass (FM), skeletal muscle mass, and extracellular water (ECW) and intracellular body water were determined. Phase angle (PhA) was deduced and whole body (50 kHz) values were compared with reference values presented by Mattiello [32], in which age-dependent PhA values <5.6 to 7.2° for men and <5.1 to 6.2° for women were considered too low. FFMI and fat mass index (FMI) were calculated (i.e., FFM/m² and FM/m²) and if indicated, FFM was corrected for fluid overload (i.e., ECW/total body water ratio >0.390). In case of fluid overload, estimated values derived from ECW were recalculated to dry weight using a standardized ratio of 0.380 for healthy persons [33]. Values <10th percentile were considered too low and >90th too high [34]. For interpretation of skeletal muscle mass index reference values from the European Working Group on Sarcopenia in Older People (EWGSOP2) were used [35], in which values <7 kg/m² for men and <5.5 kg/m² for women were defined as low.

Physical status

Physical status was determined using handgrip strength (HGS) in all patients. HGS was measured with a handhold dynamometer (Jamar; Patterson Medical, Bolingbrook, IL, USA) and the test was performed with patients in a sitting position. The highest value of six measurements was compared with the reference values of Dodds [36], in which values <10th percentile were considered too low [37]. Additional functional tests (i.e., 6-min walk test [6MWT] and 1-min sit-to-stand test [1MSTST]) were obtained in patients who also participated in the CO-FLOW study in the [Blinded for peer review] [25]. For logistical reasons it was not possible to perform these functional tests in all patients. During the 6MWT, patients were instructed to walk as far and as fast as possible back and forth on 30-m track to obtain the 6-min walk distance (6MWD) [38,39]. The 6MWD was compared to reference values of Enright and Sherrill [40]. During the 1MSTST, patients performed as many repetitions of sit-to-stand (1MSTST repetitions) in 1 min as possible without using arm support [41]. 1MSTST repetitions were compared with reference values of Strassmann et al. [42].

Nutritional status assessment

Assessment of NS upon ICU admission was based on the ESPEN guidelines (i.e., low BMI and/or unintended weight loss) before ICU stay [43]. NS 1-y post-ICU stay was based on, among others, the Global Leadership Initiative on Malnutrition (GLIM) [44] and EWGSOP2 criteria [35] as presented in Table 1.

Statistical analysis

Data of characteristics and NA were analyzed by means of descriptive statistics: mean (SD) in case of normally distributed values or otherwise as median (interquartile range [IQR]), and numbers (%), where appropriate. Difference of BMI

Table 1
Assessment criteria for nutritional status based on the GLIM [44] and EWGSP2 criteria [35].

Assessment of nutritional status	
Nutritional status	Criteria
Normal (not malnourished)	At least one of the following phenotypic criteria: <ul style="list-style-type: none"> • Weight loss: <5% involuntary within past 6 mo • BMI: between >20 and <30 kg/m² if <70 y or between >22 and <30 kg/m² if ≥70 y • FFMI: between >10th and <90th percentile* • FMI: between >10th and <90th percentile* • HGS: >10th and <90th percentile† In combination with at least one etiologic criteria: <ul style="list-style-type: none"> • Nutritional intake: ≥50% of calculated requirements for >1 wk or <ul style="list-style-type: none"> • Disease state: no acute illness or chronic disease-related inflammation
Moderately malnourished	At least one of the following phenotypic criteria: <ul style="list-style-type: none"> • Weight loss: ≥5% within past 6 mo or >10% beyond 6 mo • BMI: <20 kg/m² if <70 y or <22 kg/m² if ≥70 y • FFMI: between 5th and 10th percentile* • FMI: between 5th and 10th percentile* • HGS: between 5th and 10th percentile† In combination with at least one of the following etiologic criteria: <ul style="list-style-type: none"> • Nutritional intake: <50% of calculated requirements for >1 wk or <ul style="list-style-type: none"> • Disease state: acute illness or chronic disease-related inflammation
Severely malnourished	At least one of the following phenotypic criteria: <ul style="list-style-type: none"> • Weight loss: >10% within past 6 mo or >20% beyond 6 mo • BMI: <18.5 kg/m² if <70 y or <20 kg/m² if ≥70 y • FFMI: <5th percentile* • FMI: <5th percentile* • HGS: <5th percentile† In combination with at least one of the following etiologic criteria: <ul style="list-style-type: none"> • Nutritional intake: <50% of calculated requirements for >1 wk or <ul style="list-style-type: none"> • Disease state: acute illness or chronic disease-related inflammation
Obesity	<ul style="list-style-type: none"> • BMI: >30 kg/m² • FMI: >90th percentile*
Sarcopenic obesity†	<ul style="list-style-type: none"> • BMI: >30 kg/m² • FFMI: <10th percentile* • FMI: >90th percentile* In combination with: <ul style="list-style-type: none"> • HGS: <10th percentile†
Sarcopenia‡	<ul style="list-style-type: none"> • BMI: between 20 and 30 kg/m² • FFMI: <10th percentile* • FMI: <10th percentile* In combination with: <ul style="list-style-type: none"> • HGS: <10th percentile†

BMI, body mass index; EWGSP2, European Working Group on Sarcopenia in Older People; FFMI, fat-free mass index, FMI, fat mass index; GLIM, Global Leadership Initiative on Malnutrition; HGS, handgrip strength; FFMI based on measured FFM with bio-electric impedance analysis

*Reference values of Schutz et al [34].

†Reference values of Dodds et al. [36].

‡Different work groups maintain certain age categorization for primary sarcopenia, but because secondary sarcopenia is not age related, we not account for age when diagnosing sarcopenia.

and mREE upon admission and 1-y post-ICU stay were analyzed with a paired sample *t* tests. A two-sided *P* < 0.05 was considered statistically significant. Data analysis was performed using SPSS version 25.0 (IBM, Armonk, NY, USA).

Results

Study population

Of the 85 eligible patients, 35 (41%) withdrew because they were too tired for (further) participation. As two patients had incomplete NA (no indirect calorimetry), 48 patients were included (Supplementary Fig. 1), of whom 35 patients (73%) came from the CO-FLOW study. As presented in Table 2, the study population consisted mostly of middle-aged men (73%). Upon ICU admission, median BMI was 29 kg/m² [IQR 25;30], 7 of the patients (15%) were classified as moderately malnourished, 12 as severely malnourished (25%), 24 as obese (50%; BMI >30 kg/m²), and 5 (10%) as normal (not malnourished; Supplementary Fig. 2). Median unintended weight loss before ICU admission was 5% [IQR 0.5;10]. During hospitalization, median total weight loss was 13% [IQR 10;16]. Median APACHE IV upon ICU admission was 19% [IQR 13.8;21] and median ICU LOS was 19 d [IQR 10;30]. Median number of days spent on mechanical ventilation was 18 [IQR 11;30] and 17% (n = 8) of the patients received CRRT during their ICU stay, with a mean duration of 2 d (±6).

One-y post-ICU stay, 12% [IQR 7;16] of the unintended weight loss was regained and patients had a median BMI of 26 kg/m² [IQR 23;30], of which 11 patients (23%) remained living with obesity (BMI >30 kg/m²; Table 2). The prevalence of obesity based on BMI had decreased to 23%. The obese patients had high FMIs and were diagnosed with obesity according to our criteria. None of the patients were diagnosed with (obese) sarcopenia and none displayed either a phenotypic and a etiologic criteria for diagnosing malnutrition (Table 3 and Supplementary Fig. 3). Thirty-six of the patients (75%) followed a rehabilitation process after discharge, but indicated that they were unable to continue exercising independently afterward. The most common comorbidity was type 2 diabetes mellitus, as reported in 11 patients (24%).

Nutrient balance

Metabolism

One-y post-ICU stay, the mREE was 1899 kcal [IQR 1678;2111] and median respiratory quotient was 0.81 [IQR 0.76;0.86]. Normo-metabolism was predominantly observed (62%), followed by hypermetabolism (30%) and hypometabolism (8%). In a subgroup of 22 patients, the mREE, which was measured during ICU admission, was compared with mREE 1-y post-ICU stay. In 13 of these patients (59%), mREE decreased with a mean of 21%, whereas in 9 patients (41%), mREE increased with a mean of 28% 1-y post-ICU stay (Supplementary Fig. 3). In this subgroup eight patients (36%) remained hypermetabolic. The mREE values during ICU admission and 1-y post-ICU stay did not significantly differ (*P* = 0.31).

Nutritional intake and requirements

Median reported nutritional intake was 90% [IQR 75;109] of mREE and 80% [IQR 66;92] of the total calculated energy and 77% [IQR 66;87] of protein requirements. In 34 patients (70%), reported nutritional intake was >80% of mREE. None of the patients received tube and/or sip feeding. Sixteen (33%) patients used (multi)vitamin supplementation and 10 (21%) patients (deliberately) changed their fat or sugar consumption in favor of their health.

Nutrition-related complaints and losses

Eight patients (16%) had at least one nutrition-related complaint. Two (4%) patients had combination of three complaints.

Table 2
Patient characteristics of the included patients with COVID-19 1-y post-ICU stay (N = 48)

Men, n (%)	35 (73)		
Age (y)	60 [52;65]		
Median ICU stay, d	23 [14;32]		
Ventilation d	18 [11;30]		
Total hospital LOS, d	25.5 [15; 36]		
Comorbidities, n (%)			
Type 2 diabetes mellitus	11 (24)		
Cardiac diseases	12 (25)		
Respiratory disease	6 (13)		
Gastrointestinal disease	8 (17)		
Cancer	5 (10)		
Enteral nutrition during ICU stay	80%–95%		
Upon and during ICU admission/hospitalization	1 y after ICU admission		
Percentage weight loss before ICU admission	5 [0.5;10]		
BMI (kg/m ²) upon admission	29 [25;30]*	BMI (kg/m ²) 1 y after admission	26 [23;30]*
Normal weight, n (%)	19 (40)	Normal weight, n (%)	27 (56)
Overweight, n (%)	5 (10)	Overweight, n (%)	8 (17)
Obese, n (%)	24 (50)	Obese, n (%)	11 (23)
Percentage weight change during hospitalization	–13 [10;16]	Percentage weight change 1 y after ICU admission	+12 [7;16]

BMI, body mass index; ICU, intensive care unit; LOS, length of stay

Data presented as median [IQR] unless otherwise indicated.

Overweight defined as BMI >27.5 kg/m² and obese as BMI >30 kg/m²

*Significant change ($P < 0.001$).

Median appetite degree was 9 of 10 [IQR 7;10]. Four (8%) patients had at least one GI symptom. Of these, two patients had combination of two symptoms (Supplementary Table 1).

Body composition and physical status

Table 4 presents whole body composition values for all patients and Figure 1 [45,46] shows an overview of the measured FM, FFM, and TBW compared with the dry weight reference values for men and women separately. In 6 patients (13%), FFM was corrected for fluid overload. Nine patients (19%) had low FFMI and 24 (50%) had high FMI. A combination of high FFMI and FMI was present in 7 patients (15). Of these, 6 (13%) were living with obesity (BMI >30 kg/m²). Only seven patients had low PhA (15%) and one had low SMI (2%). Percentage of normative values reached in HGS was 92%, and 4% of the patients had low HGS. In a subgroup of 35 patients (73%), 6MWT and 1MSTST were performed. In these patients, the mean 6MWD was 516 m (± 105). Overall, patients performed 95% (± 19) of predicted level of normal and six patients (17%) had a 6MWD below the lower limit of normal, of which two (33%) patients had low FFMI. The mean 1MSTST repetitions was 30 (± 12) and patient performance was 79% (± 30) of predicted.

Discussion

The main finding of this study with adult post-ICU COVID-19 patients is that unintended weight loss was almost fully regained 1y after ICU discharge, often in combination with a high FMI (50%). A low nutritional intake was reported in 80% to 90% of the patients compared with the total calculated or measured REE. Nutrition-related complaints and GI symptoms were seen in $\leq 16\%$ of the patients, of which swallowing problems were most often reported. A low physical status was only seen in the minority of the patients.

Most of our cohort almost fully regained their weight 1y after their stay in the ICU. This observation is in line with a study where 97% of weight loss in patients with COVID-19 was regained by 3 mo post-ICU stay [19]. In our study, obesity based on BMI significantly decreased to 23% compared with ICU admission, which is in line with other reports in which 7% to 40% of patients with COVID-

19 were living with obesity up to 3 mo after discharge [49,50]. Because we found a high FMI combined with a decrease in obesity prevalence, most observed weight gain was likely composed of fat mass. Unfortunately, body composition was not measured during ICU stay in most of these patients, limiting our ability to make intraindividual comparisons.

None of our patients could be classified as being malnourished, however, the elevated FMI reflects an unhealthy NS. The presence of malnutrition in other studies varied from 15% to 100% in patients with COVID-19, but follow-up was only ≤ 3 mo after ICU discharge and in these studies also different definitions for malnutrition other than the GLIM criteria were used [19,49,50]. In contrast, 29% of our patients had one phenotypic criteria without a combination with one etiologic criteria for malnutrition. Although these patients were not diagnosed as malnourished, 19% had (prolonged) low muscle mass. These results underline the importance of measuring body composition during and after ICU stay to evaluate NS.

During critical illness, most patients with COVID-19 were found to be hypermetabolic [51] and in a catabolic state for a prolonged period [3]. However, how metabolism evolves after hospital discharge is unknown. In a subgroup of 22 patients in our study, we measured the REE during their ICU stay. One y after discharge, we found a broad range of mREE fluctuations ranging from a 41% decrease to a 59% increase of which 36% remained hypermetabolic. No association was found between intraindividual REE measurements. In this subgroup, this might be due to both the resolution of the hypermetabolic state and/or the altered body composition with a high fat mass and lower FFMI of the patients.

Concerning nutrient balance, the reported nutritional intake 1-y post ICU-stay was $\sim 90\%$ of mREE and 80% compared with total calculated energy and protein requirements. Whereas this might be influenced by underreporting, nutrition-related complaints and GI symptoms seemed no barrier to achieve a higher nutritional intake. Furthermore, physical activity level values may be lower than estimated for energy requirements since most patients with COVID-19 might experience exercise intolerance post-ICU stay [52]. Concerning physical status, only 4% of our patients had a low HGS and 17% of the patients had a 6MWD under the lower limit of

Table 3
Diagnosing nutritional status in patients with COVID-19 1 y after ICU discharge (N = 48)

	Criteria	n (%)
Normal (not malnourished)	At least one phenotypic criteria:	
	• <5% weight loss past 6 mo	47 (98)
	• Normal weight	27 (56)
	• FFMI between >10th and <90th percentile	39 (81)
	• FMI between >10th and <90th percentile	37 (77)
	• HGS between >10th and <90th percentile	44 (92)
	At least one etiologic criteria:	46 (96)
	• Normal nutritional intake for >1 wk	42 (88)
	• Chronic inflammation	37 (76)
	Combination of both a phenotypic and etiologic criteria	
Moderately malnourished	At least one phenotypic criteria:	
	• >5% weight loss past 6 mo	1 (2)
	• Underweight	2 (4)
	• FFMI 5th to 10th percentile	9 (19)
	• FMI 5th to 10th percentile	0 (0)
	• HGS 5th to 10th percentile	2 (4)
	At least one etiologic criteria:	2 (4)
	• Reduced nutritional intake for >1 wk	6 (12)
	• Chronic inflammation	0 (0)
	Combination of both a phenotypic and etiologic criteria	
Severely malnourished	At least one phenotypic criteria:	
	• >10% weight loss past 6 mo	0 (0)
	• Severe underweight	0 (0)
	• FFMI <5th percentile	0 (0)
	• FMI <5th percentile	0 (0)
	• HGS <5th percentile	0 (0)
	At least one etiologic criteria:	2 (4)
	- Reduced nutritional intake for >1 wk	6 (12)
	- Chronic inflammation	0 (0)
	Combination of both a phenotypic and etiologic criteria	
Obese	High BMI and high FMI	11 (23)
Obese sarcopenia	High BMI and high FMI and low HGS	0 (0)
Sarcopenia	Low FFMI and low HGS	0 (0)

BMI, body mass index; FFMI, fat-free mass index; FMI, fat mass index; HGS, handgrip strength; ICU, intensive care unit

Severe underweight defined as BMI <18.5 kg/m² if <70 y or <20 kg/m² if ≥70 y, underweight as BMI <20 kg/m² if <70 y or <22 kg/m² if ≥70 y, and obese as BMI >30 kg/m² [44].

High FMI defined as P>90th percentile and both low FFMI [34] and low HGS defined as P<10th percentile [36].

Reduced nutritional intake defined as <50% of energy requirement for >1 wk [44].

normal, even though low FFMI was not frequently observed in these patients. Overall, most patients reached 95% of predicted 6MWD and 79% of predicted 1MSTST. This is in line with other studies reporting 90% to 110% of norm 6MWD in patients with COVID-19 1-y post-ICU stay [53,54]. In fact, significant improvement in these physical status parameters has been reported after 1 to 3 mo rehabilitation [22,49,55] and this trend continues during long-term follow-up. Importantly the rate and degree of recovery seems much better than in non-COVID ICU survivors [9,56,57]. This might be explained by a different effects of the primary disease on the patient's body (viral pneumonia versus for instance severe septic shock due to a bacterial infection) or by the development of dedicated rehabilitation programs for post COVID-19 patients [56].

Despite good physical recovery, chronic fatigue might prevent frequent physical exercise in our study population. It should be noted that 41% of the patients did not participate in this follow-up study because they were too tired. Most of our patients did follow a rehabilitation program after discharge but were possibly unable to continue exercising independently afterward despite good

Table 4
Whole body composition values in patients with COVID-19 1-y post ICU discharge

Dry weight values	Reference (range) values	All patients (N = 48)	P-values*
Dry weight (kg) (SE)	80.7 (0.5) [†]	93 [81;103]	<0.001
Fat mass (kg)	9.1–17.7 [‡]	29 [17;42]	0.009
Fat mass index (kg/m ²)	5.7–8.3 [‡]	11 [8;14]	<0.001
Percentage fat mass (%)	10–20 [‡]	32 [23;38]	0.009
Fat-free mass (kg)	51–62.3 [‡]	62 [52;72]	0.016
Fat-free mass index (kg/m ²)	16.4–19.4 [‡]	21 [19;22]	<0.001
Skeletal muscle mass index (kg/m ²)	6.77–8.89	10 [9;12]	0.002
Total body water (L)	37.4–45.8 [‡]	46 [39;54]	0.001
Intracellular body water (L)	23.2–28.4 [‡]	28.2 [24;33]	0.001
Extracellular body water (L)	14.2–17.4 [‡]	17 [13;21]	0.440
50 kHz Phase angle (°)	5.1–7.2 [¶]	6 [5.5;6.5]	0.332

ICU, intensive care unit.

Data presented as median [IQR].

*Comparison of dry weight values of all patients with reference values.

[†]Dutch population reference values for men and women (55–65 y of age) based on public records of 2021.

[‡]Mean population references based on the individual minimal and maximal ideal body composition values provided by the InbodyS10 device [45–56].

[§]Mean reference values (50th percentile) by Schutz et al. [34] depending on sex and age.

^{||}Mean SMI for healthy white men and women of respectively 67 y by Lee et al. [48].

[¶]Reference values by Mattiello et al. [32] depending on sex and age.

physical recovery because of persistent tiredness. This might not be detected by our assessment of physical status, but might the combination of (prolonged) fatigue and limited activity as seen in patients with COVID-19 [52,58–60] could explain the relatively high FMI in weight regain in our patients. This high FMI needs attention in relation to the lower reported nutritional intake than calculated and a rehabilitation program which must be extended for >2 to 3 mo. A high FMI is not favorable for long-term health outcomes [61–63]. Combined lifestyle interventions, especially nutrition in combination with exercise, are needed to improve body composition and thus NS and health outcomes.

Although to our knowledge, this is the first long-term follow-up study to assess complete NA in patients with COVID-19, some limitations should be addressed. First, the number of patients was limited and there was no control group; therefore, results should be interpreted with caution. However even without a control group, these data are of importance as it provides initial insight into the recovery of the COVID-group. Later studies should include comparisons with a control group. Second, selection bias may have occurred since participation in follow-up was voluntary. A considerable number of the eligible patients withdrew because they were too tired for (further) participation. Third, we used norm values largely based on a healthy population despite our population having a high prevalence of comorbidities. We opted for this approach because of a lack of pre-morbid data.

Conclusion

Because of the persistent elevated FMI, the NS remained impaired in our group of adult post-ICU COVID-19 patients, even though most patients fully regained body weight and had good physical recovery 1-y after their ICU stay. This might be explained by limited physical exercise due to persistent fatigue. Our findings emphasize the importance of NA measurements during and after ICU discharge to provide tailored individual nutritional support. Future studies must focus on the effect of nutritional and exercise interventions on maintaining muscle mass and preventing increase of fat mass after discharge from the ICU.

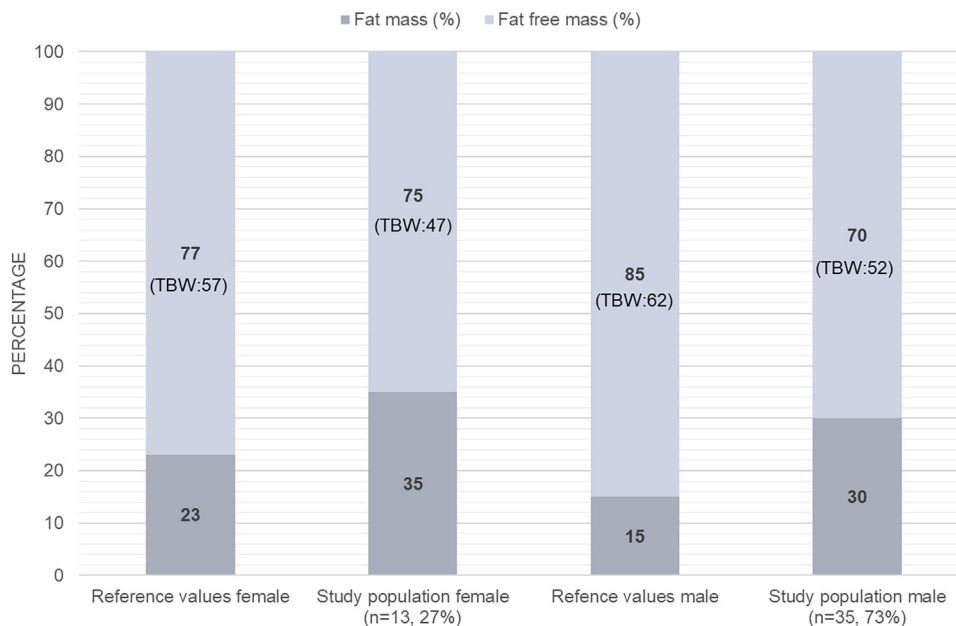


Fig. 1. Measured body composition (percentage fat mass, fat free mass, and TBW) in 48 men and women with COVID-19 1-y post-ICU stay compared with sex-dependent dry weight reference values [45,46]. TBW, total body water.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.nut.2023.112025](https://doi.org/10.1016/j.nut.2023.112025).

References

- [1] Bedock D, Lassen PB, Mathian A, Moreau P, Couffignal J, Ciangura C, et al. Prevalence and severity of malnutrition in hospitalized COVID-19 patients. *Clin Nutr ESPEN* 2020;40:214–9.
- [2] Wierdsma NJ, Kruijenga HM, Konings LAML, Krebbers D, Jorissen JRMC, Joosten M-HI, et al. Poor nutritional status, risk of sarcopenia and nutrition related complaints are prevalent in COVID-19 patients during and after hospital admission. *Clin Nutr ESPEN* 2021;43:369–76.
- [3] Lakenman PLM, van der Hoven B, Schuijjs JM, Eveleens RD, van Bommel J, Olie-man JF, et al. Energy expenditure and feeding practices and tolerance during the acute and late phase of critically ill COVID-19 patients. *Clin Nutr ESPEN* 2021;43:383–9.
- [4] Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr* 2019;38:48–79.
- [5] Alencar ES, Muniz L, Holanda JLG, Oliveira BDD, Carvalho MCF, Leitao AMM, et al. Enteral nutritional support for patients hospitalized with COVID-19: results from the first wave in a public hospital. *Nutrition* 2022;94:111512.
- [6] Prescott HC, Girard TD. Recovery from severe COVID-19: leveraging the lessons of survival from sepsis. *JAMA* 2020;324:739–40.
- [7] Armstrong RA, Kane AD, Cook TM. Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies. *Anaesthesia* 2020;75:1340–9.
- [8] Ahmed H, Patel K, Greenwood D, Halpin S, Lewthwaite P, Salawu A, et al. Long-term clinical outcomes in survivors of coronavirus outbreaks after hospitalisation or ICU admission: a systematic review and meta-analysis of follow-up studies. *J Rehabil Med* 2020;52. [jrm00063](https://doi.org/10.1080/16501977.2020.1811111).
- [9] Wischmeyer PE, San-Millan I. Winning the war against ICU-acquired weakness: new innovations in nutrition and exercise physiology. *Crit Care* 2015;19:1–14.
- [10] Rawal G, Yadav S, Kumar R. Post-intensive care syndrome: an overview. *J Transl Int Med* 2017;5:90.
- [11] Denehy L, Skinner EH, Edbrooke L, Haines K, Warrillow S, Hawthorne G, et al. Exercise rehabilitation for patients with critical illness: a randomized controlled trial with 12 months of follow-up. *Crit Care* 2013;17:1–12.
- [12] Rousseau A-F, Minguet P, Colson C, Kellens I, Chaabane S, Delanaye P, et al. Post-intensive care syndrome after a critical COVID-19: cohort study from a Belgian follow-up clinic. *Ann Intensive Care* 2021;11:1–9.
- [13] Martillo MA, Dangayach NS, Tabacof L, Spielman LA, Dams-O'Connor K, Chan CC, et al. Postintensive care syndrome in survivors of critical illness related to coronavirus disease 2019: cohort study from a New York City Critical Care Recovery Clinic. *Crit Care Med* 2021;49:1427–38.
- [14] Nanwani-Nanwani K, López-Pérez L, Giménez-Esparza C, Ruiz-Barranco I, Carrillo E, Arellano MS, et al. Prevalence of post-intensive care syndrome in mechanically ventilated patients with COVID-19. *Sci Rep* 2022;12:1–11.
- [15] Bear DE, Wandrag L, Merriweather JL, Connolly B, Hart N, Grocott MPW. The role of nutritional support in the physical and functional recovery of critically ill patients: a narrative review. *Crit Care* 2017;21:1–10.
- [16] Vanderheyden S, Casaer MP, Kesteloot K, Simoons S, De Rijdt T, Peers G, et al. Early versus late parenteral nutrition in ICU patients: cost analysis of the EPaNIC trial. *Crit Care* 2012;16:1–10.
- [17] Crispo A, Bimonte S, Porciello G, Forte CA, Cuomo G, Montagnese C, et al. Strategies to evaluate outcomes in long-COVID-19 and post-COVID survivors. *Infect Agent Cancer* 2021;16:62.
- [18] Gibson RS. Principles of nutritional assessment. Oxford University Press; 2005.
- [19] Fiorindi C, Campani F, Rasero L, Campani C, Livi L, Giovannoni L, et al. Prevalence of nutritional risk and malnutrition during and after hospitalization for COVID-19 infection: preliminary results of a single-centre experience. *Clin Nutr ESPEN* 2021;45:351–5.
- [20] Slotegraaf AI, de van der Schueren MAE, Wierdsma NJ, Weijs PJM, Kruijenga HM. Nutritional problems of patients with COVID-19 receiving dietetic treatment in primary care [Epub ahead of print]. *J Hum Nutr Diet* 2022.
- [21] van den Borst B, Peters JB, Brink M, Schoon Y, Bleeker-Rovers CP, Schers H, et al. Comprehensive health assessment 3 months after recovery from acute coronavirus disease 2019. *Clin Infect Dis* 2021;73:e1089–98.
- [22] Imamura M, Mirisola AR, FdQ Ribeiro, De Pretto LR, Alfieri FM, Delgado VR, et al. Rehabilitation of patients after COVID-19 recovery: an experience at the Physical and Rehabilitation Medicine Institute and Lucy Montoro Rehabilitation Institute. *Clinics* 2021;76.
- [23] van Veenendaal N, van der Meulen IC, Onrust M, Paans W, Dieperink W, van der Voort PHJ. Six-month outcomes in COVID-19 icu patients and their family members: a prospective cohort study. *Healthcare* 2021;9:865.
- [24] Barazzoni R, Breda J, Cuerda C, Schneider S, Deutz NE, Wickramasinghe K, et al. COVID-19: Lessons on malnutrition, nutritional care and public health from the ESPEN–WHO Europe call for papers. *Clin Nutr* 2022;41:2858–68.
- [25] Bek LM, Berentschot JC, Hellemons ME, Huijts SM, Aerts JGJV, van Bommel J, et al. CO-FLOW: Covid-19 Follow-up care paths and Long-term Outcomes Within the Dutch health care system: study protocol of a multicenter prospective cohort study following patients 2 years after hospital discharge. *BMC Health Serv Res* 2021;21:847.

- [26] Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, et al. Bowel disorders [Online ahead of print]. *Gastroenterology* 2016.
- [27] Oshima T, Berger MM, De Waele E, Guttormsen AB, Heidegger C-P, Hiesmayr M, et al. Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group. *Clin Nutr* 2017;36:651–62.
- [28] Haugen HA, Chan LN, Li F. Indirect calorimetry: a practical guide for clinicians. *Nutr Clin Pract* 2007;22:377–88.
- [29] United Nations University, World Health Organization. Human energy requirements: report of a Joint FAO/WHO/UNU Expert Consultation. Rome, 17–24 October 2001. Food and Agriculture Organization; 2004.
- [30] Lakenman PLM, van Schie JC, van der Hoven B, Baart SJ, Eveleens RD, van Bommel J, et al. Nutritional intake and gastro-intestinal symptoms in critically ill COVID-19 patients. *Clin Nutr* 2022;41:2903–9.
- [31] McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. *JPEN J Parenter Enteral Nutr* 2016;40:159–211.
- [32] Mattiello R, Amaral MA, Mundstock E, Ziegelmann PK. Reference values for the phase angle of the electrical bioimpedance: systematic review and meta-analysis involving more than 250,000 subjects. *Clin Nutr* 2020;39:1411–7.
- [33] Moonen HPFX, van Zanten FJL, Driessen L, de Smet V, Slingerland-Boot R, Mensink M, et al. Association of bioelectric impedance analysis body composition and disease severity in COVID-19 hospital ward and ICU patients: The BIAC-19 study. *Clin Nutr* 2020;40:2328–36.
- [34] Schutz Y, Kyle UUG, Pichard C. Fat-free mass index and fat mass index percentiles in Caucasians aged 18–98 y. *Int J Obes* 2002;26:953–60.
- [35] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;48:16–31.
- [36] Dodds RM, Syddall HE, Cooper R, Kuh D, Cooper C, Sayer AA. Global variation in grip strength: a systematic review and meta-analysis of normative data. *Age Ageing* 2016;45:209–16.
- [37] Langius JW, Kruijzena H, Reijnen N. Measuring handgrip strength. *Nutritional Assessment Platform*. The Netherlands: Maastricht; 2017. <https://www.dietetic-pocketguide.com/wp-content/uploads/2017/08/SOP-handgrip-strength.pdf>.
- [38] Poulain M, Durand F, Palomba B, Ceugniet F, Desplan J, Varray A, et al. 6-minute walk testing is more sensitive than maximal incremental cycle testing for detecting oxygen desaturation in patients with COPD. *Chest* 2003;123:1401–7.
- [39] ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;166:111–7.
- [40] Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med* 1998;158:1384–7.
- [41] Koufaki P, Mercer TH, Naish PF. Effects of exercise training on aerobic and functional capacity of end-stage renal disease patients. *Clin Physiol Funct Imaging* 2002;22:115–24.
- [42] Strassmann A, Steurer-Stey C, Lana KD, Zoller M, Turk AJ, Suter P, et al. Population-based reference values for the 1-min sit-to-stand test. *Int J Public Health* 2013;58:949–53.
- [43] Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition—an ESPEN consensus statement. *Clin Nutr* 2015;34:335–40.
- [44] Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition—a consensus report from the global clinical nutrition community. *J Cachexia Sarcopenia Muscle* 2019;10:207–17.
- [45] Heyward VH, Wagner DR. Applied body composition assessment. *Human Kinetics*; 2004.
- [46] Sartorio A, Malavolti M, Agosti F, Marinone PG, Caiti O, Battistini N, et al. Body water distribution in severe obesity and its assessment from eight-polar bioelectrical impedance analysis. *Eur J Clin Nutr* 2005;59:155–60.
- [47] Length and weight of persons, underweight and overweight; from 1981. Available at: <https://www.cbs.nl/nl-nl/figures/detail/81565NED?dl=4E468>. Access March 29, 2023.
- [48] Lee MM, Jebb SA, Oke J, Pinaras C. Reference values for skeletal muscle mass and fat mass measured by bioelectrical impedance in 390 565 UK adults. *J Cachexia Sarcopenia Muscle* 2020;11:487–96.
- [49] Hoyois A, Ballarin A, Thomas J, Lheureux O, Preiser JC, Coppens E, et al. Nutrition evaluation and management of critically ill patients with COVID-19 during post-intensive care rehabilitation. *JPEN J Parenter Enteral Nutr* 2021;45:1153–63.
- [50] Haraj NE, El Aziz S, Chadli A, Dafir A, Mjabber A, Aissaoui O, et al. Nutritional status assessment in patients with Covid-19 after discharge from the intensive care unit. *Clin Nutr ESPEN* 2021;41:423–8.
- [51] Whittle J, Molinger J, MacLeod D, Haines K, Wischmeyer PE, Whittle J, et al. Persistent hypermetabolism and longitudinal energy expenditure in critically ill patients with COVID-19. *Crit Care* 2020;24:581.
- [52] Soares MN, Eggelbusch M, Naddaf E, Gerrits KHL, van der Schaaf M, van den Borst B, et al. Skeletal muscle alterations in patients with acute Covid-19 and post-acute sequelae of Covid-19. *J Cachexia Sarcopenia Muscle* 2022;13:11–22.
- [53] Wu X, Liu X, Zhou Y, Yu H, Li R, Zhan Q, et al. 3-month, 6-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study. *Lancet Resp Med* 2021;9:747–54.
- [54] Huang L, Yao Q, Gu X, Wang Q, Ren L, Wang Y, et al. 1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study. *Lancet* 2021;398:747–58.
- [55] Rodrigues M, Costa AJ, Santos R, Diogo P, Gonçalves E, Barroso D, et al. Inpatient rehabilitation can improve functional outcomes of post-intensive care unit COVID-19 patients—a prospective study. *Disabil Rehabil* 2022;1–11.
- [56] Al Chikhanie Y, Veale D, Schoeffler M, Pépin JL, Verges S, Hérent F. Effectiveness of pulmonary rehabilitation in COVID-19 respiratory failure patients post-ICU. *Respir Physiol Neurobiol* 2021;287:103639.
- [57] Moonen HPFX, Strookappe B, van Zanten ARH. Physical recovery of COVID-19 pneumosepsis intensive care survivors compared with non-COVID pneumosepsis intensive care survivors during post-intensive care hospitalization: the RECOVID retrospective cohort study. *JPEN J Parenter Enteral Nutr* 2022;46:798–804.
- [58] Heesakkers H, van der Hoeven JG, Corsten S, Janssen I, Ewalds E, Simons KS, et al. Clinical outcomes among patients with 1-year survival following intensive care unit treatment for COVID-19. *JAMA* 2022;327:559–65.
- [59] Hellemons ME, Huijts S, Bek LM, Berentschot JC, Nakshbandi G, Schurink CAM, et al. Persistent health problems beyond pulmonary recovery up to 6 months after hospitalization for COVID-19: a longitudinal study of respiratory, physical, and psychological outcomes. *Ann Am Thorac Soc* 2022;19:551–61.
- [60] Bek LM, Berentschot JC, Heijenbroek-Kal MH, Huijts S, van Genderen ME, Vlakte JH, et al. Symptoms persisting after hospitalization for COVID-19: 12 months interim results of the CO-FLOW study. *ERJ Open Res* 2022;8:00355–2022.
- [61] Arnold M, Pandeya N, Byrnes G, Renehan AG, Stevens GA, Ezzati M, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. *Lancet Oncol* 2015;16:36–46.
- [62] Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet* 2014;384:755–65.
- [63] Samuel VT, Shulman GI. Mechanisms for insulin resistance: common threads and missing links. *Cell* 2012;148:852–71.