



SCIENTIFIC LETTER

Muscle wasting in ICU-patients with COVID-19 - Descriptive analysis and risk factors identification



Desgaste muscular en pacientes críticos con COVID-19 - Análisis descriptivo e identificación de factores de riesgo

Skeletal muscle atrophy is commonly associated to critical illness. Muscle mass in critically ill patients can rapidly atrophy after Intensive Care Unit (ICU) admission due to prolonged bed rest, sedatives and neuromuscular blocking agents prescription and other clinical conditions such as hypermetabolism with increased protein catabolism.^{1,2} Furthermore, muscle mass atrophy is associated with adverse clinical outcomes.³ Therefore, the aim of this study was, first, to describe changes in skeletal muscle mass in critically ill patients with COVID-19 and, second, to identify predictors of muscle atrophy during ICU stay.

This was a prospective cohort of critically ill patients with ARDS due to COVID-19 that were admitted in the Intensive Care Unit. Only patients with computed tomography (CT) scans for diagnostic purposes, performed in the first 24–48 h after admission and a second CT during ICU length of stay on mechanical ventilation were included. This study was reviewed and approved by the Institutional Review Board.

Nutritional assessment, within 24–48 h of ICU admission, included measurements such as mid-arm circumference, calf circumference, abdominal circumference, and half arm span, using a tape with 0.1 cm precision (SECA 201, Germany). Weight and height were estimated using validated equations,⁴ and BMI was calculated. Nutritional risk was assessed using a modified NUTRIC-Score, considering factors such as age, SOFA score, APACHE II score, comorbidities, pre-ICU hospital length of stay, and the first 24 h of mechanical ventilation (MV). High nutritional risk was defined as a score ≥ 5 .⁵ Prescribed drugs (e.g., midazolam, fentanyl, vecuronium, propofol) were also documented from medical records daily between CT scans.

Abdominal non-contrast CT scans were performed in a supine position using a 64-slice Siemens Healthineers scanner. A transverse CT-image at the level of the third lumbar vertebra (L3) was used for skeletal muscle area (SMA) assessment, and change between CT-assessments was calculated.

DICOM files were analyzed with coreslicer.com software. Participants were categorized by time between scans (<10 days, 10–20 days, >20 days).

Orogastric tubes were routinely placed. Calories and protein were prescribed following ESPEN guidelines (25 kcal/kg, 1.3 g/kg, respectively).⁶ Adjusted body weight was used to calculate the energy requirement in patients with a BMI > 30 kg/m². Daily recording of energy and protein provision was done. Total energy provided was calculated from non-nutritional calorie sources and enteral nutrition (EN) prescriptions. Cumulative protein (CPD) and energy (CED) deficits on the day of the second CT scan were also determined.

Quantitative variable distribution was evaluated using the Shapiro-Wilk test. Descriptive statistics included categorical variables (absolute and relative frequency) and quantitative variables (mean \pm SD or median with IQR). The total change and per day of the SMA were reported in cm² and percentage (%) of change. Differences between genders were assessed with the Mann-Whitney *U* test. The daily and total CPD and CED of each group were analyzed comparing the SMA of the initial measurement vs the subsequent measurement using *t*-Student test for paired samples. Linear regression examined factors associated with SMA loss percentage. Analysis was conducted with Stata Intercooled (Version 14). Statistical significance was set at $P < .05$.

Fourteen critically ill patients were included in this analysis (50% females). Severity of disease score was 10 ± 3 using SOFA and 18 ± 6 for APACHE II. The nutritional risk was 4 ± 1 using NUTRIC-Score; only 4 (28.6%) patients were detected with high nutritional risk.

No significant differences in muscle mass loss percentage were found between patients with low versus high nutritional risk (18.1 [10.7–24.5] vs 12.9 [12–15.6], $P = .671$). The total CED and CPD to the day of second CT were 6141 (3850–9584) kcals and 313 (219–516) g, respectively (Table 1).

Significant SMA loss was observed in both genders (Supplementary Table 1). An average muscle wasting of 14.5% was observed for the study period (loss of 1.05% per day). Additionally, significant decrease in SMA was observed along the three groups (<10 days, 10–20 days and >20 days), with reported changes of 11.7, 13.7 and 21.2% respectively (Supplemental Table 2). Linear regression analysis was performed to identify predictors of muscle wasting. No statistical predictors were observed in univariate analysis. Using stepwise regression, only age ($P = .04$) and SOFA score ($P = .02$) showed association (Table 2).

Table 1 Clinical characteristics of critically ill patients.

Patient	Age (years)	Gender	BMI (kg/m ²)	Comorbidities	First CT SMA (cm ²)	Subsequent CT SMA (cm ²)	Days between CT scans	SMA total change cm ² (%)	SMA change per study day cm ² (%)	Cumulative Energy Deficit (total kcal/kcal per day)	Cumulative Protein Deficit (total g /g per day)
1	44	F	29.1	T2D	66.97	55.26	7	11.71 (17.49)	1.46 (2.49)	1416.5/202.3	76.3/10.9
2	29	F	31.1	T2D, HT, OB	109.4	96.55	8	12.85 (11.75)	1.61 (1.47)	6259/782.3	373/46.5
3	48	F	35.3	T2D, HT, OB, AKI	120.3	107.4	9	12.9 (10.72)	1.43 (1.19)	8076/897.3	516/57.3
4	31	M	29.1	AKI	167.8	142.1	11	25.7 (15.32)	2.14 (1.28)	3549.1/322.6	218.74/19.9
5	28	F	40.2	OB	166	152.8	11	13.2 (7.95)	1.1 (0.66)	3850/350	81.4/7.4
6	49	F	34.2	HT, OB	87.26	65.83	12	21.43 (24.5)	1.79 (2.05)	5692.5/474.3	269.6/22.4
7	43	M	28.8	OB, AKI	181.5	136.3	12	45.2 (24.9)	3.77 (2.8)	4177/348.8	251.5/20.9
8	60	M	23.6	None	123.2	108.3	14	14.9 (12.1)	1.06 (0.86)	9584/684.5	356/25.4
9	53	F	41	T2D, OB, fibromyalgia	82.05	70.79	15	11.26 (13.72)	0.75 (0.91)	6022.8/401.5	405/27
10	40	M	25.8	HT, hypothyroidism	165.3	145.6	17	19.7 (11.92)	1.04 (0.63)	2449/144.6	103.5/6.1
11	25	M	28.2	Dyslipidemia	160.8	127.2	20	33.6 (20.9)	1.34 (0.84)	22156.3/1107.8	705.7/35.8
12	62	F	25.3	OB	110.3	70.79	23	39.51 (35.82)	1.72 (1.56)	6480/281.7	236/10.3
13	33	M	24.8	T2D	119.5	116.7	23	2.8 (2.34)	0.12 (0.1)	13,871/603.9	590/25.65
14	19	M	26.9	None	185.2	145.3	28	39.9 (21.54)	1.29 (0.69)	13123.2/468.6	636/22.7

F: Female, M: Male, T2D: type 2 diabetes, HT: hypertension, OB: obesity, AKI: acute kidney injury, SMA: skeletal muscle area, CT: computed tomography, BMI: body mass index.

Table 2 Predictors of skeletal muscle area wasting measured by computed tomography.

Univariate			Multivariate	
Predictors of muscle wasting	β , CI 95%	P-value	β , CI 95%	P-value
Age (years)	0.19 (−0.18 to 0.57)	.28	0.35 (0.009–0.69)	.04*
SOFA score	−1.3 (−3.2 to 0.42)	.12	−2.04 (−3.7 to −0.34)	.02*
APACHE II	0.018 (−0.85 to 0.89)	.96		
NUTRIC-Score	−2.48 (−6.38 to 1.4)	.18		
Energy Deficit (1000 kcal)	−0.022 (−0.98 to 0.93)	.96		
Protein Deficit (10 g)	−0.03 (−0.29 to 0.22)	.76		
Days receiving midazolam	0.61 (−1.18 to 2.42)	.44		
Days receiving fentanyl	−0.07 (−0.78 to 0.63)	.82		
Days receiving propofol	0.03 (−1.13 to 1.21)	.94		
Days between CT scans	0.33 (−0.48 to 1.14)	.39		
Gender (men)	−1.85 (−12.06 to 8.34)	.69		

SOFA: Sequential Organ Failure Assessment, APACHE II: Acute Physiology And Chronic Health Evaluation II.

* P value < .05.

Our study provides data about the rate of skeletal muscle area wasting in COVID-19 critically ill patients, we found a decrease of 17.3 (12.85–33.6) cm² in SMA, which represents a muscle loss of 14.5% in an average time of 15 days. The daily percentage of muscle wasting reported by another study was 1.09% during the first 13 (9–18) days of ICU stay,⁷ this is close to our results where the included population had a daily muscle loss of 1.05% (0.69%–1.55%) during the first 15 days in ICU. Longer ICU stays correlate with increased muscle mass loss.¹ We reported that the muscle wasting varies with time elapsed between measurements (<10 days, 10–20 days, >20 days), with changes of 11.7%, 13.7%, and 21.2% respectively. This progression of muscle loss may be attributed to clinical factors like higher CPD, CED, and extended use of sedatives, neuromuscular blocking agents, and immobilization.⁸ However, in our study, only age and SOFA score showed association. Age independently correlates with the percentage of SMA wasting, this result aligns with existing evidence indicating a lower anabolic response in the elderly compared to younger adults.⁹ Contrary to found by Gutiérrez-Zárate et al.,¹⁰ our analysis did not confirm a relationship between muscle loss and disease severity assessed by the SOFA score, possibly due to sample size limitations.

This study's strength lies in including patients with CT scans around ICU admission, enabling early muscle mass assessment and monitoring during ICU stay. CPD and CED were considered, nutritional indicators potentially related to greater muscle catabolism. However, limitations include: single-center enrollment, limited sample size, no data about physical rehabilitation interventions or clinical outcomes were recollected.

Muscle mass loss is a common and multifactorial problem in COVID-19 critically ill patients. Future research to assess nutritional therapies need to be tested.

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Conflict of interest

All authors declare that they have no conflict of interests.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.medine.2024.04.010>.

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High rate-trauma: the new world order?



Trauma relacionado a alta frecuencia: ¿El nuevo orden mundial?

When the lung parenchyma is exposed to cyclic stress, lung compliance inevitably begins to decrease.¹ Respiratory rates higher than 25 per minute, generate a higher energy transfer,² which leads to a higher heterogeneous strain mainly due to a lower lung resilience capacity.³ High respiratory rates produce hypocapnia and respiratory alkalosis, but also cause direct injury through chemical effects as a consequence of the alteration of mechanoreception reflexes, which is ultimately associated with greater morbidity and mortality.⁴

If the oscillatory frequency of the lung tissue exceeds the maximum limit of its elastic behavior, the heterogeneous variability of the strain⁵ and the affectation in the capacity of the parenchyma to assimilate the transmitted energy (stress), will result in a decrease of the tissue resistance with a tendency to zero, which will lead to the appearance of micro ruptures of the pulmonary cytoskeleton.⁶

The recent study published by the Mechanical Power Day [MPD] group,⁷ by applying the formula proposed by Gattinoni et al.,⁸ showed a mean mechanical power (MP) of 19.20 J/min (SD 8.44) for patients on pressure-controlled ventilation (PC-CMV) and 16.01 J/min (SD 6.88) for those on volume-controlled ventilation (VC-CMV). However, the researchers propose an interesting formula for the calculation of MP, using strain and strain-rate subrogates, based on

solid concepts of materials engineering and thermodynamics, which have already been used in other clinical studies.⁹ A relevant point is the time factor, which is also implicit in the subrogation of the strain-rate according to the formula proposed by the MPD group. In VC-CMVs, the strain-rate corresponds to Flow ratio/PEEP and DP to strain; whereas in PC-CMVs, the strain-rate corresponds to subrogated strain (ETv/PEEP)/inspiratory time.

The authors reported a mean of 17 breaths per minute in both groups (PC-CMVs and VC-CMVs), with no significant difference (Welch, $p=0.12$).

We performed an analysis post hoc of the MPD using frequentist statistics to evaluate the behavior of the respiratory rate, analyzing the variables that are part of the MP equation proposed by González-Castro et al.,⁷ of the multicenter and international cross-sectional cohort.⁷ We decided to dichotomize the sample between those with high-energy MP (>17 J/min) and compare them with those with low-energy MP (<17 J/min), as supported by current evidence.⁸

Bivariate analysis showed that respiratory rate behaved as a risk factor for high-energy MP, regardless of the ventilatory mode used (PC-CMVs; OR 1.56; 95% CI: 1.32–1.84; $p < 0.01$ /VC-CMVs; OR 1.46; 95% CI: 1.29–1.65; $p < 0.02$). In the multivariate analysis [Table 1], although PEEP was the variable that showed the greatest association with risk of high-energy MP, the behavior of respiratory rate was very similar in both ventilatory modes, showing a greater probability of association with high-energy MP both in those patients ventilated in PC-CMVs (OR 1.96; 95% CI: 1.50–2.55; $p < 0.01$), as well as in those on VC-CMVs (OR 1.41; 95% CI: 1.23–1.62; $p < 0.01$) [Table 1 and Fig. 1].