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RESEARCH ARTICLE

Ultrasonography: New Insights in its Applicability to Explore Muscle Mass and Musculoskeletal Inflammation in Critically ill Patients

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Objective: The main aim of the study was to explore muscle mass changes and to investigate musculoskeletal inflammation in critically ill patients. **Methods**: A pure observational study that comprised two musculoskeletal analyses was conducted. Ultrasonography was used to determine the inflammatory process and muscle mass modifications. We assessed the presence of musculoskeletal inflammation and muscles area reduction. We recruited 26 patients and we performed both imaging investigations (shoulder and hip joints, biceps brachii and rectus femoris areas) and anthropometric measurements (mid-upper arm circumference). **Results**: More than 70% of patients were classified with low muscle mass, over one half of sarcopenic patients being over-weight and 17% being obese. The relationship between the length of stay in intensive care unit, mechanical ventilation and presence of low mid-upper arm circumference, highlighted a significant difference when comparing sarcopenic and non-sarcopenic groups. Musculoskeletal inflammation expressed by step-down lesions, calcifications and osteophytes, is common in these patients. Statistically significant results were obtained when comparing the dimensions of the investigated muscles. Good inter-observer variability in day 3 of assessment for biceps brachii and rectus femoris was noticed. **Conclusions**: More than 1/3 of critically ill patients included in the present study was classified with low muscle mass. The length of stay in intensive care unit and the length of mechanical ventilation had an important impact on sarcopenic patients. Musculoskeletal impairment was frequent, reflected by presence of enthesitis lesions in joints and by dynamic reduction of muscle area.

Keywords: ultrasonography, low muscle mass, sarcopenia, critically ill patients

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Introduction

Various concepts have been proposed in order to define critical illness, both acute and chronic. There is not a precise mark of differentiation between acute critical illness and chronic critical illness, the evolution from acute to chronic being progressive [1, 2]. Considering that critically ill patients are distinguished by the needs of special care and large numbers of intensive care unit (ICU) resources, their management should comprise not only the life support treatments, but also the prevention of the short and long-term negative sequela [3]. Taking into account the frailty syndrome and disability that characterize critically ill patients, the assessment of other comorbidities should be made.

Sarcopenia, muscle mass impairment and musculoskeletal inflammation as pre-existing comorbid diseases are vehement predictors of life quality in post-ICU patients [4]. Designed as a major public health issue, the highest prevalence estimation shows a 63.8% increase from 2016 to 2045 (from 19.740.527 to 32.338.990 persons) [5]. The European Working Group on Sarcopenia in Older People (EWGSOP) enclosed in the diagnostic criteria of sarcopenia the presence of both low muscle mass and low muscle function (strength and performance) [6]. There are many tools to assess sarcopenia (muscle mass: computed tomography, magnetic resonance imaging, dual energy X-ray absorptiometry, bioimpedance analysis; muscle strength: handgrip strength, knee flexion/extension; physical performance: short physical performance battery, usual gait speed, stair climb power test) [6], but there are few data regarding the use of ultrasonography and its applicability to explore muscle mass and musculoskeletal inflammation in critically ill patients.

The main purpose of this study was to explore the muscle mass changes and to investigate the musculoskeletal inflammation in critically ill patients. It is important to recognise muscle impairment by repeating dynamically the same measurements in the same patients, in order to find out the ubiquity of sarcopenia in critically ill patients and to optimize the diagnostic.

Material and method

We conducted a pure observational, non-interventional study that comprised two musculoskeletal analyses.

On the one hand, we assessed the presence of musculoskeletal inflammation in critically ill patients. As ultrasonography is considered a valuable tool to determine the inflammatory process, some of the joints' pathological features were examined in the interest of detection of en-

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thesitis. For 15 critically ill patients both scapulo-humeral and coxo-femoral joints were observed, by looking for changes in muscular inflammation: bursitis, osteophytes, entesophits, calcifications, erosions, Doppler signal [7], by an experienced operator.

On the other hand, a group of 11 critically ill patients followed three ultrasonographic determinations on the biceps brachii and recuts femoris area, corresponding to 5 days period (day 1, day 3, day 5), in order to identify muscle area reduction. These tests were completed by two operators (novice and experienced) in the furtherance of inter-variability assessment.

Anthropometric measures have been used to estimate muscle mass. Calculations based on mid-upper arm circumference (MAC) and skin fold thickness were adopted. Applying the following formula: *MAC= mid-upper arm circumference – (3.14*skin fold thickness)*, low muscle mass was classified with MAC <21.1cm for men and MAC <19.2cm for women [8].

We completed a data base where the following information were noted: demographic data, reasons of admission in the ICU, anthropometric measurements, results of imaging investigations, length of stay in ICU, necessity of mechanical ventilation (MV), severity scores: GCS (Glasgow Coma Scale), APACHE II (Acute Physiology and Chronic Health Assessment), SOFA (Sequential Organ Failure Assessment) and secondary effects of intensive care hospitalisation (metabolic, protein, renal dysfunctions).

To operate statistical analysis Microsoft Office Excel package, GraphPad Prism 6 and SPSS were used. To verify Gaussian distribution Kolmogorov-Smirnov test was used and a p ≤0.05 was set as reference, with a confidence interval (CI) of 95%. Intraclass correlation coefficient (ICC) was used to attest inter-variability between two operators.

Prior to the onset, the approval from the Ethics Committee of Targu Mures Clinical County Emergency Hospital was obtained. All data used have no personal character and conformed to the Helsinki Declaration.

Results and Discussions

Twenty six critically ill patients (62% men, 38% female) that met inclusion criteria (critically ill patients admitted to the ICU for a stay of at least 24 hours; patients over 18 years old; patients for whom imaging investigations and anthropometric measurements have been performed) were included in the study.

Type of admission was acute medical for 65% patients and acute surgical for 35% patients. The most common cause of admission was respiratory failure (31%), followed by neurologic degradation (21%), after-surgery life support necessity (14%) and sepsis (11%). 85% of these patients presented pre-existing comorbidities, nearly one third being diagnosed with diabetes. With a high prevalence of diabetes worldwide, this result confirmed Bianchi's hypothesis that diabetes was a risk factor contributing to several complications including muscle frailty and sarcopenia [9].

Taking into consideration demographic data and anthropometric measurements, two groups of conditions were formed: sarcopenic group (muscle mass (MAC) under the cut-off) and non-sarcopenic group (muscle mass (MAC) above the cut-off). More than 1/3 of patients were classified with low muscle mass by following the method indicated in Gariballa's article published in Clinical Nutrition. These groups were homogenous with no significant difference regarding the age (average age 62.77±15.17 years old) or body mass index (BMI) (Table I.) Despite of this, the study pointed out that 53% of sarcopenic patients are over-weight and 17% are obese. Sarcopenic obesity was described by Baumgartner as low muscle mass index less than 2 SD below the sex-specific reference for a young, healthy population [10]. Besides diabetes, sarcopenic obesity should be considered a risk factor for critically ill patients, acting synergistically to develop multiple negative outcomes by increasing morbidity and mortality [11].

We assessed the short term impact of sarcopenia in critically ill patients. We identified a significant difference between sarcopenic and non-sarcopenic patients when we considered length of stay (LOS), MV and low MAC. (Table II.)

Severity scores based on laboratory results and clinical data (GCS, APACHE II, SOFA) were noted for each patient, but there was no significant difference between sarcopenic and non-sarcopenic patients (p>0.05). (Table III)

Regarding musculoskeletal inflammation, the most common lesions observed both at scapulo-humeral and coxo-femoral joints were step-down lesions (28% shoulder, 25% hip), calcifications (22% shoulder, 35% hip), and osteophytes (24% shoulder, 28% hip) (Figure 1, Figure 2). As consequence, musculoskeletal inflammation could be a pre-existing comorbidy or the critical care environment and immobility could predispose to muscle impairment.

Table I. Patients' characteristics (sarcopenic versus non-sarcopenic)

	p
Age	0.069
BMI	0.281

Age: patients >18 years old were included; BMI: weight/ (height x height), considering BMI >25.00 overweight; BMI >30.00 obesity

Table II. Short term impact of low muscle mass in critically ill patients

	p	R squared	CI (95%)
Length of stay	0.006	0.269	3.452 – 19.130
MV (hours)	0.003	0.013	-6.167-3.475

Table III. Severity scores in sarcopenic versus non-sarcopenic patients

	p	R squared	CI (95%)
GCS	0.569	0.013	-6.167- 3.475
APACHE II	0.267		
SOFA	0.430	0.026	-9.885- 4.351

In order to investigate rapid reductions in muscle mass, two operators consecutively checked every patient by using ultrasound diminution in the area of biceps brachii (BB) and rectus femoris (RF) in day 1, day 3 and day 5 as presented in Table IV. and Table V.

Both observer 1 and observer 2 obtained statistically significant results when comparing the dimensions of the investigated muscles. There was a statistically significant decrease in muscle mass at BB level between the first two evaluations and the third assessment (p = 0.032, r = 0.0380, CI = -0.612-0.032; p = 0.033, r = 0.379, -0.523- -0.027). Also, there was a decrease in the ultrasound measured area at the left BB between the second and third investigations (p = 0.037, r = 0.474). At the level of the lower limbs, both observer 1 and observer 2 surprised a diminished area measured at the left RF level between evaluation 1 and assessment 2 (p = 0.038, r = 0.370, CI = -0.568-0.018; p = 0.001, r = 0.690, CI = -0.610 -0.208). These results sustain Nakanishi's observations that skeletal muscle weakness is common in critically ill patients. The letter published in Intensive Care Med (2018) showed atrophy in muscle of critically ill patients in both upper and lower limbs.

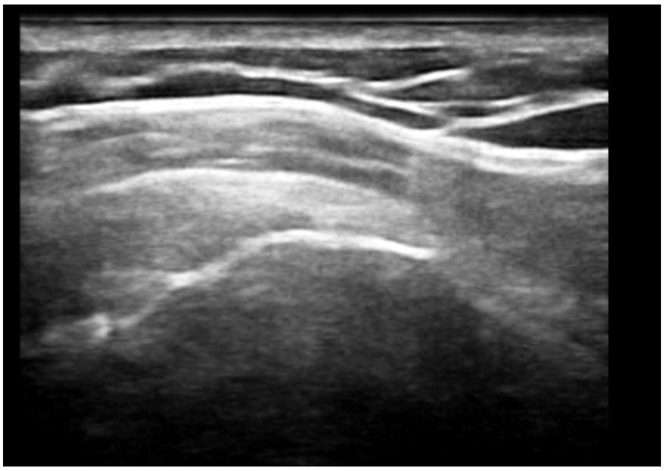

Fig. 1. Osteophytes and erosions shoulder joint

Fig. 2. Calcifications and erosions hip joint

The secondary objective was to evaluate inter-observer variability of the results, analysing the same subjects. It has been pointed out in the literature that a kappa value of between 0.7-0.9 gives confidence in results [13]. In the current study, Intraclass Correlation Coefficient (ICC) proves good inter-observer variability at the following levels: BB right assessment 3, RF left assessment 3, RF right evaluation 1 (Table VI.). (Insert table VI). These results demonstrate that more practice improves the quality of the investigation.

Conclusions

Even if more than half of the critically ill patients were obese at admission, they were classified with low muscle mass. Results sustained that the LOS in ICU and the length of MV negatively impact sarcopenic patients. Musculoskeletal impairment is frequent as pre-existing condition or due to ICU immobility, reflected by presence of enthesitis lesions in joints and by dynamic reduction of muscle area both in upper and lower limbs.

Authors' contribution

OEB – Conceptualization, data curation, formal analysis, investigation, methodology, writing original draft
ARJ – Formal analysis, investigation, methodology

Table IV. Dynamic changes in muscle mass (observer 1)

	p	R	CI (95%)
BB right ev 1/2	0,705	0,014	-0,317- 0,223
BB right ev 1/3	0,032	0,380	-0,612- -0,032
BB right ev 2/3	0,033	0,379	-0,523- -0,027
BB left ev 1/2	0,564	0,038	-0,381- 0,655
BB left ev 1/3	0,695	-0,407	
BB left ev 2/3	0,037	0,474	
RF right ev 1/2	0,492	0,340	
RF right ev 1/3	0,105	0,291	
RF right ev 2/3	0,058	0,731	-0,541- 0,011
RF left ev 1/2	0,038	0,370	-0,568- -0,018
RF left ev 1/3	0,131	0,356	-0,443- 0,066
RF left ev 2/3	0,261	0,446	-0,091- 0,302

Ev 1/2, 1/3, 2/3 refers to the comparation between muscle mass assessments day 1 / day 2/ day 3

Table V. Dynamic changes in muscle mass (observer 2)

	p	r	CI (95%)
BB right ev 1/2	0,885	0,024	-0,346- 0,395
BB right ev 1/3	0,240	0,123	
BB right ev 2/3	0,097	0,388	
BB left ev 1/2	0,999	0,224	
BB left ev 1/3	0,425	0,307	
BB left ev 2/3	0,064	0,620	
RF right ev 1/2	0,556	0,413	
RF right ev 1/3	0,112	0,154	-0,726- 0,090
RF right ev 2/3	0,625	0,248	
RF left ev 1/2	0,0087	0,247	-0,698- 0,130
RF left ev 1/3	0,0011	0,690	-0,610- 0,208
RF left ev 2/3	0,951	0,622	-0,189- 0,200

Table VI. Inter-observer variability assessment

	Significance	ICC	CI (95%)
RF right ev 1	0.005	0.804	0.342-0.946
BB right ev 3	0.041	0.714	-0.137-0.929
RF left ev 3	0.041	0.701	-0.151-0.920

RGB – Formal analysis, investigation, methodology
SMC – Conceptualization, methodology, supervision, visualization
MC – Conceptualization, methodology, supervision, validation, visualization

Conflict of interest

None to declare.

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