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"GEORGE EMIL PALADE" UNIVERSITY OF MEDICINE, PHARMACY, SCIENCES AND TECHNOLOGY FROM TÎRGU MUREŞ

PHD THESIS: STATE-OF-THE-ART IN MUSCLE CHANGES IN CRITICALLY ILL PATIENTS: SARCOPENIA, MUSCLE WASTING AND QUALITY OF LIFE

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In Romania, the issue of examining the skeletal and diaphragmatic muscles, respectively the investigation of muscle dysfunction is rarely addressed in critically ill patients. Also, the medical literature offers an extremely small number of national studies on muscle impairment in the critically ill. In this context, this PhD thesis introduced the following general objectives:

- Assessment of the attitude of anaethesia and intensive care doctors regarding the sarcopenia of the critically ill patient and of the perioperative patient;
- Evaluation of muscle wasting in ceitical setting through static imaging and exposure of the CT scan role's in determining diaphragmatic and psoas muscle alterations, in critical COVID-19 patients and in non-COVID-19 patients with thoracic trauma;
- Examining the quality of life of critical COVID-19 patients after hospitalization in the ICU.

The hypothesis proposed by these studies and by the determination of the results refers to the possible recognition of muscle alterations in the early stages of critical illness that could facilitate the implementation of strategies to limit the development of the pathology.

The general methodology of the thesis includes the following aspects: for the evaluation of bibliographic references and the review in the general part, it was used the population, intervention, comparison and results (PICO) design, representing the search criterion in systematic reviews. According to the World Medical Association, all studies conducted in this thesis used the Declaration of Helsinki to guide the protection of human participants in clinical research. Due to the observational nature of the studies, STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) features were applied to each of the six studies.

In this context, this doctoral thesis analyzes an important medical problem, referring to sarcopenia, muscle wasting and the quality of life of the critical patient after hospitalization in the Anesthesia and Intensive Care Clinic. The complexity is noted through the lens of the critical patient approach and the studies carried out with the aim of contributing to supplementing the data from the specialized literature with new and up-to-date results. The importance of the obtained results is reflected by the increased awareness of the muscular alterations identified in the critical patient of the doctors of the Anesthesia and Intensive Care Clinic, at the local and national level.

The main studies included in the thesis refer to: the evaluation of the attitude and knowledge of anesthesiologists and intensivists about sarcopenia in the critical patient and in the perioperative patient, being the first national study to investigate this aspect; appreciation of the role of static imaging, CT in the evaluation of muscle alterations in the critical patient, both the peripheral skeletal muscles and the respiratory muscles being analyzed, and the main groups of patients including critical COVID-19 patients and non-COVID-19 patients admitted for chest trauma; respectively, determining the quality of life of COVID-19 patients after hospitalization in the Anesthesia and Intensive Care Clinic.

Study 1: RO ANESTHESIA&ICU SARCOPENIA – The attitude and knowledge of Aesthesia and Intensive Care doctors about sarcopenia in the critically ill and in the perioperative patient: the first national study of current clinical practice

This is the first survey applied to clinicians in the Anestesia and Intensive Care specialty, in Romania, representing the first step in exploring the knowledge, opinions and perspectives regarding sarcopenia in perioperative and critically ill patients. Responses of the 150 participants demonstrate that although there is an understanding of the meaning of the sarcopenia definition and use of muscle parameters in the assessment and monitoring of sarcopenia, there is also a deficiency in practical implementation in the perioperative and critically ill patient. Thus, the integration of strategies to address muscle dysfunction in clinical practice could have the potential to improve screening and monitoring procedures, with a possible favorable outcome on the patient's prognosis.

Study 2: Computed tomographic evaluation of diaphragmatic changes in 20 critical patients with COVID-19

During the 4th wave of the COVID-19 pandemic, 20 critical patients benefited from the assessment of the diaphragm thickness by CT scans in dynamics, with the average time between CT1 and CT2 scans of 7.9 days, determining that the right diaphragm was altered by -7.83 ± 11.11%, and the left diaphragm by -5.57 ± 10.63% for half of the sample. All patients presented a marked inflammatory status, a high level of physiological stress and altered acid-base balance, respectively weak correlations were determined between diaphragm changes and different types of oxygen therapy, non-invasive ventilation and mechanical ventilation.

Study 3: Evaluation of the decrease in diaphragm thickness in critical patients with COVID-19 - is computed tomography an advantage in the assessment of diaphragm muscle mass?

This study identified all positive COVID-19 patients in critical condition admitted to the Anestheia and Intensive Care Clinic from August 2020 to December 2022. Out of 1427 patients, 75 were included in the study, adults, hospitalized in the clic for at least 24 hours, who required any type of oxygen therapy and had at least two CT examinations during hospitalization (more than 24 hours apart). For the 150 scans, the mean difference between CT investigations (CT1 and CT2) was -0.58 mm for the right diaphragm and -0.54 mm for the left diaphragm. Between the two CT investigations, diaphragm thickness was significantly decreased on both the right and left sides ($p=0.02$). Decreased diaphragm thickness was negatively but not statistically significantly associated with length of stay in ICU and total length of stay. No statistically significant differences were observed between the group with decreased diaphragm thickness and the group without decreased diaphragm thickness in terms of inflammatory and metabolic responses ($p>0.05$). Also, AUC and cut-off values for mortality risk in ICU, prolonged mechanical ventilation, respectively OR for mechanical ventilation, length of hospitalization in ICU, total length of hospitalization and outcome were analyzed.

Study 4: Assessment of total psoas area and psoas density in critically ill COVID-19 patients using CT imaging - can muscle mass alteration be determined during intensive care hospitalization?

In this study, two CT scans performed during hospitalization were analyzed. The total area and density of the psoas in dynamics were compared. For the 22 included patients, good reliability was demonstrated in both psoas measurements for two examining radiologists. With minor mean differences in the total area and density of the right and left psoas, no statistically significant differences were recorded ($p>0.05$), yet the dynamic decrease was detected in the total area of the psoas (right TPA=-0.12cm2, $p=0.88$; left TPA=-0.59 cm2, $p= 0.56$) and in psoas density (right psoas HU= -4.24, $p=0.17$; left psoas HU= -3.99, $p= 0.17$).

Study 5: Outcome of critically ill patients admitted for chest trauma – analysis of hospitalized patients over a one-year period, single-centre study

In the absence of specific national data, the current study aimed to analyze the cohort of patients hospitalized in a level 3 Anesthesia and Intensive Care Clinic over a one-year period, focusing specifically on chest trauma cases This study identified 52 patients with closed or penetrating thoracic trauma, in critical condition, hospitalized in the clinic, between January 01, 2021 and December 31, 2021, for whom a CT analysis of the diaphragm was performed, of which 39 patients also benefited from a CT analysis of the psoas. Results of this study represent a complex analysis of critically ill patients hospitalized for chest trauma. After implementation of the standard protocol of therapy and support of vital functions, it was found that all patients included in the study had a correct hemodynamic and respiratory response. On the other hand, the CT scan has also a purpose that extends beyond the identification of life-threatening injuries, as it could provide valuable assistance in the assessment of musculoskeletal, respiratory and peripheral musculature, with emphasis on diaphragm thickness, area and density of the psoas. Although no significant differences in prognosis were found between survivors and deceased, the results could serve as a predictor for injury severity.

Study 6: Assessment of the quality of life and LONG-COVID syndrome in COVID-19 patients after hospitalization in intensive care by applying the WHOQoL-BREF questionnaire

The sample included 67 critically ill patients, aged ≥18 years, who complied with the WHO case definition for COVID and RT-PCR testing, and who responded to the validated BREF-WHOQoL questionnaire in Romanian. The multidimensional nature of the BREF-QoL questionnaire allowed the assessment of the main result of this study, which demonstrated that critical COVID-19 patients reported low levels of QoL in the assessed domains. Clinically, such evaluations can be performed to determine the potential benefits of implementing rehabilitation therapies.

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