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Letter to the Editor

When Appearances Can be Deceiving: Sarcopenia and Obesity Paradox. Unsolved Issues in Critically Ill Surgical Patients

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Abstract

Faced with the complexity of emergency surgery and the aging of the population, it is increasingly common to have to deal with critically ill patients who require intensive care postoperatively. Surgical stress amplifies senescence mechanisms where the organism is called to face the establishment of both early and late pathophysiological mechanisms disrupting homeostasis.

In this scenario, sarcopenia represents a prognostic factor with a multifactorial etiology that can lead to fearful complications in the early postoperative period. As an octogenarian adaptation, its multifactorial genesis allows to act and counterbalance the action of concomitant modifiable factors through post-operative optimization strategies.

Keywords: Sarcopenia, obesity paradox, emergency surgery, ICU

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Critically ill patients after emergency surgery in an intensive care setting often experience several organ dysfunctions leading to an indisputable increase in postoperative morbidity and mortality.

Although emergency laparotomies are time-sensitive stretagies, mortality rates still remain high, ranging from 14-20%.[1]

Notwithstanding technical and strategical improvements, reported incidences suggest emergency surgical patients are older than ever, making to face to preexistent comorbidities and functional decline whose detrimental effects on prognosis still claim debate. Several scoring systems have been promoted to predict clinical outcomes in intensive care unit (ICU) patients, such as the Acute Physiology And Chronic Health Evaluation – II or Sequential Organ Failure Assessment.[2]

Sarcopenia, characterized by progressive wasting of both muscle strenght and mass, is usually reported in ICU patients as a consequence of previous comorbidities, inflammation, sepsis, severity of surgical emergencies and prolonged hospital stay, with an increasing prevalence with aging up to 50% of patients.[3]

Recently, several studies have investigated the prognostic role of sarcopenia in these patients with inconsistent results and evidences, though a putative prognostic role of sarcopenia would be conceivable. Data would suggest a

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direct implication on prognosis in patients undergoing supra-mesocolic surgery, such as gastric or esophageal one. But experiences and evideces are usually limited to an elective setting or to optimized oncological patients.

In a recent systematic review including fourteen studies, Zhang et al.[4] reported a pooled prevalence of sarcopenia in ICU patients of 41% with a significant statistical correlation with a two-fold increased risk of mortaliy compared with patients without sarcopenia (OR: 2.28, 95%CI: 1.83-2.83, p<0.001) and a three-fold increased risk regardless any 1-year mortality type (OR: 3.23, 95%CI: 2.08-5.00). Similarly, Yang et al.[5] demonstrated sarcopenia should be considered a short-term prognostic [OR: 2.42, 95%CI: 1.93-5.05, p<0.00001) and risk factor for ICU admission after surgery [MD: 0.55, 95%CI: 0.05-1.06, p=0.03], hospital lenght of stay [MD: 2.33, 95%CI: 1.33-3.32, p<0.00001] as far as postoperative complications [OR: 1.78, 95%CI: 1.41-2.26, p<0.00001].

Predict or define sarcopenia is often inaccurate and challenging. Several studies have focused on prediction tools, but evidences suggest a poor sensitivity leading to a generalized underestimation and, therefore, to a lack of a prompt diagnosis in high-risk cohorts of patients.[6] The only recognized and reliable indicator is the cross-sectional evaluation of the psoas major area (PMA) on abdominal computed-tomographies.[7]

Moreover, available models and normograms are too far from a universalistic applicability and usability as they do not concretely respond to inevitably interfering socio-demographic variable. Ethnicities, lifestyles, socio-economic welfare, psychosocial variables, environments, availability and access to cares are only aspects leading to an unlikely common definition and cut-off values.[8]

It would therefore not be surprising to speculate on a significant higher prevalence of sarcopenic patients subjected to an erroneous nosological classification, where vicious circles would establish and augment interactions between previous comorbidities and postoperative malnutrition.

A proper primary survey in ICU patients in the post-operative period would reduce the abovementioned misevaluations as in case of obese subjects. Obesity, in fact, frequently leads to a common paradox, known "obesity paradox" and it does not exclude the coexistence of sarcopenia, as results of wasting concurrent phenomena (immobility and long-term hospitalization).

Crucial aspects to improve clinical outcome in patients with sarcopenia in ICU setting after emergency surgery should be amended to specific clinical pathways focusing to optimization; but, nowadays, unanswered questions about these appropriate measures on modificable factors still remain. In this regard, there is no choiche for a preoperative optimization in an emergency setting, reling any effort to the only postoperative period where physiological dearrengements would be more severe and complex, leading to prolonged intubation and difficut-to-wean scenarios, reintubation within 48 hours of extubation (weaning failure) due to impaired muscolar functions and negative impact of surgical outcome.[9] Therefore, the reduction of postoperative catabolic effects would be at least a priority to minimize well known complications, such as sepsis, impaired mental status, prolonged hospitalizations and in-hospital deaths. Post-operative ICU optimization should rely on meintenance of physiological homeostasis, as it would seem anachronistic to expect a cure of previous chronic epiphenomena from the inevitable failure of metabolic reserves. A controversial point would be to discern where to act.

Sarcopenia is generally multifactorial, with environmental causes, comorbidities, tissue growth factor-beta (TGF-β) inflammation pathways activation, senescence of neuromuscular junctions and hormonal changes, depicting a clinical scenario with unmodifiable postoperative items (age, muscle senescence, hormonal changes, reduction in motoneuron density, lipodystrophy) and modifiable ones (inflammation and nutrition) (Fig. 1). It would seem, therefore, that the management of sarcopenic surgical critical patients in intensive care cannot be separated from these two common denominators. Ferrucci et al.[10] reported serum levels of the inflammatory cytokine interleukin-6 were directly related to a rapid decline in muscle dynamics, disability and loss of muscle strength. Another aspect is catabolism and nutritional support appears a priority. Adequate timing and nutritional optimization in critically ill ICU patients after emergency surgery is essential. The recent guidelines from the Europen Society for Clinical Nutrition and Metabolism (ESPEN)[11] recommend early enteral feeding (within 24 hours) over a late resumption and parenteral nutritional

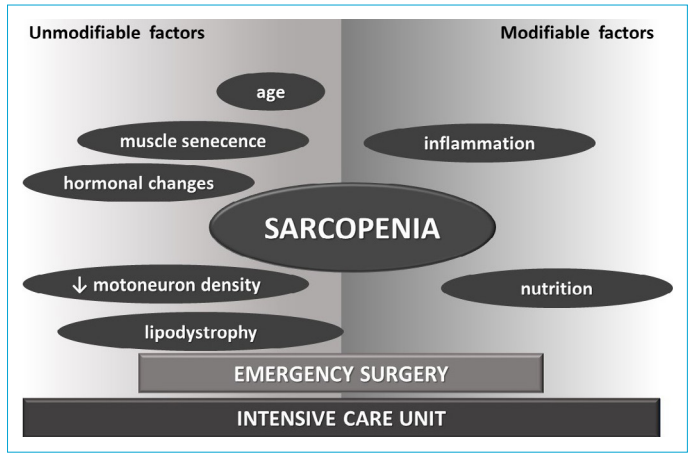

Figure 1. Factors contributing to sarcopenia.

support. There are only a few exceptions that could justify a delay (such as small bowel obstruction, bowel ischemia, uncontrolled shock, gastrointestinal bleeding and high gastrointestinal residual volume). However, recent evidence deriving from a post hoc analysis of the results emerged from the NUTRIREA-II trial suggests that, in the face of the premature increase in citrulline levels (indicator of the enterocytic thight-junctions breakdown), the only strategy to prevent bacterial translocative processes, sepsis and shock would be only early enteral nutrition.[12] The post-surgical phase and the related inflammatory processes result into an increased metabolism, insulin resistance and catabolic responses (glycogenolysis and release of fatty acids). However, catabolism should not to be inhibited as being a physiological adaptation, rather it should be counterbalanced by a step-up approache focusing on a progressive caloric intake to prevent overfeeding and normoprotein supplementation strategies acting on the preservation of the nutritional status by suppressing autophagic processes, as reported in the TARGET trial[13] (Fig. 2).

In conclusion, sarcopenia in critically ill post-surgical ICU patients remains an unsolved issue, whose prevention strategies are still far from an exhaustive solution. A proper risk stratification could be mystified by predictive models too far from an objective, universal and reproducible validation. To this date, efforts should focus on the maintenance aspects of homeostasis rather than on improvement of sarcopenia and its well-established prognostic effects on patients undergoing emergency surgery.

Disclosures

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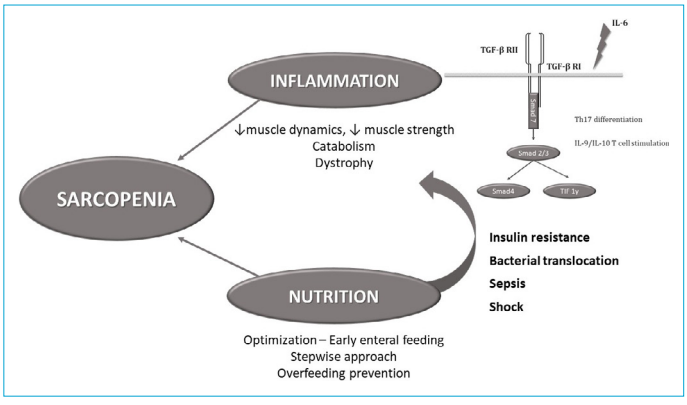

Figure 2. Strategies for optimizing sarcopenia in critically ill surgical patients and secondary pathophysiological mechanisms.

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