EDITORIAL

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Predicting outcome in abdominal sepsis: putting the puzzle together

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Acquired muscular weakness and muscle wasting are frequently observed in critically ill patients, especially after a prolonged time in the intensive care unit (ICU).[1] Patients with severe pulmonary and/or abdominal infections are at increased risk for *intensive care unit-acquired weakness* (ICUAW), which may present as *critical illness myopathy, critical illness polyneuropathy,* and/or their combination —*critical illness polyneuromyopathy.*[2,3] Both ICUAW and muscle wasting are serious medical conditions, observed in up to 40% of respective patients.[1,4] Current data indicate that impaired weaning from mechanical ventilation and additional neuromuscular dysfunction are frequent in patients with severe abdominal infections.[5] Despite aggressive medical treatment, patients suffering from abdominal sepsis regularly require prolonged treatment in the ICU; this can cause a vicious cycle of prolonged bed rest and/or need for sedation that contributes to pronounced ICUAW, unfavourable clinical outcomes, and mortality rates remained high for decades.[6]

More than two decades ago, single prediction scores such as the 'Acute Physiology And Chronic Health Evaluation' II or the 'Mannheim Peritonitis Index' were used to prognosticate clinical outcomes in patients with severe peritonitis and intra-abdominal sepsis.[7] More recently, we have learned that no single score can reliably predict outcomes in individuals suffering from peritonitis and that complex patient-related criteria and treatment-specific parameters should best define the outcomes of affected ICU patients. For example, Petersen *et al*. demonstrated in 2021 that outcome prediction in peritonitis significantly increases when multiple patient-derived factors and treatment-specific variables are integrated into a multidomain prediction model.[8]

In patients suffering from critical illness, acute muscle wasting often develops early (i.e. in the first few days of ICU treatment) and is accelerated in the presence of additional (multi-) organ dysfunction.[9,10] Retrospective data indicate that decreased muscle mass is a predictor of increased in-hospital mortality in elderly patients with sepsis.[11] In this issue of the *Journal of Cachexia, Sarcopenia, and Muscle*, Cox *et al*. provide important prospective data about the impact of acute muscle mass loss and sarcopenia on long-term outcome in critically ill patients with intra-abdominal sepsis.[12] The authors included 47 ICU patients suffering from intra-abdominal sepsis and followed them up for 1 year. Abdominal computed tomography scans were performed to assess skeletal muscle index.[12] This study confirmed that loss of muscle mass starts acutely and early in sepsis and persists over time, leading to a considerable delay in clinical recovery.[12] The authors observed that pre-existing sarcopenia, a condition which may be observed in a variety of chronic illnesses, is a predictor of poor functional outcome and increased mortality after 1 year.[12] While this study focused exclusively on patients with intra-abdominal sepsis, the results are in line with other studies evaluating sarcopenia, thus strengthening its value in predicting outcomes.[13,14]

The predictive synthesis of patient-related parameters and treatment-specific criteria can be amplified by the integration of molecular findings.[15] Inexpensive cell-derived biomarkers used to detect bacterial infection—such as the delta-haemoglobin equivalent and granularity index—are readily available and easily measured in a standard laboratory.[16] These simple lab tests, together with a multidomain prediction model and CT scans for skeletal muscle index measurement, could be integrated into a diagnostic/

predictive arsenal, alerting clinicians to which peritonitis patients are at higher risk for adverse outcomes. While the acute loss of muscle mass in patients suffering from abdominal sepsis may be difficult to prevent, maximal therapy could be tailored to individuals deemed 'high risk'.[17,18]

Cachexia and sarcopenia have already been established as risk factors for unfavourable clinical outcomes in chronic disease; we are however still gaining a better understanding of the relevance of acute muscle loss in acute abdominal sepsis. Cox *et al*. provide important additional prospective evidence for putting this particular puzzle together. Sarcopenia and muscle wasting are not just innocent bystanders in abdominal sepsis but play a significant role in determining patient outcome.

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Author contributions

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Conflict of interest

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References

1. Schefold JC, Wollersheim T, Grunow JJ, Luedi MM, Z'Graggen WJ, Weber-Carstens S. Muscular weakness and muscle wasting in the critically ill. *J Cachexia Sarcopenia Muscle* 2020;**11**:1399–1412.
2. Schefold JC, Bierbrauer J, Weber-Carstens S. Intensive care unit-acquired weakness (ICUAW) and muscle wasting in critically ill patients with severe sepsis and septic shock. *J Cachexia Sarcopenia Muscle* 2010;**1**:147–157.
3. Vanhorebeek I, Latronico N, Van den Berghe G. ICU-acquired weakness. *Intensive Care Med* 2020;**46**:637–653.
4. Fan E, Cheek F, Chlan L, Gosselink R, Hart N, Herridge MS, et al. An official American Thoracic Society Clinical Practice guideline: the diagnosis of intensive care unit-acquired weakness in adults. *Am J Respir Crit Care Med* 2014;**190**:1437–1446.
5. Zuercher P, Moret CS, Dziewas R, Schefold JC. Dysphagia in the intensive care unit: epidemiology, mechanisms, and clinical management. *Crit Care* 2019;**23**:103.
6. Bohnen J, Boulanger M, Meakins JL, McLean AP. Prognosis in generalized peritonitis. Relation to cause and risk factors. *Arch Surg* 1983;**118**:285–290.
7. Bosscha K, Reijnders K, Hulstaert PF, Algra A, van der Werken C. Prognostic scoring systems to predict outcome in peritonitis and intra-abdominal sepsis. *Br J Surg* 1997;**84**:1532–1534.
8. Petersen S, Huber M, Storni F, Puhl G, Deder A, Prause A, et al. IOutcome in patients with open abdomen treatment for peritonitis: a multidomain approach outperforms single domain predictions. *J Clin Monit Comput* 2021 Jul 10;https://doi.org/10.1007/s10877-021-00743-8 Online ahead of print.
9. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, et al. Acute skeletal muscle wasting in critical illness. *JAMA* 2013;**310**:1591–1600.
10. Kress JP, Hall JB. ICU-acquired weakness and recovery from critical illness. *N Engl J Med* 2014;**370**:1626–1635.
11. Shibahashi K, Sugiyama K, Kashiura M, Hamabe Y. Decreasing skeletal muscle as a risk factor for mortality in elderly patients with sepsis: a retrospective cohort study. *J Intensive Care* 2017;**5**:8.
12. Cox MC, Booth M, Ghita G, Wang Z, Gardner A, Hawkins RB, et al. The impact of sarcopenia and acute muscle mass loss on long-term outcomes in critically ill patients with intra-abdominal sepsis. *J Cachexia Sarcopenia Muscle* 2021.
13. Joyce PR, O'Dempsey R, Kirby G, Anstey C. A retrospective observational study of sarcopenia and outcomes in critically ill patients. *Anaesth Intensive Care* 2020;**48**:229–235.
14. Kaplan SJ, Pham TN, Arbabi S, Gross JA, Damodarasamy M, Bentov I, et al. Association of radiologic indicators of frailty with 1-year mortality in older trauma patients: opportunistic screening for sarcopenia and osteopenia. *JAMA Surg* 2017;**152**:e164604.
15. Heinisch PP, Meineri M, Luedi MM. Biomarkers in cardiac surgery: inch by inch toward perioperative organoprotection. *Anesth Analg* 2021;**132**:1545–1547.
16. Zimmermann M, Yürek S, Konzack R, Walter M, Schober P, Luedi MM, et al. Delta-hemoglobin equivalent and granularity index as cell-derived biomarkers for the

detection of bacterial infections. *Clin Lab* 2021; In Press.
17. Trethewey SP, Brown N, Gao F, Turner AM. Interventions for the management and prevention of sarcopenia in the critically ill: a systematic review. *J Crit Care* 2019;**50**:287–295.
18. Akan B. Influence of sarcopenia focused on critically ill patients. *Acute Crit Care* 2021;**36**:15–21.
19. von Haehling S, Morley JE, Coats AJS, Anker SD. Ethical guidelines for publishing in the Journal of Cachexia, Sarcopenia and Muscle: update 2019. *J Cachexia Sarcopenia Muscle* 2019;**10**:1143–1145.

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