SIGNA VITAE 2017; 13(SUPPL 3): 30-31

An update on muscle wasting in ICU

ZUDIN PUTHUCHEARY

Adult Intensive Care Unit, Royal Brompton Hospital, UK

Corresponding author:
Zudin Puthucheary
Adult Intensive Care Unit
Royal Brompton Hospital
United Kingdom
Phone: 00 44 2076790840
E-mail: Zudin.puthucheary.09@ucl.ac.uk

ABSTRACT

Mortality rates from critical illness are decreasing worldwide, but survivors suffer from significant functional disability as a result of muscle wasting. In the short-term the functional effects are seen in increased time of mechanical ventilation, and increased length of stay. Muscle wasting is the most common complication of critical illness, occurring in 25-50% of patients. In a longitudinal observational study, daily loss of muscle mass averaged 2-3% over the first 10 days. The scale of wasting was related to the severity of organ failure and of acute lung injury.

Changes in muscle mass are underpinned by alterations in muscle protein homeostasis. In stable isotope infusion experiments, muscle protein synthesis was reduced to levels of fasted controls despite the initiation of enteral feed. Protein synthetic levels recovered variably over the first week to levels comparable to fed controls. As a result, muscle protein breakdown was increased relative to muscle protein synthesis, leading to a net catabolic state.

There is a need for secondary prevention measures to be instituted in current practise. Increased nutritional delivery cannot be recommended at this stage during acute critical illness and early mobilisation has been demonstrated to increase functional status. This is best achieved through the ABCDEF bundle. This bundle constitutes a co-ordinated package of care with sedation control to facilitate spontaneous breathing and decreasing delirium. This facilitates early mobilisation, which is currently the only preventative measure with an evidence base to decrease skeletal muscle wasting associated functional disability.

Key words: muscle wasting, critical illness, muscle mass

Mortality rates from critical illness are decreasing worldwide, secondary to improved technology and bedside patient care. (1) This is coupled with an increase in admissions to critical care, secondary to both communicable and non-communicable diseases.

In 2003 Herridge et al demonstrated the functional disability that patients with Acute Respiratory Distress Syndrome suffer from 1-year post discharge. Half of these patients had still not returned to work, and a third needed caregiver assistance for their activities of daily living. (2) The average age was 44. Many groups around the world have reproduced these findings, and we now know that these functional disabilities can last for up to 5 years. (3)

Patients and researchers both recognize muscle wasting and weakness as the greatest contributor to this functional disability. In the short-term the functional effects of muscle wasting are seen in increased time of mechanical ventilation (4), and increased length of stay. (5)

Muscle mass and quality pre-critical illness are equally important- in retrospective studies of Computer Tomography scans low admission muscle mass (6) and density (7), or the presence of increased intra-muscular adipose tissue were associated with increased mortality. Dissecting pre-existing low muscle mass from pre-existing frailty, disability and or chronic disease are extremely difficult: these conditions are intertwined in a complex fashion. Recently more details have emerged on the relationship between acute muscle wasting and long-term outcomes. Firstly patients' trajectories of weakness post hospital discharge vary considerably, and persistent weakness is associated with worse survival. (8) Secondly the older patients with co-morbidities are more likely to experience physical decline and weakness post discharge. (9)

Muscle wasting is the most common complication of critical illness, occurring in 25-50% of patients. (4) Given the significant ramifications of acute muscle wasting for patients, families and carers, (10, 11) clinicians need to understand the pathophysiology of muscle wasting and develop tools for interventions.

In our longitudinal observational study of critically ill patients, daily loss of muscle mass averaged 2-3% over the first 10 days. (13) Myocellular protein:DNA ratio fell steeply (3.0%/day) over the same period. The scale of wasting was related to the severity of organ failure and of acute lung injury: Over ten days, those in single organ failure did not lose appreciable muscle mass. Those in 2-3 organ failure lost on average 20% of muscle mass over 10 days and those with greater than 4 organ failure lost on average 26% of muscle mass over the same period.

In addition to changes in muscle mass, changes in muscle quality were also seen. Forty percent of patients demonstrated patchy myofibre necrosis, with an associated fasciitis. These changes were seen on muscle biopsy, but were easily detectable by qualitative muscle ultrasound. (13)

Changes in muscle mass were underpinned by alterations in muscle protein homeostasis. Muscle protein homeostasis is the balance of muscle protein breakdown and muscle protein synthesis. In health, muscle protein synthesis is increased in response to protein ingestion and/or resistance exercise, and muscle protein breakdown switched off by insulin release. In humans, unlike rodents, alterations in muscle protein synthesis drive the majority of dynamic changes in this balance, including the response to diverse stimuli such as inflammation, immobilization, starvation and aging. In stable isotope infusion experiments, muscle protein synthesis was reduced to levels of fasted controls despite the initiation of enteral

feed. Protein synthetic levels recovered variably over the first week to levels comparable to fed controls. As a result, muscle protein breakdown was increased relative to muscle protein synthesis, leading to a net catabolic state. The observed changes in muscle protein homeostasis were mirrored by changes in intracellular anabolic and catabolic signalling pathways. (12)

These results have been reproduced by other groups in other countries. (14) Whilst ongoing work focuses on developing interventions for primary prevention, there is a need for secondary prevention measures to be instituted in current practise. Increasing nutritional delivery has not been demonstrated to increased muscle mass: in the study described above, increased protein delivery was associated with increased muscle wasting. Similarly, the EDEN trial demonstrated that trophic feeding did not result in decreased muscle strength or function either during the acute critical illness or at 1 year. (15) Lastly the EPaNIC study (where early parenteral nutrition was used to supplement enternal nutrition) demonstrated decreased muscle mass, decreased autophagy and increased intramuscular fat with increasing nutritional delivery. (16)

Whilst increased nutritional delivery cannot be recommended at this stage during acute critical illness, early mobilisation has been demonstrated to increase functional status within the critical care setting and translate to better functional outcomes at hospital discharge. (17) This is best achieved through the ABCDEF bundle. (18) This bundle constitutes a co-ordinated package of care with sedation control to facilitate spontaneous breathing and decreasing delirium. This facilitates early mobilisation, which is currently the only preventative measure with an evidence base to decrease skeletal muscle wasting associated functional disability.

CONCLUSION

Acute skeletal muscle wasting occurs rapidly and commonly in critical illness. Currently early mobilisation is the only secondary preventative measure with an evidence based to decrease the associated functional disability.

REFERENCES

1. Kaukonen, K.M., Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. JAMA, 2014. 311(13): p. 1308.
2. Herridge, M.S., One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med, 2003. 348(8): p. 683.
3. Herridge, M.S., Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med, 2011. 364(14): p. 1293.
4. De Jonghe, B., Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA, 2002. 288(22): p. 2859.
5. De Jonghe, B.M.B.-G., Sylvie MD, PhD; Durand, Marie-Christine MD; Malissin, Isabelle MD; Rodrigues, Pablo MD; Cerf, Charles MD; Outin, Herve MD; Sharshar, Tarek MD, PhD; for Groupe de Reflexion et d'Etude des Neuromyopathies En Reanimation Respiratory weakness is associated with limb weakness and delayed weaning in critical illness Crit Care Med, 2007. 39(9): p. 2007.
6. Weijs, P.J., Low skeletal muscle area is a risk factor for mortality in mechanically ventilated critically ill patients. Crit Care, 2014. 18(1): p. R12.
7. Looijaard, W.G., Skeletal muscle quality as assessed by CT-derived skeletal muscle density is associated with 6-month mortality in mechanically ventilated critically ill patients. Crit Care, 2016. 20(1): p. 386.
8. Dinglas, V.D., Muscle Weakness and 5-Year Survival in Acute Respiratory Distress Syndrome Survivors. Crit Care Med, 2017. 45(3): p. 446.
9. Pfoh, E.R., Physical declines occurring after hospital discharge in ARDS survivors: a 5-year longitudinal study. Intensive Care Med, 2016. 42(10): p. 1557.
10. Kamdar, B.B., Joblessness and Lost Earnings After ARDS in a 1-Year National Multicenter Study. Am J Respir Crit Care Med, 2017.
11. Ruhl, A.P., Healthcare Resource Use and Costs in Long-Term Survivors of Acute Respiratory Distress Syndrome: A 5-Year Longitudinal Cohort Study. Crit Care Med, 2017. 45(2): p. 196.
12. Puthucheary, Z.A., Acute skeletal muscle wasting in critical illness. JAMA, 2013. 310(15): p. 1591.
13. Puthucheary, Z.A., Qualitative Ultrasound in Acute Critical Illness Muscle Wasting. Crit Care Med, 2015. 43(8): p. 1603.
14. 14. Parry, S.M., Ultrasonography in the intensive care setting can be used to detect changes in the quality and quantity of muscle and is related to muscle strength and function. J Crit Care, 2015.
15. Needham, D.M., One year outcomes in patients with acute lung injury randomised to initial trophic or full enteral feeding: prospective follow-up of EDEN randomised trial. Bmj, 2013. 346: p. f1532.
16. Casaer, M.P., Role of disease and macronutrient dose in the randomized controlled EPaNIC trial: a post hoc analysis. Am J Respir Crit Care Med, 2013. 187(3): p. 247.
17. Schweickert, W.D., Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet, 2009. 373(9678): p. 1874.
18. Barnes-Daly, M.A., Improving Hospital Survival and Reducing Brain Dysfunction at Seven California Community Hospitals: Implementing PAD Guidelines Via the ABCDEF Bundle in 6,064 Patients. Crit Care Med, 2017. 45(2): p. 171.