Moving towards a better identification and management of frailty in ICU survivors

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Frailty is a geriatric syndrome that is defined as 'a physiologic state of increased vulnerability to stressors due to decreased physiologic reserves, and dysregulation, of multiple physiologic systems'.[1] Frailty syndrome partly overlaps with sarcopenia, the latter encompass states of loss of muscle mass and function related to ageing alone.[2] Frail patients present with an increased burden of symptoms including muscle weakness, excessive muscle fatigue during daily activities and reduced tolerance to medical and surgical interventions.[3]

Along these lines, studies have demonstrated that frailty is a common phenomenon observed in approximately 30% of adult intensive care unit (ICU) admissions.[4] Patients with pre-ICU frailty have a higher prevalence of in-hospital mortality, long-term morbidity and mortality and poorer quality of life after hospital discharge compared with non-frail ICU patients.[4] Nevertheless, limited knowledge exists as to whether post-ICU frailty impacts on long-term mortality and recovery to activities of daily living after hospital discharge.

In this issue of *Thorax*, Baldwin *et al*[5] examined 185 elderly (>65 years old), acute respiratory failure (ARF) survivors to identify distinct frailty subtypes. Authors applied a novel statistical approach (ie, *latent class analysis*) for assessing whether different frailty phenotype domains[5] (ie, grip strength, gait-speed, feelings of exhaustion, weight loss and physical activity) and differences in cognitive impairment status (ie, delirium presence/absence) may cluster in this study population. Assessments were performed in the week before patients' hospital discharge after patients had left the ICU. Mortality and recovery of activities of daily living to prehospitalisation levels were followed up for 6 months after hospital discharge. Authors identified five clinically relevant post-ICU frailty subtypes with distinguished patterns of mortality rate ratios and recovery to baseline activities of daily living within 6 months after hospital discharge. Table 1 summarises the key characteristics of the five frailty subtypes.

A key message of the study by Baldwin *et al*[5] is that routine frailty screening before and after ICU discharge may provide clinicians prognostic information for long-term survival and physical recovery for their frail ICU patients. Early identification and treatment of patients who struggle to recover to baseline activities of daily living levels after ICU discharge might be a key element when considering financial healthcare planning to better select management and post-ICU intervention programmes.[3] Indeed, discovering frailty subtypes may facilitate the decision of targeted post-ICU interventions such as physical rehabilitation, cognitive rehabilitation exercises and palliative care interventions aiming to improve ICU survivor outcomes.

Although the study by Baldwin *et al*[5] contributes substantially to frailty research in critical care, it is important to highlight that several areas remain underexplored. The integration of frailty assessments into clinical practice is emerging and future studies have to validate the five frailty subtypes reported by Baldwin *et al*[5] including younger ICU survivors with critical illnesses other than ARF. Furthermore, successful detection of early manifestations leading to a 'frailty syndrome' requires an understanding of the natural history of frailty development. However, frailty remains an evolving concept lacking clear diagnostic criteria to be used in clinical practice and epidemiological studies.[6] The most frequently used instruments for the diagnosis of frailty are primarily based on a multidimensional self-reported questionnaire of subjective signs and symptoms while few of these instruments have been validated against well-defined community populations of older people.[3 7] Therefore, there is a clear need to develop more objective, simple, valid and sensitive-to-change instruments that in combination with the existing validated tools will contribute towards a better assessment of frailty and measure its severity in routine clinical practice and critical care. For instance, concerning important symptoms of frailty namely 'muscle weakness and fatigue', technologies such as muscle ultrasound, magnetic stimulation (twitch force) and near-infrared spectroscopy (NIRS) might be attractive—as non-invasive, real-time and practical instruments that are independent of patient effort (can be used in uncooperative patients)—and sensitive to subtle early changes in peripheral muscle structure, functional capacity and oxygenation status, respectively, in critically ill patients.[8–10] Concerning NIRS application, studies in critically ill patients[11] show that this technology is able to detect alterations in peripheral muscle oxygenation, microvascular reactivity and microvascular dysfunction, the latter mechanisms have been demonstrated to play an important role in the development of muscle weakness and fatigue.[12] Besides, the information acquired by the aforementioned technologies might also serve to guide tailored early intervention in the post-ICU frailty subtypes reported by Baldwin *et al*.[5]

Another important finding of the study by Baldwin *et al*[5] is that frailty subtypes with slower recovery to baseline activities of daily living (ie, subtypes 3–5, table 1) exhibited also greater systemic inflammation, impaired innate immunity and higher anabolic hormone levels compared with frailty subtypes with greater recovery to baseline activities of daily living (ie, subtypes 1, 2, table 1), suggesting that these pathobiological factors may inhibit physical and functional recovery. Under these circumstances, the optimal timing of initiation of exercise interventions for enhancing muscle functional capacity such as strength training or bed cycling has to be a matter of future research, especially in patients exhibiting frailty subtypes 3–5. Besides, future studies have to investigate whether interventions aimed at reducing inflammatory levels and therapies that promote anabolic hormone replacement provide a therapeutic option for enhancing physical recovery following hospital discharge.

Muscle frailty status in the elderly population is partially reversible with the implementation of specific muscle reconditioning interventions, such as resistance exercise training, physical activity promotion programmes and nutritional supplementation.[13] For critically ill patients

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Table 1 Prevalence of prehospitalisation and postintensive care unit (ICU) frailty, cognitive impairment, recovery and survival within 6 months after hospital discharge of the five frailty subtypes

	Subtype 1	Subtype 2	Subtype 3	Subtype 4	Subtype 5
	'Robust' 'No Frail'	'Recoverable Frail'	'Acutely Frail'	'Chronically Frail'	'End-stage Frail'
Prehospitalisation Frailty*	0%	44%	26%	65%	>90%
Post-ICU Frailty†	0%	57%	89%	93%	100%
Cognitive impairment‡	9.5%	13%	31%	0%	100%
Recovery to baseline ADLs§	100%	83%	60%	60%	45%
Survival	100%	93%	80%	80%	67%

Assessed by: *Clinical Frailty Scale; †Fried frailty phenotype domains; ‡Confusion Assessment Method & Mini-cog Test; §Duke Activity Status Index.
ADLs, activities of daily living.

early mobilisation including transferring patients from the bed to the chair, resistance exercises, walking, bed cycling, neuromuscular electrical stimulation and inspiratory muscle training might be beneficial since they increase functional capacity and have the potential to restore locomotor and respiratory muscle weakness acquired in the ICU.[14 15] Yet, the acute and long-term effects of early mobilisation on improving ICU outcomes, restoring muscle function and potentially modifying frailty subtypes remain unknown in post-ICU frail patients and would be of specific interest to be investigated in future studies.

Contributors ZL and DL wrote, revised and approved the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

To cite Louvaris Z, Langer D. *Thorax* 2021;**76**:322–323.

Accepted 18 January 2021
Published Online First 11 February 2021

Linked

► http://dx.doi.org/10.1136/thoraxjnl-2020-214998

Thorax 2021;**76**:322–323.
doi:10.1136/thoraxjnl-2020-216530

REFERENCES

1 Hamerman D. Toward an understanding of frailty. *Ann Intern Med* 1999;130:945–50.
2 Dodds R, Sayer AA. Sarcopenia and frailty: new challenges for clinical practice. *Clin Med* 2016;16:455–8.
3 Clegg A, Young J, Iliffe S, *et al*. Frailty in elderly people. *Lancet* 2013;381:752–62.
4 Muscedere J, Waters B, Varambally A, *et al*. The impact of frailty on intensive care unit outcomes: a systematic review and meta-analysis. *Intensive Care Med* 2017;43:1105–22.
5 Baldwin MR, Pollack LR, Friedman RA. Frailty subtypes and recovery in older survivors of acute respiratory failure: a pilot study. *Thorax* 2021;76:351–60.
6 Theou O, Brothers TD, Mitnitski A, *et al*. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc* 2013;61:1537–51.
7 Buckinx F, Rolland Y, Reginster J-Y, *et al*. Burden of frailty in the elderly population: perspectives for a public health challenge. *Arch Public Health* 2015;73:19.
8 Parry SM*et al*. Ultrasound evaluation of quadriceps muscle dysfunction in respiratory disease Cardiopulm. *Phys Ther J* 2020;15:79–88. doi:10.2147/COPD.S222945
9 Laghi F, Khan N, Schnell T, *et al*. New device for nonvolitional evaluation of quadriceps force in ventilated patients. *Muscle Nerve* 2018;57:784–91.
10 Donati A, Damiani E, Domizi R, *et al*. Near-Infrared spectroscopy for assessing tissue oxygenation and microvascular reactivity in critically ill patients: a prospective observational study. *Crit Care* 2016;20:311.
11 Creteur J. Muscle StO_2 in critically ill patients. *Curr Opin Crit Care* 2008;14:361–6.
12 Tickle PG, Hendrickse PW, Degens H, *et al*. Impaired skeletal muscle performance as a consequence of random functional capillary rarefaction can be restored with overload-dependent angiogenesis. *J Physiol* 2020;598:1187–203.
13 Angulo J, El Assar M, Álvarez-Bustos A, *et al*. Physical activity and exercise: strategies to manage frailty. *Redox Biol* 2020;35:101513.
14 Castro-Avila AC, Serón P, Fan E, *et al*. Effect of early rehabilitation during intensive care unit stay on functional status: systematic review and meta-analysis. *PLoS One* 2015;10:e0130722.
15 Gosselink R, Langer D. Recovery from ICU-acquired weakness; do not forget the respiratory muscles! *Thorax* 2016;71:779–80.