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Frailty increases mortality among patients ≥ 80 years old treated in Polish ICUs

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Abstract

Background: The increasing population of very old intensive care patients (VIPs) is a major challenge currently faced by clinicians and policymakers. Reliable indicators of VIPs' prognosis and appropriateness of their admission to the intensive care unit (ICU) are urgently needed.

Methods: This is a report from the Polish sample of the VIP1 multicentre cohort study (NCT03134807). Patients ≥ 80 years of age admitted to the ICU were included in the study. Information on the type and reason for admission, demographics, utilisation of ICU procedures, ICU length of stay, organ dysfunction and the decision to apply end-of--life care was collected. The primary objective was to investigate the impact of frailty syndrome on ICU and 30-day survival of VIPs. Frailty was assessed with the Clinical Frailty Scale (≥ 5 points on a scale of 1–9).

Results: We enrolled 272 participants with a median age of 84 (81–87) years. Frailty was diagnosed in 170 (62.5%) patients. The ICU and 30-day survival rates were equal to 54.6% and 47.3% respectively. Three variables were found to significantly increase the odds of death in the ICU in a multiple logistic regression model, namely: SOFA score (OR = 1.16; 95% CI: 1.16–1.24); acute mode of admission (OR = 5.1; 95% CI: 1.67–15.57); and frailty (OR = 2.25; 95% CI: 1.26–4.01).

Conclusion: Measuring frailty in critically ill older adults can facilitate making more informed clinical decisions and help avoid futile interventions.

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Key words: frailty, intensive care units, medical futility, critical care

It is estimated that by the year 2050 people at the age of 80 years and older will represent almost 10% of the European population [1]. Progressive ageing remains one of the leading issues in contemporary critical care [2]. The increasing proportion of elderly patients admitted to ICUs requires substantial resources, while many countries are facing a shortage of ICU beds [3–5]. Although our knowledge concerning outcomes in this population is growing, there are currently no local reports from Poland [6, 7].

The long-term prognosis of "very old intensive care patients" (VIPs) is often poor, which requires careful weighing of potential costs and benefits associated with intensive care [8]. There is a growing recognition of the fact that clinical features used in traditional disease severity scores, such as APACHE and SAPS, may be insufficient to accurately predict the outcome in VIPs [2]. Population-specific conditions, such as sarcopenia, dementia, delirium and frailty, could be incorporated into the evaluation of elderly patients in the setting of critical illness in order to help better define their prospects of recovery [9–12].

Of the above-mentioned factors, frailty syndrome seems to be the most reliable indicator of biological age [13]. Frailty is defined as a clinically recognisable state of increased vulnerability resulting from ageing-associated decline in reserve and function across multiple physiologic systems such that the ability to cope with everyday or acute stressors is compromised [14]. Its impact on patients' outcomes is established in geriatric and surgical settings, with less evidence available in the field of intensive care. A systematic review and meta-analysis by Muscedere *et al.* [15] showed a significant impact of frailty on hospital and long-term mortality in critically ill patients. However, the relevance of these results is limited by a moderate quality of included studies.

The Very Old Intensive Care Patient: A Multinational Prospective Observation Study (VIP1) was designed to reliably address this issue. Its main goal was to assess the prevalence of frailty among VIPs and assess its impact on their outcomes in the ICU. In the current paper, we would like to present results of the VIP1 study based on Polish population with a particular interest in frailty and life-sustaining treatment limitations, further referred to as end-of-life care interchangeably.

METHODS

The study was approved by the local ethics committee (Jagiellonian University Ethics Committee), while the protocol complied with the Declaration of Helsinki. According to ethics committee`s verdict, patient consent was not required.

VIP1 was a prospective multicentre study coordinated by the Health Services Resource and Outcome (HSRO) section of the European Society of Intensive Care Medicine (ESICM). The enrolment and data collection processes were described in detail in the original VIP1 Study [16]. In this paper, we reported data from the Polish VIP1 cohort.

Patients of 80 years of age or older admitted to Polish ICUs were considered eligible for the study. We collected information on the mode and reason for admission, demographics, utilisation of ICU procedures (i.e. type of respiratory support, administration of vasoactive drugs, initiation of renal replacement therapy), ICU length of stay, organ dysfunction assessed with SOFA score and the decision to

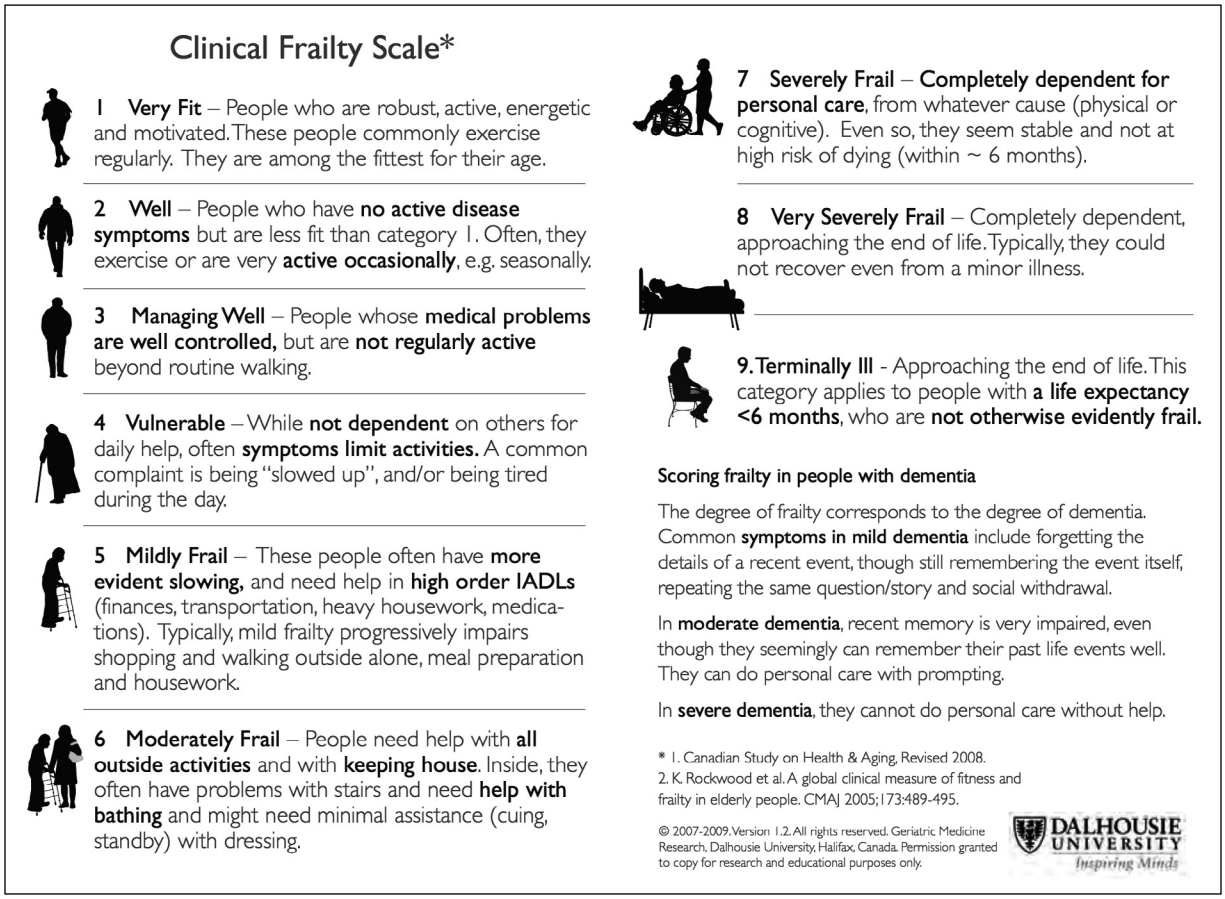

Figure 1. Clinical Frailty Scale

introduce end-of-life care (withholding and/or withdrawal of further treatment). Specific definitions had been previously described elsewhere [16].

The main objective of the study was to investigate the ICU and 30-day survival in relation to the presence of frailty syndrome before the onset of acute illness and to characterise the intensity of treatment in this group. Frailty was assessed with the Clinical Frailty Scale (CFS), a simple tool used by the ICU staff according to a visual description to categorise patients as frail or non-frail (≥ 5 points or < 5 points respectively on a scale of 1–9) (Fig. 1) [17].

Continuous variables were described as medians with interquartile ranges, categorical variables were reported as percentage values. The Mann-Whitney U test and chi-squared test (Pearson's chi-squared or Fisher's exact test) were used in the between-groups univariate analyses as applicable. The effect size was represented by odds ratios with 95% confidence intervals. A multiple logistic regression model was used to report adjusted odds ratios for the ICU mortality of different clinical characteristics. *P*-values < 0.05 were considered statistically significant.

RESULTS

Between November 2016 and February 2017, 272 participants were enrolled in the study. The overall ICU and 30-day survival rates were equal to 54.6% and 47.3% respectively. Data on ICU survival was available in 269 (98.9%) patients, while 239 (87.9%) individuals completed the 30-day follow-up. Frailty was diagnosed in 170 (62.5%) patients admitted to ICUs.

The median age of the studied population was 84 (81–87) years and 159 (58.5%) patients were female. The median SOFA score on admission was equal to 10 (7–14). The CFS score used to assess frailty reached a median value of 5 (4–6.75), while the median length of stay in the ICU was 4 days (1.3–15.9).

Most admissions were classified as acute, with only 42 (15.4%) patients transferred to the ICU after elective surgery. There were 48 (17.6%) patients who stayed less than 24h in the ICU (one-day stay). The median time spent in hospital before admission to the ICU was 2 days (0–5). The most common baseline diagnosis was a combination of circulatory and respiratory failure, reported in 72 (26.5%) cases. The majority of patients required intubation, mechanical ventilation and administration of vasoactive drugs (Table 1).

Table 1. Differences in clinical characteristics between frail and non-frail patients

Characteristic	Not frail n = 102	Frail n = 170	*P*-value
Age (years)	83 (81–85.25)	85 (82–88)	0.004
SOFA score	10 (6–14)	10 (7–14)	0.99
Gender (female)	57.8%	58.8%	0.87
Non-invasive ventilation	7.8%	15.9%	0.06
Intubation & mechanical ventilation	85.3%	84.7%	0.90
Vasoactive drugs	65.7%	74.7%	0.11
Renal replacement therapy	21.6%	19.4%	0.67
Respiratory failure	19.6%	18.2%	0.78
Combined circulatory & respiratory failure	23.5%	28.2%	0.39
Post-elective surgery	20.6%	12.4%	0.07
One-day stay (< 24h at ICU)	19.6%	16.5%	0.51
End-of-life care*	9.8%	16.5%	0.13
Withholding of treatment	6.9%	8.8%	0.57
Withdrawal of treatment	2.9%	7.6%	0.18
ICU length of stay (days)	5.7 (1.1–17.3)	3.1 (1.3–13.1)	0.26
ICU survival	66.3%	47.6%	0.003
30-day survival[§]	59.1%	40.4%	0.005

SOFA: Sequential Organ Failure Assessment; ICU: Intensive Care Unit; *End-of-life care: the overall proportion of patients with only withholding and patients with and appropriateness (including patients with previous of treatment; [§]Survival estimates reported after exclusion of patients lost to follow-up (11.2% and 13.7% missing 30-day observations of frail and non-frail patients respectively)

Table 2. Multiple logistic regression model — mortality in the ICU

Characteristic	Estimate	SE	P-value	Adjusted OR (95%CI)
SOFA score	0.15	0.03	< 0.001	1.16 (1.09–1.24)
Frailty	0.81	0.30	0.006	2.25 (1.26–4.01)
Acute admission	1.63	0.57	0.004	5.10 (1.67–15.57)
Age (years)	0.042	0.037	0.25	1.04 (0.97–1.12)
Gender (female)	0.15	0.28	0.58	1.17 (0.67–2.02)
Intercept	–8.96	3.19	0.005	-

SOFA: Sequential Organ Failure Assessment

In univariate analyses, patients with frailty syndrome were older and had a significantly lower ICU and 30-day survival rate than those without frailty (Table 1). The unadjusted OR for death in the ICU associated with frailty was equal to 2.17 (95% CI: 1.3–3.62; $P = 0.003$), with a similar effect on 30-day mortality and an OR of 2.13 (95% CI: 1.26–3.64, $P = 0.005$). There were no differences in terms of the baseline SOFA score and utilisation of ICU procedures based on the presence of frailty. End-of-life care was applied in 16.5% and 9.8% of the frail and non-frail patients respectively ($P = 0.13$).

Three variables that significantly increased the odds of ICU death were identified in the multiple logistic regression model, namely: SOFA score (OR = 1.16; 95% CI: 1.16–1.24); acute mode of admission (OR = 5.1; 95% CI: 1.67–15.57); and frailty (OR = 2.25; 95% CI: 1.26–4.01) (Table 2). Age was not a significant predictor of poor outcome after adjustment for other clinical characteristics. An analogous model for 30-day mortality exhibited similar findings (results not shown).

An exploratory model investigating whether patients lost to follow-up were more severely ill was provided to verify the possibility of attrition bias. We found that a combination of SOFA score, frailty and type of admission could not predict which patients would leave the study (none of these features achieved statistical significance; AUC = 0.56).

DISCUSSION

We reported data of 272 very old critically ill patients admitted to 27 ICUs that took part in the VIP1 Study in Poland [16]. The main objective of this multicentre, international study was to investigate prospectively the impact of frailty on short-term mortality and to describe the level of care in this population.

Frailty, assessed with a simple screening tool, was associated with an over two-fold increase in the odds of death independantly of the patient's age and baseline severity of organ failure. The utilisation of medical procedures was similar in patients with and without frailty, and there was no statistically significant difference between both groups in terms of life-sustaining treatment limitations.

The study had a limited sample size due to reporting partial data from a larger cohort study. This did not guarantee sufficient power to detect statistically significant differences in some characteristics and reduced the cohort's representativeness of the population — Polish VIPs had more severe organ dysfunction based on the SOFA score as well as a lower ICU and 30-day survival rate than the average reported in the VIP1 Study. These observations confirm previous reports showing that patients admitted to Polish ICUs are in poor clinical condition [18]. However, the observed mortality has recently been demonstrated to be lower than predicted by the APACHE II model, which might indicate a relatively good performance of ICUs in Poland [19].

In the ageing population, the number of critically ill elderly patients is increasing [20]. Patients ≥ 80 years old account for 10% to 20% of all admissions to the ICU, posing a global challenge to healthcare systems [21]. Limited resources necessitate careful consideration of the potential reversibility of critical illness to avoid futile interventions [11, 22, 23]. In a recent study in JAMA, Guidet *et al.* [7] have shown that a proactive strategy of admitting elderly patients to the ICU (i.e. an ICU triage) doubled the number of admissions to French ICUs and, at the same time, increased hospital mortality. These findings give rise to a question whether we could better predict which VIPs will, in fact, benefit from intensive care. Traditional disease severity scores do not capture important data on a patient's premorbid condition, such as cognitive impairment, decreased functional capacity and frailty — all described as potential modifiers of morbidity and mortality in VIPs [2].

The concept of assessing patients' biological rather than chronological age is appealing and paves its way from geriatrics to intensive care. Our results support including frailty in the assessment of critically ill elderly patients to improve the discrimination between individuals fit for additional interventions and those in whom withholding or withdrawal of treatment should be considered. This, in turn, should help physicians, along with patients and their families, make more informed decisions concerning the intensity of treatment, its appropriateness and further course. A study which was recently published by Guidet [24] placed frailty among the most influential factors with regard to life-sustaining treatment limitations, along with acute admission, age and SOFA score. The results of the upcoming VIP2 study will help establish a predictive model designed specifically for the critically ill elderly population, which will take into account the above-mentioned features [25]. Despite being calculated with a dedicated tool, risk estimates alone are unlikely to guide treatment in the ICU. However, accurate outcome prediction could facilitate clinical judgement and improve the communication between providers and recipients of care.

A decision to de-escalate treatment in a particular case is never an easy one. In the Polish cohort of VIPs, a decision to introduce end-of-life care was made in 14% of the patients, compared to 27.2% reported across all centres participating in the study. These numbers go along with results of the paper published by Guidet [24], which showed a lower frequency of life-sustaining treatment limitation in Eastern Europe. While it does not allow for making direct inferences, we should be wary about the fact that many patients approaching the end of life tend to value comfort over aggressive treatment when given the opportunity to express their preferences [26]. The evidence suggests that this an often underappreciated practice in the ICU, where the patient's opinion is rarely sought, and the preferences of the family are discordant with the care provided in many cases [27–29]. Despite the potential short-term benefit of treatment in the ICU, the long-term outcome in this population is unfavourable [30–32].

Maintenance of life-support measures in patients who have no real prospects of recovery is a broadly discussed topic. Polish guidelines on intensive care referring to this issue considered futile medical therapy as malpractice and have highlighted the role of palliative care in this setting [33]. This is an important step towards overcoming the legal, ethical and religious reservations which may all affect the decision whether to de-escalate or discontinue further treatment [24, 34]. The above-mentioned factors are likely to be more pronounced in Polish intensivists compared to nationalities with a less conservative attitude [35]. In many cases, the death of a critically ill elderly patient is a natural history of disease rather than a therapeutic failure. Amid the flurry of intensive care, we can all benefit from acknowledging end-of-life care [36, 37].

Nevertheless, we do not all age the same. An octogenarian may still have his greatest mountains to climb ahead — just like the famous Mr. Miura, who at the age of eighty, against all odds, reached the summit Mount Everest for the third time in his life [38]. Thus, adopting the assessment of

frailty in critical care has a potential to identify patients who are more likely to recover from an acute illness and to act upon it with an adequate intensity of intensive care.

CONCLUSIONS

The presence of frailty increases mortality among critically ill patients ≥ 80 years old treated in Polish ICUs. Measuring frailty in this population can facilitate making more informed clinical decisions and help avoid futile interventions.

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