Title: The Clinical Frailty Scale- Does it predict outcome of the very-old in UK ICUs?

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Acknowledgements

We would like to acknowledge the significant contribution of the following individuals involved in running these studies at the participating sites. Jason Cupitt, Emma Stoddard, Steve Rose, Aimi Collins, Irina Grecu, Richard Partridge, Christian Frey, Beverley Stidolph, Michael Reay, Karen Reid, Michael Spivey, Karen Burt, Coarlie Carle, Alan Pope, Nicola Butterworth-Cowin, Marcela Vizcaychipi, Laura Martins, Clare Bolger, Nicky Cullum, Yolanda Baird, Kerry Barnes, Carole Boulanger, Nicola Paver, Ritoo Kapoor, James Douglas, Mark Puulletz, Sarah Williams, Patricia Williams, James Wood, Miriam Davey, Phillipa Wakefield, Ashley Quinn, Amanda Cowton, Nikki Collings, Clare Bolger, Ingeborg Welters, Karen Williams, Georgina Randell, Katie Stammers, Jenny Lord Jordi Margalef, Madhu Balasubramaniam, Jenny Anderson, Alison Lewis, Agnieszka Kubisz-Pudelko, Rachel Savine, Rebecca Gale, Maria Faulkner, Laura Parry, Richard Pugh, Victoria Garvey, Tom Daubeny, Emily Bevan, Deise Griffin, Mupudzi McDonald, James Nathan, Reena Khade, Daniel Martin, Helder Filipe, Mason Pannell, Amy Collins, Kiran Salaunkey, Philip Bastone, Sally Pitts, Katie Bowman, Reni Jacob, Richard Innes, Patricia Doble, Rosie Reece-Anthony, Babita Gurung, Ben Creag-Brown, James Doyle, Nanci Doyle, Richard Savigne, Laura Montague, Rachel Oguntimehin and Carlos Castro Delgado.

Conflicts of Interest and Sources of Funding:

No conflicts of interest declared. The ESICM supported VIP1 with a research award. Free support for running the electronic database and was granted from Aarhus University, Denmark. Financial support for creation of the e-CRF and maintenance of the database was possible from a grant (open project support) by Western Health region in Norway) 2018.

Abstract

**Introduction.** The age of patients admitted into critical care in the UK is increasing. Clinical decisions for very-old patients, usually defined as over 80, can be challenging. Clinicians are frequently asked to predict outcomes as part of discussions around the pros and cons of an ICU admission. Measures of overall health in old age, such as the clinical frailty scale (CFS) are increasingly used to help guide these discussions. We aimed to understand the characteristics of the very-old critically unwell population in the UK and the associations between frailty and outcome of an ICU admission in our healthcare system (National Health Service, NHS). **Methods** Baseline characteristics, ICU interventions and outcomes (ICU- and 30-day mortality) were recorded for sequential admissions of elderly patients to UK ICUs as part of the European VIP 1 and 2 studies. Patient characteristics, interventions and outcome measures were compared by frailty group using standard statistical tests. Multivariable logistic regression modelling was undertaken to test association between baseline characteristics, admission type and outcome. **Results** 1858 participants were enrolled from 95 ICUs the UK. Median age was 83. Median CFS was 4 (IQR 3–5). 30-day survival was significantly lower in the frail group (CFS>4, 58%) compared to vulnerable (CFS=4, 65%) and fit (CFS<4 68%, p=0.004).SOFA score, reason for admission and CFS were all independently associated with increased 30-day mortality (p<0.01). **Conclusion** In the UK, frailty is associated with an increase in mortality at 30-days following an ICU admission. At moderate frailty (CFS 5–6), 3 out of every 5 patients admitted survived to 30-days. This is a similar mortality to septic shock.

Introduction

The mean age of admission to critical care in the United Kingdom (UK) is 60, and over 40% of admissions are aged 65 and over1. Caring for older people is therefore an integral part of critical care medicine. Part of this role is helping patients and their families make decisions about their care. For the very-old, usually defined as over 802, this can be particularly challenging. This age group's relatively shorter life-expectancy brings sharply into focus the question of what adverse effects of a critical care admission are tolerable for each individual. Decisions about care for any patient necessitate careful evaluation of the potential benefits of a therapy and its risks of failure or harm. In order to fully communicate the balance between these competing forces to patients and their families, clinicians frequently derive probable outcomes for an individual, from data about the populations they care for. However, data in the very-old age group is lacking, with ‘elderly’ care studies often having a lower age limit between 60 and 70 years 3, 4. Chronological age alone is an insufficient predictor of outcome from critical illness, as there is often significant variation in the physical and physiological reserve of older people 2. A preferred descriptor of the physiological changes associated with ageing is frailty. This term refers to both the cumulative physiological decline associated with age *and* the dramatic effect of even minor insults that accompany increasing frailty 5. There is growing awareness that measures of frailty such as the clinical frailty scale (CFS) 6 may be useful to inform decision on care by helping to predict likely outcome. Indeed, guidelines to deal with case surge in the COVID-19 pandemic from the national institute of clinical excellence (NICE), advocated using a CFS > 5 as indicative of likely poor outcome from critical care admission as part of an assessment of severely unwell patients with the disease7, 8. Utilising these scores outside of the patient groups and care settings they were validated in has recognised limitations, but mirrors the evolution of other scoring systems in critical care. For example, the sequential organ failure assessment (SOFA) score 9 was originally developed to assess population level morbidity and mortality in critical care but its use has subsequently evolved to predict individuals at high risk of mortality, most notably in the recently updated sepsis diagnostic criteria 3, 10. As yet, neither CFS nor SOFA score have been shown to provide valid and reliable risk prediction for the very old who are admitted to intensive care.

Recently, two large prospective observational studies of very old intensive care patients (VIP-1 and -2) have reported their findings of the outcomes of very old (over 80 years of age) patients admitted to intensive care units (ICUs) 11, 12. These studies recruited participants from over 300 critical care units in 21 countries across Europe. Results from these studies confirmed the associations between increasing frailty and 30-day mortality. In addition, they found regional variations in the characteristics of patients admitted to ICU. This is perhaps unsurprising, given the recognised variation in healthcare provision across the continent 13, but does raise an important question about how the clinician can best interpret findings from across healthcare systems and apply them to their own and consequently help inform decisions about care.

In our view, it is necessary to understand the characteristics of the very-old critically unwell population in our own healthcare system (National health service, NHS). As such, we have undertaken an analysis of participants in the VIP-1 and -2 studies from ICUs in the UK. Using similar methodology to a recently published analysis of patients from Germany 14, the aim of this work is to describe the characteristics of very old patients admitted to the ICU in the UK and determine whether the associations between frailty and sickness severity scores and outcome found in the continental evaluation holds true for the UK.

Methods

Study participants and data collection

Participants included in this analysis were enrolled by a UK critical care unit to one of two prospective observational studies of very old intensive care patients (VIP-1 and -2) 11, 12. Briefly, participating critical care units in the UK enrolled consecutive admissions of patients over 80-years old in a 3-month period in 2016–17 (VIP-1) or a 6-month period in 2018–19 (VIP 2). VIP-2 included only unplanned admissions; VIP-1 also included elective admissions (e.g. following major surgery). Ethical approval for this work was provided by the NHS Health Research Authority (REC references 16/LO/1642 and 18/WA/0193) and the studies were registered on clinicaltrials.gov (IDs: NCT03134807 and NCT03370692). Participant consent was obtained prospectively where possible and assent for participation sought from relatives where patients lacked capacity. Ethical approval was granted to include those participants who died prior to consent being obtained.

Demographic data for each participant included age, sex and reason for admission to critical care. CFS was calculated for each participant, based on pre-morbid state (i.e. frailty prior to admitting condition)6. Assessment of CFS was undertaken by a healthcare professional or member of the research team at each study site. Information to calculate CFS was provided by the patient, a relative or carer or the patient record. Participants were categorised as fit (CFS <4), vulnerable (pre-frail) (CFS=4) or frail (CFS>4) 12. Sickness severity was measured by sequential organ failure assessment (SOFA) score in the first 24-hours 9. Provision of life-supportive measures such as ventilation (including non-invasive), vasoactive drugs and renal replacement therapy were recorded, along with documentation of whether life-supportive care was withheld or withdrawn. Outcome was measured as critical care survival and 30-day survival from critical care admission.

Statistical analysis

Patient characteristics, interventions and outcome measures were compared by frailty group using standard statistical tests (Chi-squared, Kruskal-Wallis, Fisher’s exact). Uni- and multi-variable logistic regression modelling was undertaken to test association between baseline characteristics (age, gender, CFS, SOFA and type-of admission [unplanned vs planned] and outcome). Statistical analyses, tables and plots were undertaken and created using R: A language and environment for statistical computing (version 3.6.3) 15. These statistical analyses match those undertaken on the subset of participants from German critical care units by Muessig et al 14.

Results

Table 1 shows the characteristics of the 1858 participants enrolled from 95 ICUs in the UK to VIP-1 (n=1036) and -2 (n=822). 991 (53%) of admissions were male. The median age was 83 (IQR 81, 86) and the oldest patient was 100. 1352 (73%) participants had unplanned admissions. Elective admissions accounted for 29.6% of participants from VIP-1, where reason for admission was known. These admissions occurred early on in the hospital stay with a median length of hospital stay prior to ICU admission of 1 day (IQR 0, 3). Acute medical admissions had a higher median SOFA score than other reasons for admission (p<0.001, ANOVA). The number of admissions by frailty scale was approximately normally distributed, with the majority of participants having frailty scale of 3–5 (figure 1).

Resource utilisation and outcomes by frailty category are shown for unplanned (table 2) and elective admissions (table 3). For participants with an unplanned critical care admission (table 2), those categorised as frail were more likely to have limitations placed on their ceiling of care (p<0.001). Where such a decision was made, it occurred earlier in the critical care stay for frail compared to non-frail patients (median time to decision 1-day vs 2-days, p=0.04). Of the life-sustaining treatments recorded, participants categorised as frail were less likely to receive invasive ventilation compared to those categorised as fit (33% vs 44% respectively). Provision of other therapies was similar across frailty categories with approximately 8–9% of participants receiving renal replacement therapy and 57–60% of participants receiving vasoactive drugs. Rates of withdrawal of therapies was similar across frailty categories (16–20% of unplanned admissions). Whilst ICU survival was similar across frailty categories (73–77%), 30-day survival was significantly lower in the frail group (58%) compared to vulnerable (66%) and fit (68%) participants (p<0.01). Figure 2 shows mortality by frailty scale 1–9, with a clear trend to increasing mortality with increasing frailty scale. 30-day survival was 25–41% for CFS scale of 7 or more (supplementary table 1).

The characteristics and outcomes for participants with a planned admission (table 3) were broadly similar across all frailty categories. Elective admissions were less likely to receive invasive ventilatory support than unplanned admissions (21% vs 38–49%, p<0.001), with a similar finding for vasoactive drugs (32% vs 50–61%, p<0.001). 30-day survival was >94% across all frailty categories. There was a similar trend of increasing mortality with increasing frailty group (figure 2), but numbers were small.

Results from the logistic regression models are presented in tables 4 and 5. SOFA score, reason for admission and frailty were all independently associated with increased mortality at 30-days (p<0.01). The odds of death at 30-days was increased for frailty when tested as a category (odds ratio 1.5, p=0.002) or a linear scale (odds ratio 1.15 per point increase in CFS, p<0.001). The odds ratio of death at 30-days was 2.96 (p<0.001) for medical and 4.53 (p<0.001) for trauma admissions compared to acute surgical admissions. Age did not have a significant association with mortality outcome.

## Discussion

We have presented detailed data on the largest very old cohort of patients admitted to critical care in the UK, both in terms of number of patients and number of ICUs. Data was provided on over 1800 patients from 95 critical care units. With a median age of 83 years, these data provide a good snapshot of the use of critical care by the very old (>80 years) across the country and healthcare system (NHS). This cohort covers the full remit of critical care provision, including medical, trauma and surgical, planned and unplanned admissions. With an increasing prevalence of admissions of the very old, clinicians frequently find themselves trying to explain the risks and benefit of an ICU admission to patients, their relatives and carers. These data may help inform those decisions, as well as future resource plans.

These data show a balance of sexes admitted to critical care. This does not mirror population data on sex from the 2011 census in England, which showed that just 37% of people over 80 are men16. This perhaps can be explained by the lower life expectancy (and consequent higher chance of illness) in men over 80.

At 30-days, frailty as measured by the CFS was associated with increased mortality independent of illness severity (as measured by SOFA score). The odds of survival at 30-days reduced with increasing frailty (supplementary table 1), although numbers were smaller in the higher CFS groups. The lower 30-day survival is perhaps unsurprising in the frail group of participants. However, with 3 out of every 5 frail admissions surviving at least 30 days, it is unclear how these data will help inform decisions to admit or continue therapy. A recent guideline for admission into ICU published by the National Institute for Health and Care Excellence (NICE) during the ongoing coronavirus (COVID-19) pandemic suggested that CFS of 5 is the threshold at which clinicians should start to consider if the harms will outweigh the benefits of critical care organ support7. Survival rates for CFS 5 and 6 at 30 days post-ICU admission in this study were 63% and 59% respectively. Interestingly, this is a similar mortality to septic shock 10, where early and aggressive intervention is recommended 17. This may add weight to the argument that mortality isn’t always a helpful standalone outcome measure, but some may argue that these findings support a raising of the CFS threshold at which the benefits of a critical care admission are questioned and at the very least a time limited trial of treatment may be suitable for patients with this level of frailty. With 30-day survival of just 40% with CFS of 7 and 25% for CFS of 9 (supplementary table 1), the importance of using the full range of the CFS rather than just frail/non-frail is apparent. These findings are similar to the work by Darvall et al. that showed a significant association between CFS and mortality in only the severe/very severely frail (CFS 7 and 8) in their retrospective study of ICU admissions for pneumonia in Australia and New Zealand 8. In the most recent update to COVID-19 guidelines, NICE continue to advocate the use of CFS in guiding decision making in the elderly, although the specific reference to CFS > 5 has been removed18.

In this study, associations between frailty and mortality are mirrored in both resource utilisation and decisions to limit life supportive treatment. Although this finding may be unsurprising, it perhaps may indicate that decisions on whether or not to provide life-supportive therapies could be made earlier in the ICU stay, if not prior to admission. This is particularly true for those with a higher clinical frailty scale (CFS>6) where more than 1 in 3 patients had some limitations in care. A frailty assessment of the very old at time of ICU referral could prompt and help inform discussions on potential therapies. As noted in our regression analysis, increasing SOFA score was also associated with increased mortality. A further potential avenue for triage therefore may be to use assessment of frailty alongside acute sickness severity. Figure 3 shows a heatmap of 30-day mortality by SOFA and frailty scale, with trends toward higher mortality (darker colour) with higher SOFA and frailty. We do not propose cut-off or threshold values, but these trends could help to inform discussions with patients or their representatives.

In keeping with other studies investigating the associations between frailty and outcomes from critical illness, it would be helpful to have a comparison with those patients not admitted to critical care (i.e. where critical illness exists but where admission to an ICU has not occurred as it is felt not in the patient’s best interests). Given the potential physical and psychological trauma associated with a critical care admission, this comparison would provide important information on the benefit of care on an ICU over continued care on a general hospital ward for those in the most-frail groups where decisions on escalation of therapy are particularly challenging. Similarly, details on patients provided with non-invasive ventilation or high flow oxygen outside of the ICU (e.g. on a respiratory ward) is also missing from these data and could provide a useful comparator in future studies. In addition to longer-term mortality data (e.g. 90-days), this work is also missing quality of life and disability outcome measures. The chance of short-term survival alone may not be the most important factor for patients and their families or carers who are making complex decisions about treatment during critical illness at this stage in their lives. Patients may be more interested in understanding how likely it is they will achieve an outcome with a quality of life they find acceptable. McNelly et al. showed that functional capacity is reduced for all survivors of critical illness 18-months after discharge in a cohort (n=41, mean age 55 yrs.) of participants in the MUSCLE study 19. Other work has suggested that frailty can help to predict functional outcome, although these data are often derived from slightly younger age groups and healthcare systems outside of the UK 20-24. In a single centre study in Holland, Geense and colleagues recently showed that 42% of patients with an unplanned critical care admission had increased frailty 12-months after discharge in all-age groups admitted to critical care 22. Interestingly, survivors with higher baseline frailty scale at admission were found to have reduced frailty 12-months later. Survivorship and selection bias (with significant loss to follow up) may confound this finding, again demonstrating the difficulty and complexity of research aimed at determining predicting factors for critical care outcome. In a cohort of older patients in the United States of America (USA) (n=216 ICU survivors, mean age 84), Ferrante et al. found higher disability scores at 6-months in patients who were frail at admission to critical care, with nearly 60% nursing home discharge for frail patients 24. However, data from this cohort includes critical care admissions from 1998–2014 so whether the findings are generalisable to current cohorts or outside the USA is unknown. Finally, we must acknowledge that many clinicians already use frailty, either informally or with scores like CFS, when making decisions about care. The associations we have found in these data are likely to be influenced by this.

Conclusions

In the very-old cohort of patients admitted to critical care in the UK, frailty is associated with an increase in mortality at 30-days. The odds of death increased with increasing frailty as measured using the clinical frailty scale. At moderate frailty (CFS 5–6) 3 out of every 5 patients admitted survived to 30-days, a similar survival rate to septic shock. Associations between frailty and death were found to be independent of sickness severity (SOFA) score. These findings support the use of the clinical frailty scale to aid patients, caregivers and clinicians making decisions about critical care provision for very-old patients.

## Figure headers and legends

**Figure 1. Number of admissions by clinical frailty scale**

Distribution of clinical frailty scale amongst very-old-patients (over 80-years) admitted to UK ICUs

**Figure 2. 30-day mortality by clinical frailty scale**

Percentage mortality 30-days following ICU admission by frailty scale. There is a clear increase in mortality with increasing frailty for both unplanned and elective admissions. Number (n) of deaths at each clinical frailty scale indicated by numbers next to data points.

**Figure 3. Heatmap showing percentage mortality at 30-days referenced to SOFA and clinical frailty scale**

Number of participants shown in white text in each reference square. Darker colours represent higher mortality. Plot shows trend to higher mortality with increase in either or both scores. A combination of chronic and acute frailty scores like these could be used to inform discussions around benefits and risks of ICU admission and associated treatments.

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