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ORIGINAL

Association of frailty with short-term outcomes, organ support and resource use in critically ill patients

Fernando G. Zampieri[1,18], Theodore J. Iwashyna[2,3], Elizabeth M. Viglianti[2], Leandro U. Taniguchi[4,5], William N. Viana[6], Roberto Costa[7], Thiago D. Corrêa[8], Carlos Eduardo N. Moreira[9], Marcelo O. Maia[10], Giulliana M. Moralez[11], Thiago Lisboa[12], Marcus A. Ferez[13], Carlos Eduardo F. Freitas[14], Clayton B. de Carvalho[15], Bruno F. Mazza[16], Mariza F. A. Lima[17], Grazielle V. Ramos[11], Aline R. Silva[11], Fernando A. Bozza[11,19], Jorge. I. F. Salluh[11], Marcio Soares[11*] and for the ORCHESTRA Study Investigators

Abstract

Purpose: Frail patients are known to experience poor outcomes. Nevertheless, we know less about how frailty manifests itself in patients' physiology during critical illness and how it affects resource use in intensive care units (ICU). We aimed to assess the association of frailty with short-term outcomes and organ support used by critically ill patients.

Methods: Retrospective analysis of prospective collected data from 93 ICUs in Brazil from 2014 to 2015. We assessed frailty using the modified frailty index (MFI). The primary outcome was in-hospital mortality. Secondary outcomes were discharge home without need for nursing care, ICU and hospital length of stay (LOS), and utilization of ICU organ support and transfusion. We used mixed logistic regression and competing risk models accounting for relevant confounders in outcome analyses.

Results: The analysis consisted of 129,680 eligible patients. There were 40,779 (31.4%) non-frail (MFI = 0), 64,407 (49.7%) pre-frail (MFI = 1–2) and 24,494 (18.9%) frail (MFI ≥ 3) patients. After adjusted analysis, frailty was associated with higher in-hospital mortality (OR 2.42, 95% CI 1.89–3.08), particularly in patients admitted with lower SOFA scores. Frail patients were less likely to be discharged home (OR 0.36, 95% CI 0.54–0.79) and had higher hospital and ICU LOS than non-frail patients. Use of all forms of organ support (mechanical ventilation, non-invasive ventilation, vasopressors, dialysis and transfusions) were more common in frail patients and increased as MFI increased.

Conclusions: Frailty, as assessed by MFI, was associated with several patient-centered endpoints including not only survival, but also ICU LOS and organ support.

Keywords: Frailty, Modified frailty index, Organ support, Resource use, Outcomes, Critical care

Introduction

Frailty has been conceptually defined as diminished physiologic reserve associated with age that results from the accumulation of physiologic stresses and comorbid diseases affecting multiple physiologic systems [1–3]. Across multiple measurement strategies, frailty has been robustly associated with worse in-hospital and long-term mortality, and reduced ability to return home for both acutely and critically ill patients [4–14].

While frailty is prognostically important, we know less about how frailty impacts patients' physiology, need for organ support and resource use during critical illness. A

*Correspondence: marciosoaresms@gmail.com
[11] Graduate Program in Translational Medicine and Department of Critical Care, D'Or Institute for Research and Education, Rio De Janeiro, Brazil
Full author information is available at the end of the article

recent systematic review [4] of frailty in the ICU found that only six of 10 studies reported on mechanical ventilation (MV) and/or vasopressors use demonstrating that frail patients were no more likely to receive organ support in the ICU than non-frail [5, 7–11]. These findings seem paradoxical as we might expect patients with diminished physiologic reserve to require more physiologic support when critically ill. However, these data are limited by modest sample sizes and looking at only a small part of the spectrum of treatments and life-sustaining therapies in the ICU.

In light of these gaps, we sought a more systematic approach to measuring the needs for ICU support and outcomes of critically ill patients associated with frailty. We studied a large population of adult patients using a previously validated modified frailty index (MFI) systematically collected on ICU admissions over 2 years [2]. We then sought to measure the association of MFI with the outcomes and organ supports used by critically ill patients.

Take-home message

In a large cohort of critically ill patients, we found that frailty, assessed using the Modified Frailty Index (MFI), was associated not only with mortality, but also with higher need for organ support during ICU stay (mechanical ventilation, non-invasive ventilation, renal replacement therapy, vasopressors and transfusions), lower probability of return home without need for nursing assistance, and longer ICU and hospital length-of-stay. Our results also demonstrated in general a dose-response between the frailty measure we used—the MFI—and all of our outcomes and suggested that MFI values ≥ 3 points may be most robust to identify frailty in critically ill patients.

Methods

Design and setting

We performed a retrospective study on prospectively collected data in 93 medical-surgical ICUs from 55 public and private hospitals in Brazil from January 2014 to December 2015. The local ethics committee at the D'Or Institute for Research and Education (Approval Number 334.835) and the Brazilian National Ethics Committee (CAAE 19687113.8.1001.5249) approved the study and waived need for informed consent. A complete list of the investigators is in the Electronic Supplementary Material (ESM).

Patients' eligibility criteria

We considered all ICU admissions for analysis. We excluded patients aged < 16 years old, readmissions and those with missing core data [age, location before ICU admission, main admission diagnosis, the Simplified Acute Physiology Score (SAPS) 3 [15], ICU and hospital lengths of stay (LOS) and vital status at hospital discharge].

Data collection

We retrieved de-identified patients' data from the Epimed Monitor System®, (Epimed Solutions®, Rio de Janeiro, Brazil), a cloud-based registry for ICU quality improvement and benchmarking purposes [16]. In brief, data on all admitted patients are prospectively collected at each ICU including demographics, ICU admission diagnosis, admission SAPS 3 [15] and Sequential Organ Failure Assessment (SOFA) scores [17], previous functional capacity according to the performance status 1 week before hospital admission [18], comorbidities [including all those encompassed by the Charlson Comorbidity Index (CCI)] [19], use of organ support [vasopressors, MV, noninvasive ventilation (NIV) and renal replacement therapy (RRT)], and transfusion [fresh frozen plasma, platelet and red blood cells (RBC)] during the ICU stay, ICU and hospital LOS and mortality, and discharge location after hospital discharge.

Modified frailty index (MFI)

The MFI was chosen as a proxy for frailty due to availability of its components in administrative databases as previously validated in other populations [16, 20–22]. The MFI allows frailty to be measured as a multi-step variable, not merely dichotomous, and was calculated as the sum of the number of points a given patient has in a list of 11 items (one point per item) encompassing previous functional capacity, comorbid conditions, and previous complications (ESM, Box 1) [2]. Patients were then categorized using MFI values into non-frail (MFI = 0), pre-frail (MFI = 1–2) or frail (MFI $\geq$ 3); this categorization was used for all main analyses [2, 23, 24]. Alternatively, we also supply additional analysis treating MFI as a continuous variable (truncated at 5, so the smallest category had at least 1% of the total sample size) for selected outcomes (see below).

Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes were discharge location among hospital survivors (home without need for nursing care versus any other, including hospice, home-care and other healthcare facilities), ICU and hospital LOS, and utilization of ICU resources (organ support and transfusion).

Missing data

There was no missing information regarding hospital outcome. For ICU resource use, if the number of missing values was below 1%, we imputed using the most frequent category; otherwise, we used a multiple imputation

technique. If the patients had missing data in the components necessary to calculate the MFI, we applied a multiple imputation technique using chained equations regardless of the percentage of missing data [25]. We did not impute missing MFI directly; instead, we imputed the missing values for each MFI item and then recalculated MFI.

Statistical analyses

We used frequentists tests (*t* test/ANOVA or Mann–Whitney/Kruskal–Wallis) in descriptive analyses. We assessed the association between frailty (according to MFI categories) and hospital mortality in all patients, as well as destination after discharge (home without need for nursing care versus any other) in those who survived the hospital stay in generalized linear mixed model (GLMM) regressions while correcting for age, SOFA score, admission type. GLMM model was fit using penalized quasi-likelihood method [26]. Three-way interactions among SOFA score, admission type, and frailty category were allowed. We defined variable models a priori based on clinical relevance. The ICU where the patient had been admitted was included as the random intercept. Odds ratios and their respective 95% confidence intervals (OR, 95% CI) are reported. To ease the interpretability of results including interactions, we also report the graphical probabilities of the models and ORs for fixed terms for the main mortality analysis. We performed an additional model for hospital mortality using continuous MFI values (0–5).

LOS was analyzed using a competing risk analysis (Fine and Gray model) considering death as a competitor for both ICU and hospital discharge. We specified that this model would be adjusted for age, SOFA score, admission type and MFI categories, without interactions. We censored patients at discharge or at 28 days (for ICU LOS) or 60 days (for hospital LOS). We reported results as hazard ratios (HR) of being discharged, with lower values representing a lower hazard of being discharged and, consequently, a higher LOS independently of the competitor (death). Additional models using MFI as a continuous variable were also performed.

We also performed additional mixed logistic regressions for organ support use (vasopressors, MV, NIV, and RRT) and transfusion support during the ICU stay. These models were adjusted to SAPS 3 score, allowing interactions. Patients already in use of organ support were not included in the model, that is, for example, the mixed model logistic regression for MV use included only patients requiring MV after ICU admission. Similarly to the main mortality model and LOS analyses, we also built additional models for organ support using continuous MFI values instead of MFI categories. All analyses were done in R (version 3.5.0) using *mice, tidyverse*, *Hmisc, multicomp, MASS*, and *cmprsk* packages [27].

Results

Population characteristics

During 2014 and 2015, 149,650 consecutive admissions occurred in the participating ICUs. (The cohort flowchart is shown in ESM, Suppl. Fig. 1). Of these, 129,680 patients were eligible for the analyses. The median number of patients per ICU was 1049 (IQR 708–1735). A total of 6515 (5%) patients had missing data for the calculation of MFI. The MFI distribution in our sample is shown in Supplementary Box 2 and Supplementary Figure 2. There were 40,779 (31.4%) non-frail, 64,407 (49.7%) pre-frail and 24,494 (18.9%) frail patients. The proportion of frail patients varied substantially among ICUs [median 19.4% (IQR 14.1–26.5%; range 1.5–50.0%)]. Detailed information on the patients' characteristics and outcomes stratified according to MFI categories are shown in Table 1 (further data for patients stratified according to MFI values is shown in Supplementary Tables 1 and 2). As expected, frail patients were older, had more chronic comorbidities and impairment of performance status, were more severely ill and more frequently admitted for medical reasons.

Mortality analysis

Frailty was associated with higher mortality and LOS at both ICU and hospital in univariate analysis (Table 1 and Suppl. Table 1). Hospital mortality increased from 12.5% in non-frail to 28.8% in frail patients. Mortality from MFI 0 to ≥ 5 also increased in a step wise fashion (12.5%, 16.3%, 19.5%, 26.2%, 31.9%, 36.8%, respectively). After multivariate analysis, frailty was still associated with a more than doubling of the odds hospital mortality [aOR 2.42 (95% CI 1.89–3.08), Supplementary Table 3]. Age [aOR 1.029 (1.028–1.030)], SOFA score [aOR 1.34 (1.31–1.38)] and admission type [medical, aOR 3.700 (3.109–4.402); emergency surgical, aOR 2.569 (2.003–3.295)] were also associated with mortality (Supplementary Table 3).

The association between frailty and higher mortality was more evident in patients admitted with lower SOFA scores (Fig. 1). This effect was apparent regardless of admission type (Supplementary Figure 3). Moreover, pre-frailty was not associated with mortality. When MFI was added as a continuous variable, the same pattern of a reduction in ORs for MFI as the SOFA increased was observed (Supplementary Figure 4). Of note, only MFI ≥ 3 points was clearly associated with higher mortality.

Table 1 Characteristics of included patients according to frailty status

	Non-frail	Pre-frail	Frail	*P* value
n	40,779	64,407	24,494	
Age (years) [mean (sd)]	48.55 (19.07)	65.41 (17.11)	75.68 (12.54)	< 0.001
SOFA (points) [mean (sd)]	2.72 (3.53)	3.18 (3.58)	4.05 (3.79)	< 0.001
SAPS 3 (points) [mean (sd)]	39.76 (15.06)	45.92 (15.70)	53.09 (15.63)	< 0.001
Admission type (*n*, %)				< 0.001
Elective surgery	11,766 (28.9)	17,220 (26.7)	3392 (13.8)	
Medical	25,055 (61.4)	43,149 (67.0)	19,830 (81.0)	
Urgent surgery	3958 (9.7)	4038 (6.3)	1272 (5.2)	
LOS before ICU (days) [median (IQR), mean (sd)]	0.00 [0.00, 1.00] 1.94 (6.62)	0.00 [0.00, 1.00] 2.32 (8.08)	0.00 [0.00, 1.·00] 3.82 (11.92)	< 0.001
CCI (points) [median (IQR), mean (sd)]	0 [0–1] 0.80 (1.64)	1 [0–2] 1.39 (1.76)	2 [1–4] 2.78 (1.91)	< 0.001
Performance status impairment (*n*, %)				< 0.001
Absent/minor	40,779 (100.0)	45,829 (71.2)	6688 (27.3)	
Moderate	0 (0.0)	13,583 (21.1)	12,162 (49.7)	
Severe	0 (0.0)	4995 (7.8)	5644 (23.0)	
Solid non-metastatic tumor (*n*, %)	5505 (13.5)	9149 (14.2)	2733 (11.2)	< 0.001
Solid metastatic tumor (*n*, %)	1970 (4.8)	3406 (5.3)	805 (3.3)	< 0.001
Hematological malignancy (*n*, %)	916 (2.2)	1179 (1.8)	378 (1.5)	< 0.001
Cirrhosis, Child A–B (*n*, %)	391 (1.0)	776 (1.2)	171 (0.7)	< 0.001
Cirrhosis, Child C (*n*, %)	379 (0.9)	627 (1.0)	126 (0.5)	< 0.001
COPD (*n*, %)	0 (0.0)	3146 (4.9)	4396 (17.9)	< 0·001
Heart failure NYHA Class II–III (*n*, %)	0 (0.0)	1801 (2.8)	3993 (16.3)	< 0.001
Heart failure NYHA Class IV (*n*, %)	0 (0.0)	454 (0.7)	1041 (4.3)	< 0.001
Diabetes (uncomplicated) (*n*, %)	0 (0.0)	12,121 (18.8)	9961 (40.7)	< 0.001
Diabetes (complicated) (*n*, %)	0 (0.0)	3518 (5.5)	5336 (21.8)	< 0.001
Organ support at ICU admission				
Vasopressors (*n*, %)	4082 (10.0)	6950 (10.8)	3466 (14.2)	< 0.001
MV (*n*, %)	6221 (15.3)	9234 (14.3)	4381 (17.9)	< 0.001
NIV (*n*, %)	1694 (4.2)	3966 (6.2)	2651 (10.8)	< 0.001
RRT (*n*, %)	294 (0.7)	1023 (1.6)	668 (2.7)	< 0.001
Organ support on first 24 h				
Vasopressors (*n*, %)	5249 (12.9)	9342 (14.5)	4587 (18.7)	< 0.001
MV (*n*, %)	6845 (16.8)	10,640 (16.5)	5123 (20.9)	< 0.001
NIV (*n*, %)	2129 (5.2)	5024 (7.8)	3431 (14.0)	< 0.001
RRT (*n*, %)	753 (1.8)	2377 (3.7)	1264 (5.2)	< 0.001
Organ support during ICU stay				
Vasopressors (*n*, %)	5508 (13.5)	10,590 (16.4)	5369 (21.9)	< 0.001
MV (*n*, %)	8227 (20.2)	13,766 (21.4)	6815 (27.8)	< 0.001
MV duration [days, median (IQR)]	4 [1–11]	5 [2–12]	6 [2–14]	< 0.001
NIV (*n*, %)	3182 (7.8)	7185 (11.2)	4694 (19.2)	< 0.001
RRT (*n*, %)	1473 (3.6)	4321 (6.7)	2335 (9.5)	< 0.001
Transfusion during ICU stay				
Red blood cells (*n*, %)	3756 (9.2)	6318 (9.8)	2900 (11.8)	< 0.001
Fresh frozen plasma (*n*, %)	857 (2.1)	1309 (2.0)	549 (2.2)	0.150
Platelets (*n*, %)	789 (1.9)	1208 (1.9)	499 (2.0)	0.288
Any transfusion (*n*, %)	4093 (10.0)	6932 (10.8)	3170 (12.9)	< 0.001
Outcomes				
ICU LOS (days) [median (IQR), mean (sd)]	2.00 [1.00, 4.00] 4.58 (9.34)	3.00 [1.00, 5.00] 5.40 (10.13)	4.00 [2.00, 8.00] 7.22 (13.21)	< 0.001

Table 1 continued

	Non-frail	Pre-frail	Frail	*P* value
Hospital LOS (days) [median (IQR), mean (sd)]	7.00 [4.00, 14.00] 13.59 (24.70)	8.00 [4.00, 18.00] 17.76 (126.87)	13.00 [6.00, 28.00] 27.24 (75.85)	< 0.001
Hospital mortality (*n*, %)	5095 (12.5)	11,419 (17.7)	7049 (28.8)	< 0.001
Destination after discharge (*n**, %)				< 0.001
Home without nursing support	34,263 (96.0)	50,511 (95.5)	16,274 (93.3)	
Other	1421 (4)	2477 (4.5)	1171 (6.7)	

IQR interquartile 25–75% range, *SD* standard deviation, *ICU* intensive care unit, *SOFA* Sequential organ failure assessment, *SAPS* Simplified acute physiological score, *LOS* length-of-stay, *CCI* Charlson comorbidity index, *COPD* chronic obstructive pulmonary disease, *MV* mechanical ventilation, *NIV* non-invasive ventilation, *RRT* Renal replacement therapy, *NYHA* New York Heart Association, *total number of patients = 106,117 patients

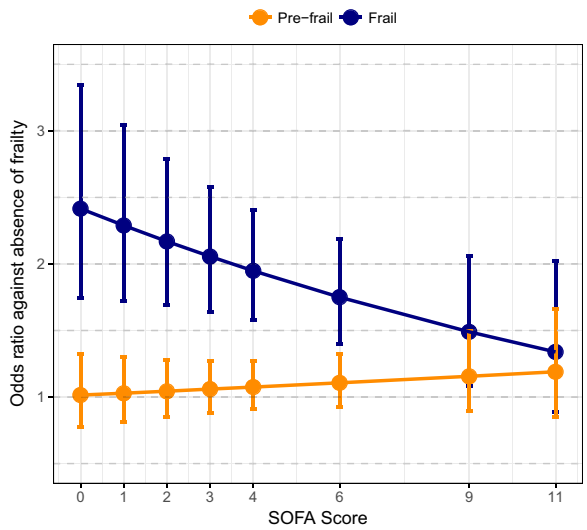

Fig. 1 Odds ratio for mortality according to frailty. Association between frailty status [pre-frail (orange) and frail (dark blue)] on hospital mortality according to the admission SOFA score. Results as odds-ratios and respective 95% confidence intervals. Model also adjusted by age and admission type

Discharge home without the need for nursing support

After multivariate analysis, frailty was associated with a lower probability of discharge home without the need for nurse support [aOR 0.363 (0.538–0.795)] (Suppl. Table 4). This association was more pronounced in medical admissions (where more than 30% of the pre-frail and frail patients were not discharged home without nurse assistance compared to less than 15% of the non-frail; Supplementary Figure 5) than in surgical ones (Supplementary Figure 6).

ICU and hospital LOS analysis

Despite being 18% of the study population, frail patients were responsible for 25% of all ICU bed/days during the study period. Frailty was associated with a lower HR of being discharged from the ICU and from the hospital (Fig. 3 and Supplementary Table 5). LOS according to MFI value stratified according to hospital survival is shown in Supplementary Figure 7. Increasing MFI scores were associated with progressive lower probability of being discharged from the ICU and hospital (Fig. 2). Similarly to the main mortality model, only MFI ≥ 3 points were consistently associated with lower HRs for ICU and hospital discharge (Fig. 2).

Organ support analysis

Frail patients used more organ support (during the first 24 h after admission and during ICU stay) and received blood transfusions more frequently (Table 1 and Supplementary Table 2). As MFI increased, use of organ support and transfusion increased (Fig. 3 and Supplementary Table 2). Multivariate results according to frailty categories adjusted for SAPS 3 are shown in Fig. 4 and Supplementary Figure 8. Frailty was associated with both higher odds of organ support and transfusions, particularly RBC. When MFI was treated as a continuous variable, odds for organ support or transfusion increased as MFI increased—continuous dose response curves were consistently present (Supplementary Figure 8). Thus, compared to non-frail patients (MFI = 0), frail patients (MFI ≥ 3) were 1.69 times more likely to receive any transfusion (95% CI 1.43–2.01); 1.61 times more likely to receive RBC (95% CI 1.35–1.92); 1.36 times more likely to receive MV (95% CI 1.05–1.75); 4.25 times more likely to receive NIV (95% CI 3.33–5.42); and 3.56 times more likely to receive RRT (95% CI 2.76–4.61); and 1.84 times more likely to receive vasopressors (95% CI 1.45–2.35), while adjusting for SAPS 3.

Discussion

In this large cohort study of critically ill patients, we found frailty to be associated with higher hospital mortality and organ support use during ICU stay. The finding that frailty is associated with subsequent mortality may be, at this point in the literature [4–14, 28], interpreted as a positive control to ensure face validity for

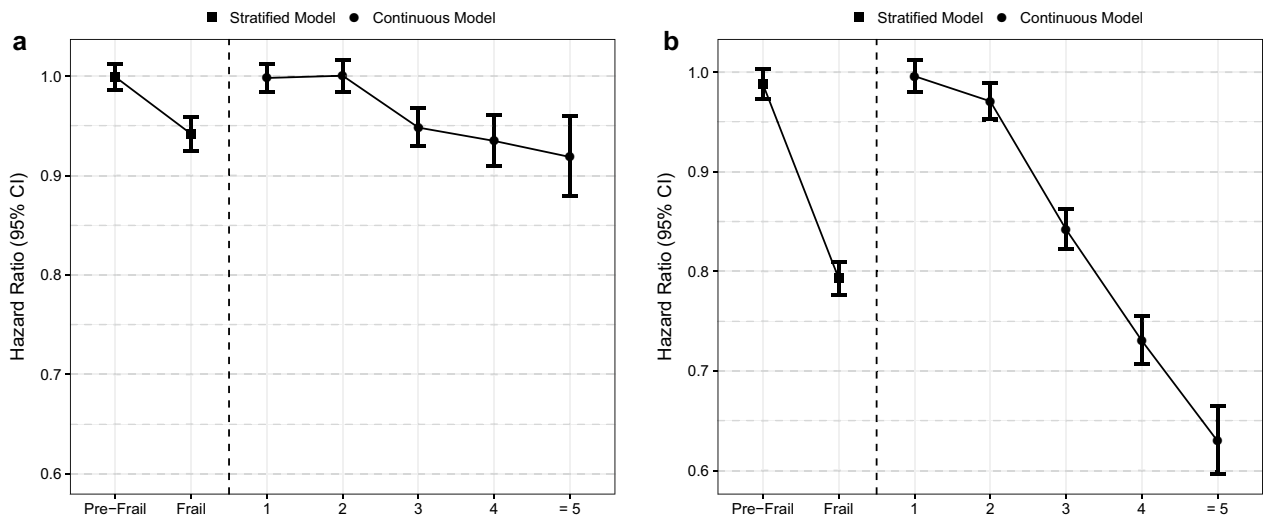

Fig. 2 Competing risk analysis. Hazard ratios with respective 95% confidence intervals for ICU (**a**) and hospital (**b**) discharge in survivors according to MFI categories (squared) and points (dots). This analysis was adjusted by age, SOFA score and admission type

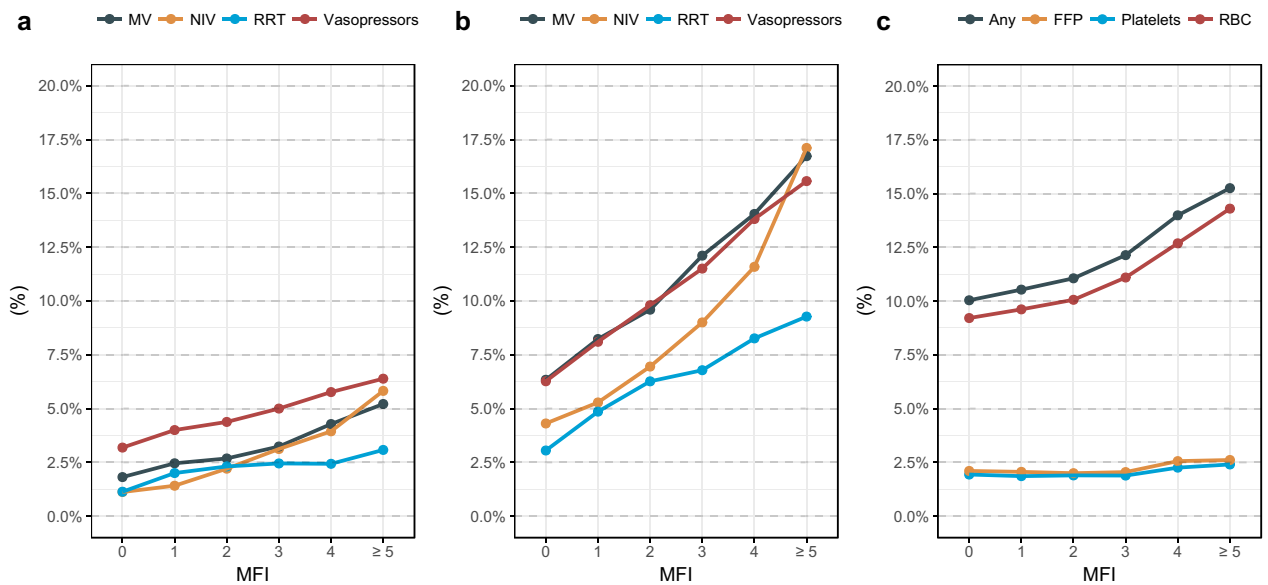

Fig. 3 Resource use during ICU stay according to MFI points. **a** Organ support use within 24 h after ICU admission; **b** organ support any time during the ICU stay after ICU admission; **c** transfusion requirements during the ICU stay

frailty measurement. Increasingly, the interesting questions may be: how is frailty associated with mortality, and at what level of frailty? Our results speak to both questions. Moreover, frailty was also associated with higher ICU and hospital LOS and lower probability of being discharged home without need for nursing assistance. In contrast to previous smaller studies [5, 7–11], frailty was associated with the need for organ support (including MV, NIV, vasopressors, RRT) and transfusions during ICU stay.

There are multiple credible hypotheses about the bedside ways in which frailty might manifest itself in ICU patients. First, frailty might lead patients with seemingly similar diagnoses and other background characteristics to present more acutely physiologically deranged. Second, conditional on the same physiological derangement

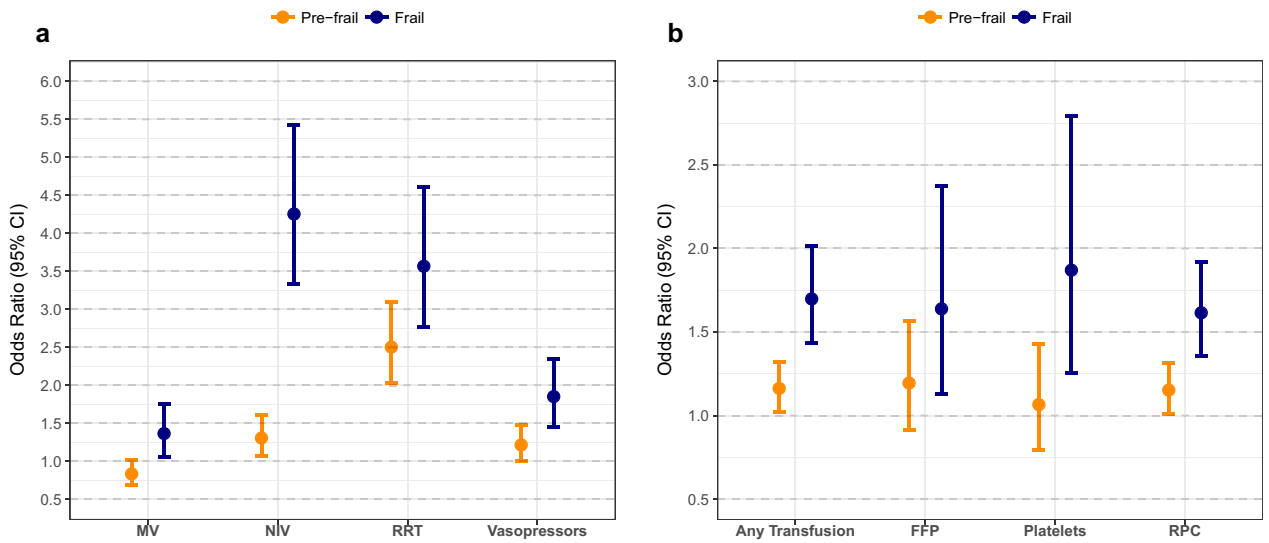

Fig. 4 Adjusted odds ratio for resource use. Adjusted odds-ratios with respective 95% confidence intervals for ICU resource use anytime during ICU stay according to MFI categories (pre-frail: orange lines; frail: dark blue lines). **a** Organ support; **b** transfusion requirements. Analyses adjusted by SAPS 3 score

on presentation, frailty might lead patients to require more aggressive physiological support to obtain similar outcomes. Third, frailty may result in reduced salvageability, with worse outcomes despite more aggressive support. Finally, frailty might be associated with mortality because it is associated with different preferences for care by patients, their surrogates, or (more concerning) the clinicians caring for those patients.

Our results show that, in fact, the mechanisms of frailty are multiple. Frail patients do present with more deranged physiology on admission, as measured by SAPS 3 or SOFA scores. Yet, even adjusting for this deranged physiology, they also receive more physiologic support initially and throughout the ICU stay. Regardless this more aggressive organ support, frailty is still associated with worse short-term mortality, suggesting there are additional unmet needs for further physiologic support. Despite the fact that we were not able to assess the implementation of end-of-life (EOL) decisions (to withhold or to withdraw treatments), the finding that frailty is also associated with lower probability of being discharged home without need for nursing care argues that the increased mortality is not simply the result of a preference of the ICU for withdrawing care in patients with frailty, but also a result of the diminished capacity of ICU care to provide full recovery for critically ill frail patients. Alternatively however, as frail patients may be less likely to withstand aggressive therapies, it is also conceivable that the very intensive support may be related to mortality in some of these patients.

We might speculate about the implications of this at the bedside. The first is that frail patients face worsened prognosis for the same traditionally measured severity of illness, and this must be taken into account in prognostication and communication. Of note, if hospitals do not all have the same rates of frailty in their catchment areas, such an uneven distribution of the frail patients may have implications for hospital comparisons. The second is that ICUs should anticipate increased resource utilization and staff in frail patients, appropriately. Rising rates of frailty may mean that the increases in ICU use projected from aging alone may underestimate future needs for critical care. Finally, the finding that frail patients are admitted with higher severity of illness raises the possibility that, in same cases, frail patients with similar risk of death to non-frail patients are denied ICU because of their frailty, or even that there is a delay in recognition for ICU admission in frail patients. If intentional and consistent with family wishes, this may be reasonable, but it also raises the prospect of inadvertent discrimination against frail patients, who are nonetheless admitted to the ICU, making it also ineffective discrimination.

Our results also suggest that past reports [4, 5, 7–11], wherein frailty was not associated with, for example, MV and vasopressors use may have been limited by their modest sample sizes to detect non-linear associations. Our results demonstrate in general a dose–response between the frailty measure we used—the MFI—and all of our outcomes. But the difference between non-frailty and or low frailty levels (pre-frailty) was variable between outcomes. The full association was most readily visible

when the entire spectrum of frailty was meaningfully examined, possible only in large population-based data. These results suggest, in our judgment, that if one must dichotomize the MFI, a dichotomization at < 3 versus ≥ 3 may be most robust, in accordance with previous publications in non-critically ill patients [23, 24, 29].

This manuscript has important strengths. Our analysis substantially increases the number of patients and centers in whom the association between frailty and these outcomes has been reported. The Muscedere et al. meta-analysis totaled 3030 patients and a recent multicenter multinational study included 5021 patients aged ≥ 80 years [4, 14]. This larger sample size allows us to examine non-parametric relationships between frailty and key measures, including important subgroups. The inclusion of diverse hospitals and ICUs increases the validity and generalizability of these results. The concordant findings across multiple organ support suggests robustness, and allow us to begin to address critical questions about the mechanisms by which frailty leads to poor outcomes—with an eye to distinguishing which are inevitable and which could be ameliorated by a more geriatrics-attuned care. Finally, our definition of frailty is not limited exclusively to coded diagnoses, but includes basic functional measures [18] and also corroborates the feasibility and potential value of collection of pre-hospitalization functional measures at scale as a part of routine care [20–22, 24].

The present study has also several additional limitations. First, MFI is not the gold standard for frailty assessment (which would involve a comprehensive multidisciplinar geriatric team, unavailable in most ICUs). While MFI comprehends comorbidities, previous complications and functional capacity, it fails to account for other important aspects, such as strength, weight loss, among others. It is also uncertain how MFI correlates with other instruments to assess frailty. Second, we drew patients from several hospitals in Brazil. While perhaps more representative of intensive care globally than selected quaternary care hospitals in North America and the United Kingdom where some frailty research has been done, these data must be generalized to other contexts with caution. The extent to which the effects of frailty are context-dependent is not yet known and should be investigated in international studies including also non-elderly patients. Third, we used routinely collected data to conduct this analysis at scale, and so some degree of information was unavailable or missing. However, we utilized robust imputation techniques to account for the missing data. Forth, few patients in our sample had extreme frailty (MFI ≥ 5) and we, therefore, could not assess whether mortality and need for support keeps rising with very high MFI values or if there is a plateau at some point. Whether this is a unique feature of our data or if it marks that very frail patients are seldom admitted to the ICU deserves exploration in further studies. However, this rareness suggests such extreme phenotypes, while scientifically interesting, may be of less population-health significance [2, 22, 24]. Fifth, we studied a population with an overall relatively low severity of illness and future studies evaluating more severe patients are wanted. Finally, we have no data on EOL decisions in this population. It is conceivable that withholding or withdrawing support could be more frequent in frail patients, which could modulate the results. These implications deserve also further investigation.

Conclusion

Frailty is independently associated with short-term outcomes and resource use in critically ill patients. This has important implications for both administrators and clinicians. Increasing resource use by growing numbers of frail patients must be anticipated, and their nonetheless worse prognosis must be accurately communicated to families and incorporated into decision-making. Nevertheless, with large numbers of frail patients being treated in the ICU and dying in greater than anticipated numbers, there may also be a role for specialized care pathways and research into optimizing organ support in these patients [10].

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-018-5342-2) contains supplementary material, which is available to authorized users.

Author details

[1] Research Institute, HCor-Hospital do Coração, São Paulo, Brazil. [2] Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA. [3] Veterans Affairs Center for Clinical Management Research, HSR&D Center for Excellence, Ann Arbor, MI, USA. [4] ICU, Hospital Sírio Libanês, São Paulo, Brazil. [5] Emergency Medicine Discipline, Hospital das Clínicas HC-FMUSP, Universidade de São Paulo, São Paulo, Brazil. [6] ICU, Hospital Copa D'Or, Rio De Janeiro, Brazil. [7] ICU, Hospital Quinta D'Or, Rio De Janeiro, Brazil. [8] Adult ICU, Hospital Israelita Albert Einstein, São Paulo, Brazil. [9] ICU, Hospital Nove de Julho, São Paulo, Brazil. [10] ICU, Hospital Santa Luzia Rede D'Or São Luiz DF, Brasília, Brazil. [11] Graduate Program in Translational Medicine and Department of Critical Care, D'Or Institute for Research and Education, Rio De Janeiro, Brazil. [12] ICU, Hospital Santa Rita, Santa Casa de Misericórdia de Porto Alegre, Porto Alegre, Brazil. [13] ICU, Hospital São Francisco, Ribeirão Preto, Brazil. [14] ICU, Hospital Esperança Olinda, Olinda, Brazil. [15] ICU, Hospital Brasília, Brasília, Brazil. [16] ICU, Hospital Samaritano, São Paulo, Brazil. [17] ICU, Hospital Esperança, Recife, Brazil. [18] ICU, Hospital Alemão Oswaldo Cruz, São Paulo, Brazil. [19] National Institute of Infectious Diseases Evandro Chagas, Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro, Brazil.

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Author contributors

FGZ, TJI, EMV and MS participated in study conception, data interpretation, and drafting of the manuscript. FGZ performed the statistical analysis and produced the figures. FAB, JIFS and MS led data collection and cleaning. LUT, WNV, RC, TDC, CENM, MOM, GMM, TL, MAF, CEFF, CBC, BFM, MFAL, GVR, ARS, FAB and JIFS participated in data acquisition and revised the manuscript for important intellectual content. All authors approved the final copy of the manuscript.

Compliance with ethical standards

Conflicts of interest

Dr. Soares and Dr. Salluh are founders and equity shareholders of Epimed Solutions®, which commercializes the Epimed Monitor System®, a cloud-based software for ICU management and benchmarking. The other authors declare that they have no conflict of interest.

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