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# The PALliative MUlticenter Study in Intensive Care (PalMuSIC). Results From a Multicenter Study Addressing Frailty and Palliative Care Interventions in Intensive Care Units in Portugal

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## Abstract

**Objective:** Frailty is a clinically recognizable state of increased vulnerability common in critical medicine. When underrecognized, it may lead to invasive treatments that do not serve the patients' best interest. Our aim was to evaluate the use of both palliative care consultation and invasive interventions in frail patients admitted to Intensive Care Units in Portugal. **Methods:** This was a prospective, observational study. All consecutive adult patients admitted for more than 24 h, over a 15-day period were enrolled. Twenty-three Portuguese Intensive Care Units were included. Informed consent was obtained from all patients or their surrogate. The doctor and nurse in charge calculated the Clinical Frailty Score as well as the reference family member **Results:** A total of 335 patients were included in the study (66% male). Mean age was 63.2 $\pm$ 16.8 and SAPS II score was 41.8 $\pm$ 17.4. Mean Clinical Frailty Score value was 3.5 $\pm$ 1.7. Frailty prevalence (mean score $\geq$ 5) was 20.9%. Frail patients were offered organ support therapy (64,3% invasive mechanical ventilation; 24,3% renal replacement therapy; 67,1% vasopressors) more often than non-frail patients. Nevertheless, limitation of therapeutic effort or a do not resuscitate order ($p < 0.001$) were more common in frail patients. Mortality rate by 6 months was higher among frail patients (50% vs. 32.3%, $p < 0.001$). Palliative Care was offered to only 15% of frail patients (3.9% overall). **Conclusions:** The authors suggest that palliative care should be universally consulted once frailty is identified in critical patients.

## Keywords

critical & intensive care, DNR, end of life, frailty, futility, ICU, limitation of therapy, palliative care

## Introduction

Frailty, a clinically recognizable state of increased vulnerability,[1] has been an emerging topic in intensive medicine. Frailty results from an accumulation of health deficits. It defies classical concepts, namely physiological age or comorbidities, as well as prognostic significance or the ability to predict the risk of death.[2-4]

Except for dementia, most medical conditions (including cancer) have unpredictable disease trajectories until few months before death[5] and therefore should not be used alone for end-of-life (EOL) care decision-making policies. By contrast, almost two-thirds of frail patients have EOL downward trajectories.[5] This should warn about the need to anticipate goals of care assessment and advance life directives on frail patients.[5,6]

Frailty is common in the Intensive Care Unit (ICU)[7,8] and is usually measured by the Clinical Frailty Score (CFS).[9] Inter-rater variability may lead to significant bias in frailty assessment since most patients in the ICU do not have the ability to communicate. Being the family members the main source of information, emotional bias can be present.[10] Inter-rater variability may lead to underrecognized frailty and

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subsequent invasive treatments that do not serve the patients' best interests.

Palliative Care (PC) in ICU offers an opportunity for open communication with patients and their families about EOL. It also offers articulation with the remaining health teams to jointly build a holistic care plan. Frail patients have known palliative needs, which are expected to be exacerbated in critical illness.[11] Although several studies addressed frailty and PC in intensive care,[7,12-14] there is scarce information on their relationship.

In this study we aim to prospectively evaluate frailty prevalence in ICU in Portugal along with PC utilization and invasive interventions and to assess adequacy of these interventions in the ICU population. We measured the prevalence of advanced directives; family meetings; PC intervention; limitation of therapeutic efforts and do not resuscitate (DNR) orders.

We aimed to address the following research questions:

a) What is the prevalence of frailty in the Portuguese ICUs?
b) Is there inter-rater variability of frailty assessment?
c) What is the EOL decision-making policy in the ICU? How many patients are referred to a palliative care consultation?
d) Should frailty be a trigger for PC intervention in the ICU? Is frailty independently related to short term mortality, either in the ICU or after discharge?

## Material and Methods

This was a prospective, multicenter, cohort observational study.

The study was approved by the Research and Ethics Committee of Hospital Vila Franca de Xira. All centers were responsible for obtaining local authorization. The study was performed in accordance with the 1964 Declaration of Helsinki and its later amendments.

### Recruitment

All 51 Portuguese multivalent ICUs were invited to the study. A total of 23 centers agreed to participate. All consecutive patients admitted to 1 of the 23 participating centers during a 15-day consecutive period were enrolled. Recruitment of patients in any single center could start anytime between March and May of 2019 and continue for 15 consecutive days. All consecutive adult patients (age > 18years) admitted in ICU for more than 24 hours were included. Each patient could only be included once.

Written informed consent was obtained from all patients, or their surrogate, previously to data collection. All centers were limited to a maximum of 30 participants to prevent an excessive weight of a single center on the overall results.

### Database

The collected information included demographic data, comorbidities, type of admission (medical or surgical), sepsis on admission, Simplified Acute Physiology Score (SAPS) II score,[15] process of care (including organ support therapies), ICU and hospital length of stay (LOS). All patients were followed until hospital discharge or death (whichever occurred first) and were again reevaluated 6 months later to assess all-cause mortality or need for hospital readmission.

All data were entered in a dedicated electronic database exclusively created for this study and managed by 2 of the authors (IC and JGP) who ensured its confidentiality. Patients were given a code number to secure their identification. Investigators could only access the data that they introduced. No financial reward was granted to participating centers.

### Frailty Assessment and Palliative Care Interventions

All included patients were prospectively assessed by the CFS performed both by the doctor and nurse in charge as well as the reference relative. We considered the reference relative as the preferred liaison contact with the ICU team (normally the spouse, son or daughter).

The CFS is a nine-point Canadian assessment tool that quantifies frailty matched to descriptors of fitness, comorbidities, vulnerabilities, disability, and life expectancy. We used the Brazilian validated version of CFS.[16] Frailty was defined as a mean CFS score $\geq 5$.[16]

Limitation of therapeutic efforts was defined as limitation of all curative therapeutic efforts. A decision to forego cardiopulmonary resuscitation attempt (in the instance of a cardiac arrest) was called a Do Not Resuscitate (DNR) order.

All clinical decisions related to limitation of therapeutic efforts and DNR orders, along with patient's advanced directives, PC interventions, goals of care assessment and family meetings were also registered.

### Statistical Analysis

A single investigator in each participating center performed data entry. Data were screened in detail by one of the authors (JGP or IC) for missing information and for implausible or outlying values.

General descriptive statistics were assessed. Continuous variables were expressed as mean $\pm$ standard deviation or median [interquartile range] according to data distribution. Categorical variables were expressed as N (%). Comparisons between groups were performed with the unpaired Student's t-test or Mann-Whitney U-test for continuous variables and Fisher's exact test and chi-square test for categorical variables, as appropriate.

We developed 2 multiple logistic regression analysis to assess the variables associated with frailty (first model) and the risk of being dead within 6 months (second model).

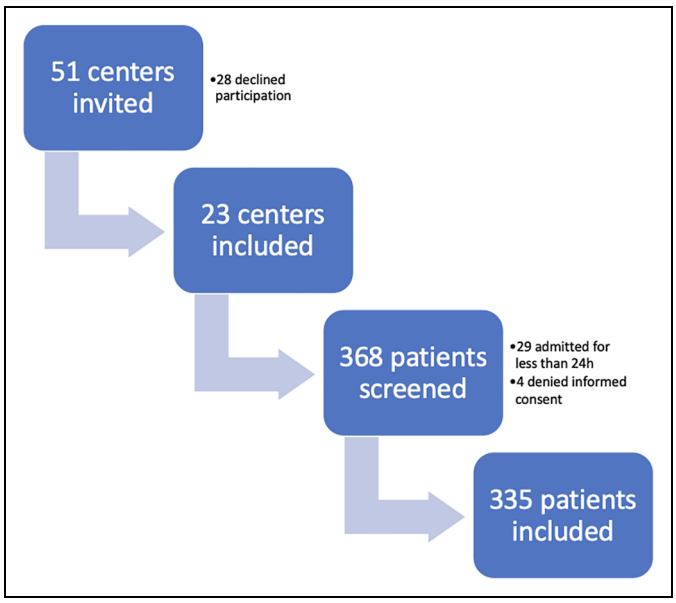


**Figure 1.** Flowchart of the included patients.

The univariate association of clinically significant variables, especially comorbidities, demographic characteristics and laboratory markers, with frailty (first model) and 6-month all-cause mortality (second model) was assessed for model building. To ensure inclusion of all clinically significant variables into the model, a p-value as high as 0.1[17] was used for selection. Moreover, if an excluded variable was considered to have a possible influence on the outcome, it was also forced into the model. Correlations between all included variables were checked. We arbitrarily used a $r < 0.3$ as low enough threshold to decrease the risk of significant multicollinearity.[18] For variables that were correlated, the one that was considered more prone to be related to the studied outcome was selected. A sub-group analysis, according to age (more or less than 60 years old) was also performed. Model fit was assessed with the Hosmer-Lemeshow goodness of fit test.

Statistical analysis was performed using IBM SPSS Statistics v.25.0 (IBM, Somers, NY, USA). All statistics were 2-tailed and the significance level was defined as $p < 0.05$.

## Results

### Demographic Data

A total of 335 patients were recruited from 23 different centers. Denial of consent was rarely reported (less than 5 episodes) as shown in Figure 1. Mean age was 63.2 ± 16.8 years and 66% were male. Their general characteristics are shown in Table 1.

Comorbidities were common (Table 2), especially chronic renal failure, coronary ischemic disease, chronic obstructive pulmonary disease and solid neoplastic disease. In 116 patients (34.6%) no comorbidity was reported. AIDS prevalence was very low.

### Frailty

Frailty was observed in 20.9% of patients. Age subanalysis showed a higher incidence in patients over 60 years of age (27.3% vs. 10.3%, $p < 0.001$).

Doctor and family's scores were strongly correlated (Pearson' correlation score, $r = 0.92$), while the nurses' score was less well correlated (nurse with doctor, $r = 0.47$ and nurse with family, $r = 0.42$, respectively). However, nurses' frailty score was the only independently associated with 6-month all-cause mortality (OR 1.962, 95% CI 1.097-3.507, $p = 0.023$), as shown in Table 3. Similar results were found in the subgroup of patients over 60 years, ($N = 218$; OR 1.260, 95% CI 1.039-1.528, $p = 0.019$).

Cardiovascular disease (OR = 3.292; 95%CI 1.288-8.409) and diabetes (OR = 1.55; 95%CI 1.061-2.264) were the only 2 comorbidities independently associated with frailty along with hemoglobin concentration (per gram/dL, OR = 0.672; 95%CI 0.583-0.776) and age (per year, OR = 1.042; 95%CI 1.018-1.066). Nevertheless, as showed in Figure 2, there is a significant overlap of age distribution between patients with and without frailty.

### Mortality and Length of Stay

There were no significant differences in ICU LOS (Mann Whitney U test, $p = 0.364$) or mortality between frail and non-frail patients. Frail patients had a median of 6 days longer hospital LOS (Mann Whitney U test $p = 0.008$, Table 4) and higher in-hospital mortality (38.6% vs. 19.2%, $p = 0.001$). Six months all-cause mortality was also significantly higher in frail patients (50% vs. 32.3%, $p < 0.001$) and this difference increased at the 6-month follow up (Figure 3).

### Discharge and Outcomes

After hospital discharge, frail patients were more often integrated in the National Continuous Care Net. This is an institutional care net, supported by the Portuguese national health system, to address those patients who need prolonged convalescence with specific clinical care. Overall, 44% of frail patients admitted to the ICU returned home after hospitalization vs. 70.9% of the non-frail patients ($p = 0.008$). Only 2.3% of discharged frail patients were referenced to palliative care units (Table 4).

### Invasive Interventions

Patients who had limitation of therapeutic efforts often received invasive procedures during their ICU stay, namely invasive mechanical ventilation, renal replacement therapy and/or vasopressors (Table 5). Age and mean frailty score were both strongly associated with a limitation of therapeutic efforts order.

Not initiating mechanical ventilation or renal replacement therapy were common decisions (8.6% and 7.8%, respectively). These limitations of therapeutic effort decisions were most often associated with DNR (Table 6) than with frailty

**Table 1.** Patients General Characteristics According to the Gender.

| | Male | Female | Total | P value[$] |
|---|---|---|---|---|
| Sex | 221 (66%) | 114 (34%) | 335 (100%) | |
| Age | 62.5 ± 16.9 (range 18-98) | 64.4 ± 16.4 (range 20-88) | 63.2 ± 16.8 (range 18-98) | 0.32 |
| ICU LOS | 5 [7] (range 1-77) | 5 [7] (range 1-79) | 5 [8] (range 1-79) | 0.75* |
| Ward LOS | 14 [27] (range 0-136) | 14 [21] (range 0-217) | 14 [23] (range 0-217) | 0.59* |
| Previous admissions | 48 (21.7%) | 27 (23.7%) | 75 (22.4%) | 0.90 |
| Sepsis on admission | 65 (29.4%) | 35 (30.7%) | 100 (29.9%) | 0.01 |
| Pos-operative | 34 (15.4%) | 14 (12.3%) | 48 (14.3%) | 0,01 |
| IMV | 139 (62.9%) | 75 (65.8%) | 214 (63.9%) | 0.63 |
| Non IVM | 43 (19.5%) | 14 (12.3%) | 57 (17%) | 0.12 |
| RRT | 25 (11.3%) | 23 (20.2%) | 48 (14.3%) | 0.03 |
| Vasopressors | 118 (53.4%) | 67 (58.8%) | 185 (55.2%) | 0.36 |
| SAPS II | 41.2 ± 18.3 (range 5-81) | 43.2 ± 15.4 (range 11-72) | 41.8 ± 17.4 (range 5-81) | 0.27 |
| Infection | 133 (60.2%) | 68 (59.6%) | 201 (60%) | 1 |
| MDR bacteria | 24 (10.9%) | 10 (8.8%) | 34 (10.1%) | 0.55 |
| Antibiotic therapy | 136 (61.5%) | 68 (59.6%) | 204 (60.9%) | 0.93 |
| DNR | 27 (12.2%) | 11 (9.6%) | 38 (11.3%) | 0.59 |
| LTE | 29 (13.1%) | 10 (8.8%) | 39 (11.6%) | 0.28 |
| ICU mortality | 25 (11.3%) | 10 (8.8%) | 35 (10.4%) | 0.57 |
| Hospital mortality | 53 (24%) | 25 (21.9%) | 78 (23.3%) | 0.79 |
| 6 month all cause mortality | 67 (30.5%) | 31 (27.2%) | 98 (29.3%) | 0.53 |
| New hospital admission** | 51 (30.4%) | 24 (28.1%) | 75 (29.2%) | 0.57 |

Data presented as N (%) or mean ± standard deviation or median [interquartile range] according to data distribution.
Abbreviations: ICU—Intensive Care Unit: LOS—length of stay; IMV—Invasive mechanical ventilation; RRT—Renal replacement therapy; SAPS—Sequential Organ Failure Assessment; MDR—Multi drug resistant; DNR—Do not resuscitate order; LTE—Limitation of therapeutic efforts order.
[$]Chi-square test unless otherwise stated; * Mann Whitney U Test; ** Only patients discharged alive from the index hospital admission.

**Table 2.** Prevalence of Comorbidities and Frailty According to the Gender.

| | Male | Female | Total | P value* |
|---|---|---|---|---|
| All patients | 221 (66%) | 114 (34%) | 335 (100%) | |
| Diabetes | 52 (23.5%) | 33 (28.9%) | 85 (25.3%) | 0.42 |
| Chronic hepatic Failure | 15 (6.7%) | 9 (8%) | 24 (7.2%) | 0.52 |
| Chronic renal failure | 30 (13.6%) | 18 (15.8%) | 48 (14.3%) | 0.85 |
| Congestive heart failure | 67 (30.3%) | 22 (19.3%) | 89 (26.6%) | 0.031 |
| COPD | 32 (14.5%) | 6 (5.3%) | 38 (11.3%) | 0.012 |
| Cerebro-Vascular disease | 19 (8.6%) | 8 (7%) | 27 (8.1%) | 0.62 |
| Peripheric vascular disease | 29 (13.1%) | 5 (4.4%) | 34 (10.1%) | 0.012 |
| Chronic ischemic coronary disease | 44 (19.9%) | 8 (7%) | 52 (15.5%) | 0.002 |
| Neoplastic disease | 38 (17.2%) | 16 (14.1%) | 54 (16.1%) | 0.41 |
| Hematologic neoplasm | 7 (3.2%) | 3 (2.7%) | 10 (3%) | 0.93 |
| Dementia | 8 (3.6%) | 3 (2.6%) | 11 (3.3%) | 0.63 |
| AIDS | 5 (2.3%) | 1 (0.9%) | 6 (1.8%) | 0.37 |
| Frailty (mean score) | 3.4 ± 1.7 (range: 1-9) | 3.7 ± 1.6 (range: 1-9) | 3.5 ± 1.7 (range: 1-9) | 0.08 |
| Frail (mean score ≥5) | 46 (20.8%) | 24 (21.1%) | 70 (20.9%) | 0.96 |

Data presented as N (%) or mean ± standard deviation.
Abbreviations: COPD—Chronic obstructive pulmonary disease; AIDS—Acquired immunodeficiency syndrome. * Chi-square test.

(84.2% vs 25.7%). Nevertheless, several patients who had a DNR order, received organ support during their ICU stay, namely invasive mechanical ventilation (N = 32), renal replacement therapy (N = 12) or vasopressors (N = 27).

## *Palliative Care*

As shown in Table 6, only a small minority of patients had a formal living will or advanced directives (2.1%), including frail patients. Additionally, advanced directives were only written in less than half of the patients' clinical records, while the DNR order was recorded in more than 85% of the cases.

Family meetings occurred in 11.6% of all patients and in 31.4% of frail patients. The majority of these patients had some form of limitation to therapeutic efforts or a DNR order.

Palliative Care intervention occurred in only 3.9% of ICU patients and in 5.7% of patients who died in the ICU. Only 15% of frail patients were offered PC.

## Discussion

To the best of our knowledge, this was the first multicenter study regarding frailty and PC in Portuguese ICUs. One out of 5 patients in Portuguese ICUs were frail. Significant differences were found in frailty assessment according to the observer, and nurses' scores were the more accurate to predict 6-month all-cause mortality. In our population, despite limitations of therapeutic efforts and DNR orders being commonly decided by the doctors in charge, those patients often received invasive procedures, which suggests that EOL decisions are mostly related to failure of therapeutic measures rather than by patient overall health condition or goals of care assessment. Palliative Care was offered only in 3.9% of the whole population and less than 15% of frail patients. This is particularly concerning since 50% of our frail patients were dead 6 months after ICU discharge.

**Table 3.** Multivariate Regression Model for All Cause Mortality at 6 Months Following ICU Admission.

| | OR | 95% CI | P value |
|---|---|---|---|
| Age | 1.029* | 1.008-1.051 | 0.008 |
| SAPS II | 1.047* | 1.029-1.065 | <0.001 |
| CHF | 1.814 | 1.017-3.237 | 0.044 |
| Frail (Nurse) | 1.962 | 1.097-3.507 | 0.023 |

Logistic regression model evaluating independently associated risk factors with 6 months all cause mortality. Frail patients were defined as having ≥5 points in Clinical Frailty Score assessed by nurse.
Abbreviations: SAPS—Simplified Acute Physiology Score; CHF—Congestive Heart Failure. *By year or point.

### *What is the Prevalence of Frailty in the Portuguese ICUs?*

Frailty was present in 20.9% of patients admitted to Portuguese ICUs. Similarly to our study, the reported prevalence of frailty in both European and non-European ICUs ranges between 20% and 35% or even up to 50% when limited to very old patients.[12,13,19,20]

In our cohort, frailty prevalence was also significantly higher above 60 years (27.3% vs. 10.3%), although we did not find a strong relationship between comorbidities and frailty. Moreover, recent studies unveiled a substantial number of patients with frailty are younger than 65 years[21] and that health deficits accumulation (not the number of diseases itself) correlates more with death risk than chronological age.

### *Is There Inter-Rater Variability of Frailty Assessment?*

We found poor correlation between nurses' mean CFS score and either doctors' or family members' mean scores. Nurses' mean score was the highest and it was the only one independently associated with 6-month all-cause mortality (OR 1.962; 95%CI 1.097-3.507).

This inter-rater variability of frailty assessment is not yet well studied, although it can introduce important bias, preventing use of frailty as an independent prognostic factor.[8]

We used the CFS to assess frailty[16] as it is easy to use, being a practical tool in the critically ill population,[4] although it did not prevent this inter-rater variability. There are other frailty scales validated for the Portuguese population, such as Tilburg Frailty Indicator, Edmonton Frailty Scale and Prisma-7.[22-24]

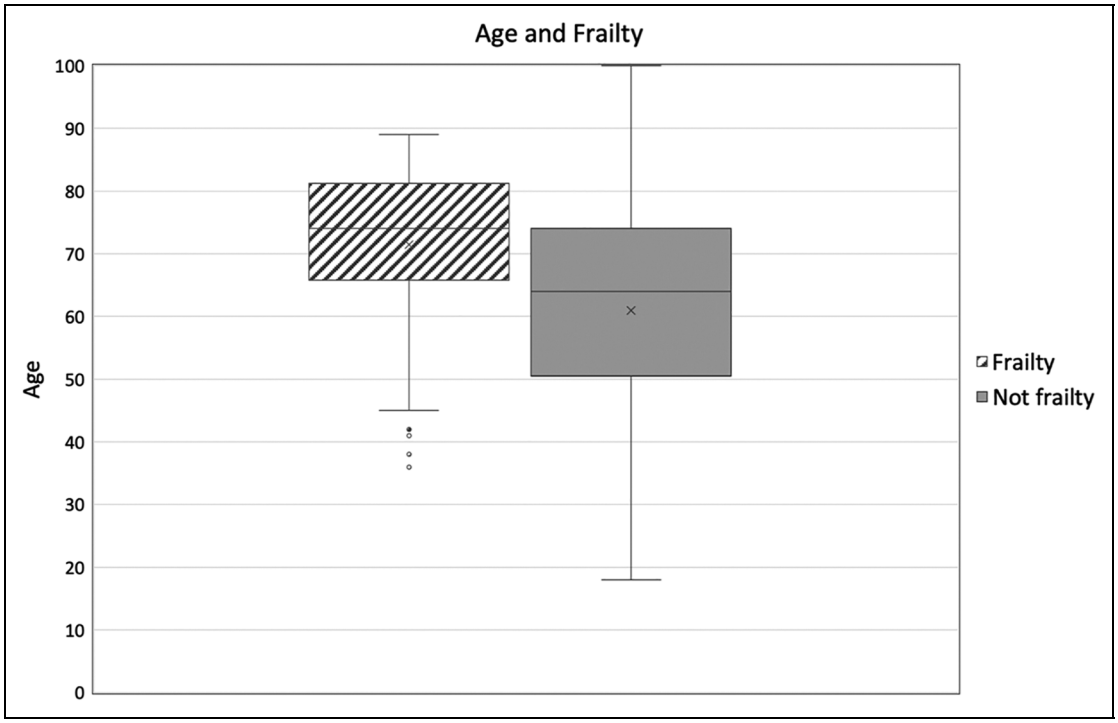


**Figure 2.** Box plots for age according to the presence of frailty.

**Table 4.** Prevalence of Frailty, Outcomes, Need for Organ Support and Destination After Discharge.

| | | Frail | No frail | P value[$] |
|---|---|---|---|---|
| All Patients | | 70 | 265 | |
| Age | | 70.8 ± 13.8 (range 36-89) | 60.6 ± 17 (range 18-98) | <0.001** |
| Organ Support | IMV | 45 (64.3%) | 169 (63.8%) | 0.937 |
| | Non IMV | 13 (18.6%) | 44 (16.6%) | 0.697 |
| | RRT | 17 (24.3%) | 31 (11.7%) | 0.008 |
| | Vasopressors | 47 (67.1%) | 138 (52.1%) | 0.024 |
| SAPS II | | 48.4 ± 17.1 (range 5-81) | 39.5 ± 16.9 (range 6-79) | <0.001** |
| Previous admissions* | | 25 (35.7%) | 50 (18.9%) | 0.004 |
| Limitations | | 18 (25.7%) | 21 (7.9%) | <0.001 |
| ICU Mortality | | 11 (15.7%) | 24 (9.1%) | 0.124 |
| Hospital Mortality | | 27 (38.6%) | 51 (19.2%) | 0.001 |
| LOS ICU | | 6 [9]. (range 1-77) | 5 [7]. (range 1-79) | 0.364*** |
| Destination after ICU discharge | | | | 0.89 |
| | High dependency unit | 67 (27.8%) | 16 (27.1%) | |
| | Medical ward | 57 (23.7%) | 18 (30.5%) | |
| | Surgical ward | 59 (24.5%) | 13 (22.0%) | |
| | Other ward | 53 (20%) | 12 (20.3%) | |
| | Home | 5 (2.2%) | 0 (0%) | |
| LOS Ward | | 26 [36]. (range 0-108) | 20 [31]. (range 0-217) | 0.008*** |
| Destination after ward discharge | | | | 0.03 |
| | RNCC | 23 (10.7%) | 9 (20.9%) | |
| | UCP | 1 (0.5%) | 1 (2.3%) | |
| | Social Care institution | 2 (0.9%) | 2 (4.7%) | |
| | Home | 188 (87.9%) | 31 (72.1%) | |

Data presented as N (%) or median [interquartile range] according to data distribution.
Abbreviations: IMV—Invasive mechanical ventilation; RRT—Renal replacement therapy. LOS—Length of stay; ICU—Intensive Care Unit; SAPS—Sequential Organ Failure Assessment; RNCC—National Continuous Care Net; UCP—Palliative Care Unit.
[$]Chi-square test unless otherwise stated; *—Number of patients with hospital admissions in the 3 months before the index admission; **—Students' T test; ***—Mann Whitney U test.

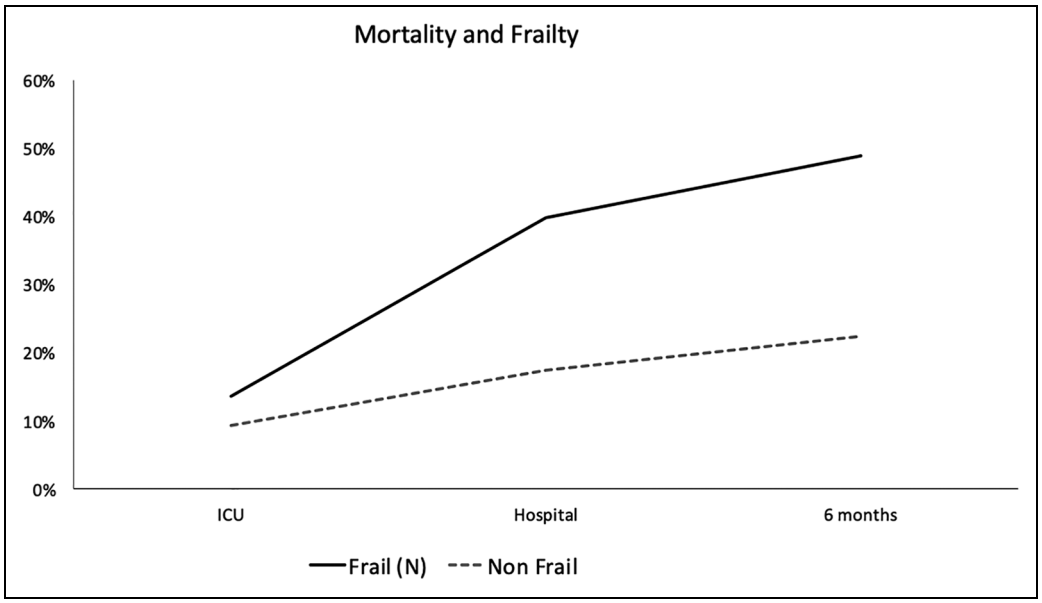


**Figure 3.** Cumulative mortality according to the presence of frailty (assessed by the nurse).

Nonetheless, all these scales imply patients' active participation, which was often not possible in our study.

Nurses are more experienced in disability scales application and patient performance status evaluation. Family evaluations are known to be overestimated, probably by emotional bias.[4] Classically, families are the main source of anamnesis in the critical care setting which may misguide doctors in their frailty evaluation. Training seems to

**Table 5.** Evaluation of Risk Factors for the Order to Limit Therapeutic Efforts.

| | LTE (N, % within condition) | No limitations (N) | Total (N, % of all patients) | P value[$] |
|---|---|---|---|---|
| All patients | 39 (11.6%) | 296 | 335 (100%) | 0.283 |
| 6 M all cause mortality | 33 (33.7%) | 65 | 98 (29.3%) | <0.001 |
| Age§ | 73.2 ± 10.6 (range: 46-89) | 61.8 ± 17.0 (range: 18-98) | 63.2 ± 16.8. (range: 18-98) | <0.001* |
| Male Sex | 29 (13.1%) | 192 | 221 (66%) | 0.239 |
| Diabetes | 9 (10.6%) | 76 | 85 (25.3%) | 0.773 |
| Chronic hepatic Failure | 3 (12.5%) | 21 | 24 (7.2%) | 0.063 |
| Chronic renal failure | 7 (14.6%) | 41 | 48 (14.3%) | 0.504 |
| Congestive heart failure | 16 (18%) | 73 | 89 (26.6%) | 0.035 |
| COPD | 6 (15.8%) | 32 | 38 (11.3%) | 0.419 |
| Cerebro-Vascular disease | 4 (14.8%) | 23 | 27 (8.1%) | 0.537 |
| Peripheric vascular disease | 6 (17.6%) | 28 | 34 (10.1%) | 0.259 |
| Chronic ischemic coronary disease | 9 (17.3%) | 30 | 52 (15.5%) | 0.166 |
| Neoplastic disease | 5 (9.3%) | 49 | 54 (16.1%) | 0.022 |
| Hematologic neoplasm | 4 (40%) | 6 | 10 (3%) | <0.001 |
| Dementia | 1 (9.1%) | 10 | 11 (3.3%) | 1.0 |
| AIDS | 1 (16.7%) | 5 | 6 (1.8%) | 0.527 |
| Sepsis on admission | 13 (13%) | 87 | 100 (29.9%) | 0.67 |
| IMV | 32 (15%) | 182 | 214 (63.9%) | 0.013 |
| CRT | 10 (25.6%) | 29 | 39 (11.6%) | 0.048 |
| Vasopressors | 10 (25.6%) | 29 | 39 (11.6%) | 0.011 |
| Frail (mean score)§ | 4.5 ± 2.1 (range: 1-8) | 3.3 ± 1.6 (range: 1-9) | 3.5 ± 1.7. (range: 1-9) | <0.001* |
| Frail (mean score ≥5) | 18 (25.7%) | 52 | 70 (20.9%) | <0.001 |

Data presented as N (%) unless otherwise stated. [$]Chi-square test unless otherwise stated; * Students' T test. § = Mean ± standard deviation; 6M = 6 months.
Abbreviations: AIDS—Acquired immunodeficiency syndrome; IMV—Invasive mechanical ventilation; RRT—Renal replacement therapy.

**Table 6.** End of Life Decisions.

| | N | Formal living will | DNR | Family meeting | Paliative care consultation | LTE |
|---|---|---|---|---|---|---|
| All patients | 335 | 7 (2.1%) (40% written in the process) | 38 (11.3%) | 39 (11.6%) | 13 (3.9%) | 39 (11.6%) |
| Frailty | 70 | 3 (4.3%) | 17 (24.3%) | 22 (31.4%) | 9 (12.9%) | 18 (25.7%) |
| Death in the ICU | 35 | 0 | 17 (48.6%) | 19 (54.3%) | 2 (5.7%) | 15 (42.9%) |
| DNR | 38 (86.8% written in the process) | 1 (2.6%) | - | 28 (73.7%) | 7 (18.4%) | 32 (84.2%) |
| LTE | 39 (100% written in the process) | 2 (5.1%) | 32 (84.2%) | 30 (76.9%) | 11 (28.2%) | - |

Data presented as N(%).
Abbreviations: DNR—Do not resuscitate order; LTE—Limitation of therapeutic efforts order; ICU—Intensive Care Unit.

minimize this subjectivity[25] and teamwork could help to minimize bias.

We did not find any influence of family member educational level on CFS score.

## *What is the EOL Decision-Making Policy in the ICU?*

In our cohort, only 3.9% of patients (and 5.9% of those who died) were given PC intervention in the ICU and in only 11.6% a family meeting was organized. These figures were only slightly higher in frail patients, 15% and 31.4% respectively. This raises concern about the quality of death and grief support in Portuguese ICU and reinforces that considerable communication barriers are still present and opportunities are being wasted.

Healthcare providers may struggle with determining when critically ill patients are approaching the EOL[26] which often delays the timing for limitation of therapeutic efforts decisions and may lead to futility.

In this study, patients who had a DNR order most often received invasive organ support interventions, notably invasive mechanical ventilation and renal support therapy. This fact suggests that EOL decisions remain mostly related with failure of therapeutic measures already taken. Setting a pre-established therapeutic ceiling and assessment of goals of care on admission could anticipate decision-making and ensure focus on patient wishes.

When PC is integrated in the ICU, communication is facilitated and goals of care assessments are made sooner and more easily.[27]

Although 70% of ICU patients might lack capacity to make EOL decisions, literature shows that, in the majority of patients who had already expressed their wishes, care will be in line with it.[28] There is a Portuguese advanced directives policy since 2012[29] but mainly for information purposes. The doctor must frame his decision based on assessment of patients' best interests.[30] Living will was rare in our cohort (2.1%) and in more than half of the cases it was not even transcribed to the clinical chart. These facts hamper goals of care established in the ICU and may cloud the election of a decision surrogate.

### *Should Frailty be a Trigger for PC Intervention in the ICU? Is Frailty Independently Related to Short Term Mortality, Either in the ICU or After Discharge?*

In-hospital mortality (38.6% vs. 19.2%, $p = 0.001$) and 6-month all-cause mortality were significantly higher in frail patients (50% vs. 32.3%, $p < 0.001$). Moreover, frail patients stayed a median of 6 days longer in-hospital. In fact, even after discharge, a lengthy convalescence seems to be associated with frailty. The low physiological reserve of frail patients (which seems to be more dependent on the extension of comorbidities)[7] may hinder the process of healing, making frailty a factor for worse prognosis.

Frail patients often exhibit more psychosocial and symptom burden (fatigue, pain, depression), communication needs, and less social support.[31] In fact, EOL frail patients present with pain, emotional distress and need of assistance with essential activities of daily living at least as much as those with terminal cancer.[5,32]

According to published literature, ICU frail patients have lower quality of life at 6 and 12 months after discharge regardless of their physical and mental status.[2,19,20] They often report preferring less invasive or intensive treatment.[32,33] Adjusting therapeutic interventions to future expectations, social conditions and family support are essential for those patients, and are also a PC cornerstone.

Clinical and empirical evidence suggests that patterns or trajectories of functional decline can be used to trigger PC intervention.[34] As described above, most of frail patients will have EOL descendent trajectories.

Frailty has been suggested as a trigger to introduce or reinforce PC along with functional dependence, cognitive impairment, symptom distress and family support needs.[34] Assessing frailty can be a feasible method to avoid futility and anticipate appropriate PC intervention, contributing to goals of care assessment and improving EOL decisions policy in the ICU.

Our study supports the idea of frailty being a trigger to call for PC intervention in ICU patients. These patients often have: longer hospital LOS; late therapeutic effort limitation; frequent DNR orders; higher in-hospital mortality; worse short-term prognosis even after discharge.

According to our data, PC interventions in ICU are suboptimal, especially in frail population (less than 15%) and mostly late. The time to call for a PC team intervention in the ICU is not clearly defined. Lack of a validated prognostic screening tool for PC in ICU is an important gap.[35]

## Study Limitations

Reliability of frailty assessment can be biased. We tried to overcome that by using the mean score value of doctor, nurse and family and by adding a limit to the number of patients that could be included from one single center.

Although in this study all consecutive patients admitted to the ICU should have been included, the selection of the starting date was left to local decision, which may have introduced unknown bias.

We used the CFS to classify frailty although this scale is not validated for the Portuguese population (only for the Brazilian population).

The timing of limitation of therapeutic efforts and DNR orders was not registered, which limits the assumptions related to those decisions.

Although this was a multicenter study, we only included Portuguese centers and this limits the generalizability of our data.

### *Implications for Practice*

This study provides quantitative data relating frailty and PC intervention during ICU stay. It included all patients, independently of their cause of admission, age and discharge status. Previous studies were commonly limited to the post-ICU setting,[11] an older age (50 years)[14] or post-mortem patients.[36] Our study reinforces the message that frailty may be a useful and valid PC trigger in the ICU.

A second important implication relates to the inter-rater variability of frailty assessment. Family and doctors commonly underestimate frailty, with a subsequent risk of depriving patients of PC or even facilitating futility. Efforts should be made to ensure ICU teams are trained enough to reduce bias.

A third implication lies on our *polaroid picture* of PC use in ICU that suggests an underuse of PC in this setting and the lack of communication with patients and families. Also, EOL decision-making policy should be redesigned to systematically include goals of care.

## Conclusions

As much as 1 in every 5 critically ill Portuguese patient may be frail. These patients are resource consuming: they often need organ failure support, long hospital stays and lengthy convalescence. They also have high mortality both in-hospital and in the first 6 months.

Our data suggests that both physicians and families underestimate frailty.

We recommend that palliative care should be universally consulted once frailty is identified in critical patients.

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