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ORIGINAL ARTICLE

Effect of pre-morbid frailty status on in hospital mortality in critically ill patients.

Ravi Kumar[1], Fakhir Raza Haidri[2], Nazia Arain[3], Adnan Abbas Rizvi[4], Heeralal[5], Ramesh Kumar[6]

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ABSTRACT… Objective: To determine the pre-morbid frailty and its association with in-hospital mortality among critically ill patients admitted in intensive care unit (ICU) of a tertiary care hospital. **Study Design:** Cross-sectional study. **Setting:** ICU of Sindh Institute of Urology and Transplantation, Karachi, Pakistan. **Period:** December 2022 to July 2023. **Methods:** Patients of age 18 years or older, admitted to the ICU were included. Frailty was defined as per Clinical Frailty Scale (CFS). Detailed history was taken to assess frailty status two weeks prior to hospital admission. Patients were classified as pre-morbid frail if their score was higher than 4. **Results:** Total 151 patients were analyzed with median age of 47 (IQR= 33-59) years. There were 106 (70.2%) male patients, whereas and 92 (60.9%) were having comorbidities. Median CFS score was 4 (IQR=3-5). Out of 151 patients admitted to ICU, 56 (37.1%) had frail. Odds of frailty were increasing with increasing age and among those who had comorbidity. Mechanical ventilation (MV) days (p=0.234), hemodynamic support days (p=0.216) and LOS (p=0.903) were not significantly different among frail and non-frail patients. Nearly half of the patients had died (49%). Mortality was noted in 74 (49.0%) patients. Need of MV, hemodynamic support, APACHEII and SOFA score were associated with mortality (p<0.05). **Conclusion:** There was considerable burden of frailty among critically ill patients admitted in ICU. However, in-hospital outcomes including mechanical ventilation, hemodynamic support and mortality were not associated with frailty status.

Key words: Critically Ill, Frailty, Intensive Care Unit, Mortality, Mechanical Ventilation.

INTRODUCTION

Clinical frailty depicts an advanced state of low physical, physiological and cognitive reserve, leading to adverse outcomes after stressors like trauma, infection, or surgery.[1] Frailty increases with age, and different people achieve frailty at different ages. Moreover, almost 25% of patients achieve frailty at age 65, and 50% achieve frailty at age 85.[2]

Frailty can also occur in the non-elderly population, most people recover fully after acute illness, but some may develop deficits at the sub cellular level. These deficits accumulate after every illness and lead to frailty, which does not always correlate with age.[3] In non-elderly populations, frail patients have similar adverse outcomes in terms of mortality, but frail increases the chances of dependency at the time of hospital discharge.[4]

Different methods can estimate frailty, but the gold standard is a comprehensive geriatric assessment that cannot be used at admission to the intensive care unit (ICU) because this requires a fully cooperative patient.[5] The frailty in ICU is frequently measured with the "clinical frailty scale (CFS)". This scale holistically assesses the patient's physical, cognitive, and functional status and chronic illness burden.[6,7] This scale consists of a pictogram with text and is easy to understand for patients, caregivers, and healthcare teams. The range of the scale is 1 to 9, with 1 to 3 representing non-frailty, 4 representing vulnerability or pre-frailty, 5 to 8 representing frailty, and 9 representing terminal sickness. If it is difficult to classify the patient according to the CFS, we sought assistance from the classification tree of the CFS.[7]

1. MBBS, FCPS (Internal Medicine), MRCP UK (Internal Medicine), Fellow Department of Critical Care Medicine, Sindh Institute of Urology and Transplantation, Karachi.
2. MBBS, FCPS (Pulmonology), FCPS (Internal Medicine), Consultant & Head Critical Care Medicine, Sindh Institute of Urology & Transplantation, Karachi.
3. MBBS, FCPS (Internal Medicine), Fellow Department of Critical Care Medicine, Sindh Institute of Urology and Transplantation, Karachi.
4. MBBS, Resident Medical Officer Intensive Care Unit, Sindh Institute of Urology and Transplantation, Karachi.
5. MBBS, MCPS, FCPS (Internal Medicine), MRCPI, (Internal Medicine), Senior Lecturer, Sindh Institute of Urology and Transplantation, Karachi.
6. MBBS, FCPS (Medicine), Senior Lecturer Intensive Care Unit, Sindh Institute of Urology and Transplantation, Karachi.

Correspondence Address:
Dr. Ravi Kumar
Department of Critical Care Medicine
Sindh Institute of Urology and Transplantation, Karachi.
ravirajbangeja@gmail.com

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Current research suggests that frailty affects the outcome of patients admitted to ICU in terms of in-hospital mortality, morbidity, length of hospital stay, readmission, and quality of life.[8] The cause of frailty is related to genetic and environmental risk factors. Understanding a mechanism leading to frailty may open a new door for intervention to delay frailty.[9] Different rehabilitation programs are designed to reverse frailty; one is a supervised multi-component exercise program (MEP), which includes physical exercises and nutritional supplementation. The supervised MEP helps reverse the frailty and improves cognition and emotional and social networking in frail patients.[10]

Much research has been done to identify pathological processes leading to frailty, concluding that frail patients have an increased risk of endocrine and immunological dysfunction after critical illness compared to non-frail.[9] Frailty does not improve to baselines after critical illness in almost 75% of patients, leading to an increased financial burden on the healthcare system, nursing homes, and caregivers.[11] There is paucity of data from Pakistan regarding frailty prevalence at the time of admission. Therefore, we planned the present study to determine frailty and its association of premorbid frailty with in-hospital mortality among critically ill patients admitted in ICU of a tertiary care hospital.

METHODS

This cross-sectional study was conducted at ICU of Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan from December 2022 to July 2023. Approval from "Institutional Ethical Committee" was obtained (SIUT-ERC-2023/A-426). Patients aged 18 years or above, admitted to the ICU and spending at least 24-hours in ICU were included. Patients were not included if comfort measures only applied to their code status. Consecutive participants were identified through daily screening of new admissions. After undergoing screening, the patients meeting the study criteria were enrolled. All participants or their surrogates provided informed consent. All patients were subsequently monitored until their discharge from the hospital or occurrence of death. Based on the previous estimate, ICU mortality among frail patients was 31.3%[12] with a margin of error of 3% and a 95% confidence interval, a total of 151 patients were taken for the study.

Detailed history was taken to assess frailty status two weeks prior to hospital admission. Frail was classified if pre-morbid frailty score was greater than 4. Treating consultant assessed the frailty which was defined using CFS Scale, a pre-validated 9-point assessment tool intended for quantifying frailty. The scale is objective in nature assigning a score to patients from 1-9, with 1 being very fit and 9 being terminally ill.[12]

In hospital mortality from all causes, served as the primary outcome indicator. The total length of hospital stay as well as the number of days spent receiving hemodynamic support and invasive mechanical ventilation were used as secondary outcome measures. At enrolment, the trained research data collectors recorded patients' demographics and clinical features. Demographic information included age and gender whereas clinical information included "Acute Physiology and Chronic Health Evaluation (APACHE)" II score, "Sequential Organ Failure Assessment (SOFA)" score, CFS score and outcome variables.

Data was entered and analyzed using IBM-SPSS version 26.0. Categorical variables were expressed as frequencies and percentages. Numerical variable were presented as median with inter-quartile range as they were non-normal. Normality assumption was tested using Shapiro-Wilk test. Binary logistic regression applied and odds ratio with 95% confidence interval were calculated. P-values <0.05 was taken as significant.

RESULTS

During the study period, 242 patients were admitted to ICU. Out of these 242, 43 were eliminated because their LOS was under 24 hours. Out of 199 potentially eligible patients, 48 of them were excluded as they did not meet inclusion criteria. Finally 151 patients were included and analyzed in this study (Figure-1).

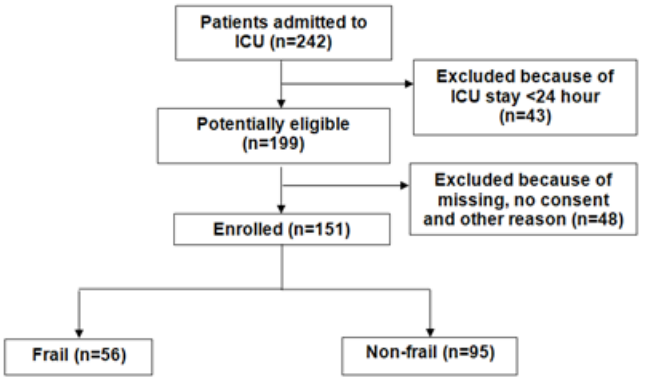

Figure-1. Flow diagram of patients enrolled and analyzed

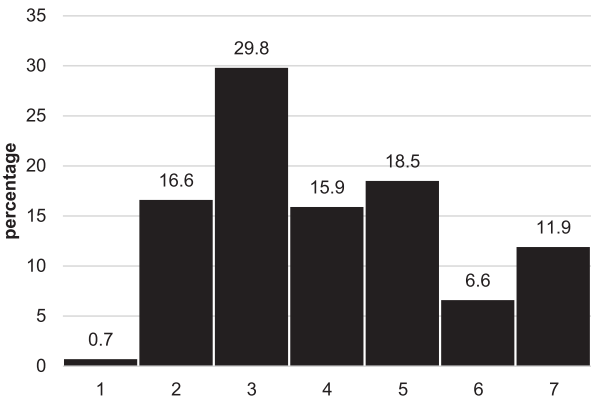

Figure-2. Distribution of clinical frailty scale scores among study subjects (n=151)

In a total of 151 patients, the median age was 47 (IQR= 33-59) years, ranging between 18-92 years. There were 106 (70.2%) male patients, whereas and 92 (60.9%) were having comorbidities. Median score for APACHE II and SOFA score were 14 (IQR=9-21) and 7 (is it IQR=3-10), respectively. Median score for CFS was 4 (IQR=3-5). Figure-2 displays CFS score distribution.

Out of 151 patients admitted to ICU, 56 (37.1%) had frail. Having comorbidity was associated with higher likelihood of frailty than those who had no comorbidity (OR: 2.70; 95% CI: 1.31-5.58; p=0.007). Gender, APACHE II score and SOFA score on admission were not associated with frailty status. Table-I displays comparison of patients' features among frail and non-frail and its association with frailty status.

Variables	Frail n (%)	Non-frail n (%)	OR (95% CI)	P-Value
Age				
<50 years	25 (31.2)	55 (68.8)	0.58 (0.30-1.14)	0.116
≥50 years	31 (43.7)	40 (56.3)	Reference category	
Gender				
Male	36 (34.0)	70 (66.0)	0.64 (0.32-1.31)	0.224
Female	20 (44.4)	25 (55.6)	Reference category	
Comorbidity				
Yes	42 (45.7)	50 (54.3)	2.70 (1.31-5.58)	*0.007
No	14 (23.7)	45 (76.3)	Reference category	
Diabetes	24 (53.3)	21 (46.7)	2.64 (1.29-5.41)	*0.008
Hypertension	24 (49.0)	25 (51.0)	2.10 (1.04-4.22)	*0.038
Chronic kidney disease	2 (50.0)	2 (50.0)	1.72 (0.24-12.57)	0.592
Chronic liver disease	5 (45.5)	6 (54.5)	1.45 (0.42-5.00)	0.553
Ischemic heart disease	4 (44.4)	5 (55.6)	1.38 (0.35-5.38)	0.639
Code Status on Admission				
Full code	50 (34.5)	95 (65.5)	-	-
DNI, DNACPR	6 (100)	-	-	-
APACHE II score on admission#	13 (10-18.7)	15 (7-22)	0.99 (0.95-1.04)	0.967
SOFA score on admission#	7.5 (4-11)	6 (2-10)	1.04 (0.97-1.11)	0.257

Table-I. Comparison of patients' features among frail and non-frail and its association with frailty status (N=151) CI: Confidence interval, OR, odds ratio, #: Non-normal variables expressed as median with interquartile range, *Significant at p<0.05

There were 115 (76.2%) patients who required mechanical ventilation, whereas hemodynamic support was required in 94 (62.3%). Median MV days, hemodynamic support days and LOS were 3 (IQR=1-8) days, 1 (0-4) days and 14 (IQR=8-21) days respectively. Figure-2 displays comparison of median MV days, hemodynamic support days and LOS among frail and non-frail patients. MV days, hemodynamic support days, and LOS did not change significantly between frail and non-frail patients (p=0.234, p=0.216, and p=0.903, respectively).

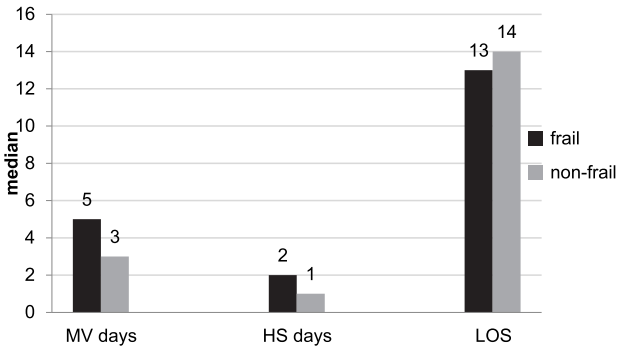

Figure-2: Comparison of median mechanical ventilator days, hemodynamic support days and length of stay

Mortality was noted in 74 (49.0%) patients. Table-II represents patients' features among alive and dead patients and relative risk. None of patients' features including frailty were found to be associated with in-hospital mortality except need of mechanical ventilation and hemodynamic support, APACHEII and SOFA score (p<0.05).

DISCUSSION

This study analyzed that frailty was prevalent among 37.1% of the ICU admitted patients. Our finding was comparable to many other studies investigating frailty in ICU admitted patients. A larger study from Brazil studying 129,680 patients reported that 31.4% patients in ICU were frail.[13] An Indian study demonstrated a frailty prevalence of 38.6%.[14] Bagshaw SM et al[15] performed a multi-center study in Alberta and found that prevalence of frailty was 32.8%. Taniguchi LU et al[16] examined the modified Frailty Index (mFI) and CFS, two frailty detection methods for critically sick patients, and found that the prevalence of frailty was 32.8% and 39.2%, respectively. Darvall et al[17] reported 39.7% patients were frail on admission in ICU.

Variables	Alive n (%)	Dead n (%)	OR (95% CI)	P-Value
Age				
<50 years	42 (52.5)	38 (47.5)	0.88 (0.46-1.67)	0.694
≥50 years	35 (49.3)	36 (50.7)		
Gender				
Male	52 (49.1)	54 (50.9)	1.29 (0.64-2.62)	0.465
Female	20 (44.4)	25 (44.4)	Reference category	
Comorbidity				
Yes	43 (46.7)	49 (53.3)	1.55 (0.80-2.99)	0.192
No	34 (57.6)	25 (42.4)	Reference category	
Code status on admission				
Full code	76 (52.4)	69 (47.6)	0.18 (0.02-1.59)	0.124
DNI, DNACPR	1 (16.7)	5 (83.3)	Reference category	
APACHE II score on admission#	10 (6-17)	17.5 (12-23.3)	1.12 (1.06-1.17)	*<0.001
SOFA score on admission#	4 (1-7)	9 (7.8-13.3)	1.35 (1.22-1.50)	*<0.001
Hemodynamic support				
Yes	30 (31.90)	64 (68.1)	10.03 (4.46-22.51)	*<0.001
No	47 (82.5)	10 (17.5)	Reference category	
Mechanical ventilation support				
Yes	52 (45.2)	63 (54.8)	2.75 (1.24-6.12)	*0.013
No	25 (69.4)	11 (30.6)	Reference category	
Frailty status				
Frail	24 (42.9)	32 (57.1)	0.59 (0.31-1.16)	0.126
Non-frail	53 (55.8)	42 (44.2)	Reference category	

Table-II. Comparison of features among frail and non-frail patients and its association with in-hospital mortality (N=151)

CI: Confidence interval, OR, odds ratio, #: Non-normal variables expressed as median with interquartile range, *Significant at p<0.05

A larger systematic review analyzing 3030 adult patients reported a lower pooled prevalence (30%) than in our study.[18] Generally, frailty is considered as age-related loss of cognitive and physiologic systems which may lead to other serious events.[1,19] In this study, patients over the age of 50 had a relatively higher prevalence of frailty than patients under 50, however this difference was not statistically significant (43.7% versus 31.2%). In agreement to our finding, a study investigating the relationship between age and frailty found no significant association.[20] However, a larger survey reported higher risk of frailty with increasing age.[21] According to Li Y et al[21] analysis of the community housing survey data from the United States, 46% of respondents were pre-frail and 9% were frail, with older adults having a higher chance of both conditions (OR=1.93, 95% CI=1.45-2.56).

This study analyzed that odds of frailty were lower among males than females but this finding did not show statistical significance. In contrast to our study, frailty was more common in women than in males, according to research by Darval JN et al[17] (44.6% vs. 35.4%). Bagshaw SM et al[15] at al also reported higher frailty among females than males (47.8% versus 34.3%). A study analyzing 15,238 patients revealed that women were more likely than men to be frail (32% vs. 27%).[22]

Patients with comorbidities utilize inpatient and ambulatory treatment more often than those without comorbidities and have inferior quality of life, functional status and overall health outcomes. Findings of the present study suggested a 2.7 times higher likelihood of frailty among patients with coexisting comorbidities than those without comorbidities. In a community-based study, Wong et al[20] showed that 82% of frail older people living in communities had comorbidities.

The SOFA scoring tool was designed to offer community level understandings into the acute morbidity in ICU settings, whereas the APACHE-II score was developed for measuring illness intensity in critically ill patients. Surprisingly, we did not discover a significant relationship between APACHE-II and SOFA, and frailty status in this research. In contrast to our study, Kalaiselvan MS et al[14] and Bagshaw et al[15] revealed higher APACHE-II and SOFA scores among frail patients. The limited sample size and inclusion of younger patients without comorbidity could be the reason of their conflicting findings.

The timely identification of the requirement for urgent hemodynamic support may be improved by clinical decision support systems that are created to continually screen and identify individuals at a high risk of developing hemodynamic instability. These systems' early use of hemodynamic treatments may help prevent consequences from organ hypoperfusion and lower mortality.[23] The current study discovered that frail patients required more hemodynamic support on average days than non-frail patients, although statistical significance was not identified. The overall mortality rate in this study was 49%. The mortality rate among frail and non-frail patients was 57.1% and 44.2% respectively. Although the mortality rate was higher among frail patients but there was no statistical significance. In fact, there was no discernible difference in ICU mortality among frail patients and non-frails. Frailty was found to be an independently predicting short-term mortality by Silva-Obregón et al.[24] Even after accounting for other factors, there was a tendency for frail patients to have higher ICU mortality than non-frail patients (37.7% vs. 26.7%), although the difference did not achieve statistical significance.

There are a few limitations in this study. Because this was a single-center study, hospital policies governing ICU admissions and care may have had an impact on the study's findings. This study did not examine issues that would have increased the length of stay in the ICU, such as delirium, ICU acquired infections, and cardiac issues. Long-term outcomes were not tracked for patients after the study ended, hence this information was not accessible. This study on frailty in critically ill patients used a lower sample size of patients; in order to confirm the results of the current study, particularly for our local Pakistani patients, we need investigations with a bigger sample size.

CONCLUSION

There was considerable burden of frailty among

critically ill patients admitted in ICU. However, in-hospital outcomes including mechanical ventilation, hemodynamic support and mortality were not associated with frailty status.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Ravi Kumar	Conceptualization, Data collection, Drafting.	
2	Fakhir Raza Haidri	Literature review, Study protocol.	
3	Nazia Arain	Literature review.	
4	Adnan Abbas Rizvi	Data collection.	
5	Heeralal	Data analysis.	
6	Ramesh Kumar	Data analysis.