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Prevalence of frailty and its effect on requirement of organ support and clinical outcomes in critically ill patients: a prospective observational single center study

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Abstract

Background Assessing pre-hospital frailty on ICU admission can help in risk stratification. We conducted this prospective, observational study to determine the prevalence of frailty in critically ill patients based on Clinical Frailty Scale (CFS) within 24 h of admission and to study effect of frailty on requirement of organ support and clinical outcome.

Methods The study was registered in Clinical Trials Registry-India (CTRI/2021/04/032782) on 13/04/2021. After approval from IEC and written informed consent, all adult patients admitted to our ICU from April 15th, 2021 to April 14th, 2022 were included. The patients were categorized as Frail & Non-Frail, defining frailty as CFS ≥ 5, two weeks before index admission. The groups were compared for requirement of organ support (vasoactive support, mechanical ventilation, renal replacement therapy) and clinical outcomes (hospital acquired infections (HAI), hospital and ICU length of stay (LOS) and hospital, ICU and 30-day mortality).

Result Out of 358 admissions, 317 were enrolled. The demographic data were comparable except for higher family income amongst frail patients, $p < 0.001$. The prevalence of frailty was 24.6%. A significantly higher number of frail patients required vasoactive support ($p = 0.006$). Incidence of HAI in frail group was significantly higher (48.7%) as compared to non-frail group (20.9%) ($p < 0.001$). The median ICU LOS was 7 days [IQR, 3–7] in frail compared to 6 days [IQR,3–10] in non-frail group, $p = 0.051$. The median hospital LOS in frail patients was 18 days [IQR,10–32] compared to 15 days [IQR, 8.25-26] in non-frail, $p = 0.005$. ICU, hospital and 30-day mortality were significantly higher in frail patients, $p < 0.01$.

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Conclusion The prevalence of frailty in ICU patients was 24.6% and a higher number of frail patients had requirement of vasopressor support and incidence of HAI. Additionally, frail patients also had longer hospital LOS and higher ICU, hospital and 30-day mortality.

Trial registration CTRI/2021/04/032782.

Keywords Frailty, Frailness, Frailty syndrome, Critically ill, Illness, critical

Introduction

The severity of illness and prognostication scores used in intensive care units (ICU) that assess the composite risk in critically ill patients are integral to the practice of critical care. Lately, there has been a lot of emphasis on the importance of frailty as a potential risk factor for poor outcomes in critically ill patients. Frailty is not equivalent to old age, disability or co-morbidity, a holistic approach would be to measure frailty, disability and co morbidity together for overall risk assessment [1].

Despite lack of a standard definition, certain core components of frailty like multifactorial etiology, varied presentation and inability to recover from insult due to lack of physiological reserve, allow clinical measurement of vulnerability of patients [2, 3]. Frail patients are more prone to adverse events and poor clinical outcomes compared to same chronological age, non-frail population [4].

A multidimensional frailty assessment tool, the Clinical Frailty Scale (CFS) is a validated and most widely practiced 9-point assessment tool that can be quickly performed in critically ill patients. It is a judgement-based tool to broadly stratify degrees of frailty [5, 6].

As frailty takes into account the clinical as well as socio-demographic factors, knowing the prevalence of frailty in a specific population is important to improve clinical decision making within critical care settings. This allows identification of individuals who will need aggressive medical treatments for reducing the length of stay and mortality, individuals who may get re-admitted to ICU, need longer follow-up and/or appropriate rehabilitation [1].

With this background, we conducted this prospective, observational study over a period of one year with the primary aim of determining the prevalence of frailty using CFS at 24 h of admission, in patients admitted to ICU in a tertiary care hospital in North India. The secondary objectives were to study the effect of frailty on requirement of organ support in terms of vasoactive support, mechanical ventilation (MV) and renal replacement therapy (RRT) and clinical outcomes including ICU length of stay (LOS), hospital LOS, hospital acquired infections (HAI), ICU, hospital and 30-day mortality and Glasgow outcome scale (GOS), wherever applicable.

Materials and methods

Study design, setting and ethics

After approval from institute ethics committee, this prospective observational study was conducted in Main ICU of our institute over a period of one-year from April 15th, 2021 to April 14th, 2022 (Institutional Ethics Committee registration number INT/IEC/2021/SPL-240 on 13/02/2021 and Clinical Trials Registry-India registration number CTRI/2021/04/032782 on 13/04/2021). The main ICU of our hospital is a 12-bedded mixed medical and surgical ICU in tertiary care academic hospital. This manuscript is reported according to Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines.

Study population, data collection and outcome

On admission, a written informed consent was taken from the patients or their surrogate and all patients (> 13 years of age) admitted to ICU during the study period were included. Patients who died or got discharged from ICU within 24 h of admission, those admitted for palliation or for organ donation and those who left against medical advice were excluded. The exclusion from study based on admission for palliation was confirmed by independent opinion of two consultants of ICU team.

The demographic parameters (age, gender, education status, marital status, family income, profession, source of admission to ICU (e.g., emergency department, ward, operating theatre) were recorded. The pre-existing co-morbid illnesses, diagnosis at the time of admission and Acute Physiology and Chronic Health Evaluation (APACHE) II score at 24 h of admission were also recorded. For all patients recruited in the study, the CFS assessment was performed within 24 h of ICU admission by the primary investigator and the frailty status two weeks before hospitalization was assessed. Another assessment of CFS was done by second assessor who had similar level of training as first assessor. Since CFS is a judgement-based tool, the agreement between the scores obtained by the two was also assessed at the end of study. In ICU studies, CFS is usually applied to pre-illness functional status in order to remove the confounding factor of acute illness [6–8].

The patients with CFS score of 5 or more, two weeks before hospitalization were considered to be frail, thereby, categorizing the study population into two

groups: Group 1 Frail & Group 2 Non-Frail [6]. All patients were followed up and following data were noted: requirement of organ support in terms of vasoactive support, MV and RRT throughout the ICU stay. The clinical outcomes including ICU LOS, hospital LOS, HAIs, ICU, hospital and 30-day mortality and GOS were also recorded.

Sample size/power analysis statement

In order to detect a prevalence of frailty of 25% with a 95% CI width of 10% and 95% power we would require a total sample size of 289. Inflating this for potential drop-outs of 10% we needed to recruit 320 patients.

Statistical analysis

The statistical analysis was done on Jamovi version 2.2.5 which is an open-source software based on R statistical language. Statistical averages e.g. mean ± standard deviation or median with inter quartile range were calculated as applicable. All categorical data (gender, marital status, source of admission, binary outcomes like requirement of organ support, ICU/hospital/30-day mortality, HAI) was compared using chi-square test. The ordinal (age group, education level, number of comorbidities) were compared in a contingency table using chi-square test. The APACHE II score at 24 h of admission and continuous variables (age, family income, ICU and hospital LOS) were assessed using independent sample t test e.g., Welch test, student t test or Mann Whitney U test. A p value of less than 0.05 was considered significant.

Logistic regression was used for multivariable modelling of ICU mortality. The set of variables for multivariable adjustment were derived from domain knowledge. The variables with an SMD (Absolute Standardized Mean Difference) > 0.25 between survivors and non-survivors were considered for multivariate modelling. From this set, the variables which were correlated with each other (Pearson correlation coefficient > 0.4) were removed before assessing them as predictors in multivariate models. Frailty is an indirect reflection of the impact of comorbidity burden on the functional status of the patient [9, 10] As comorbidity burden is a known predictor of frailty, they were considered correlated and frailty was used as a predictor in multivariate modelling of mortality. This was also evidenced in our dataset by the correlation coefficient of 0.52 between the number of comorbidities and CFS score. Age was colinear with CFS score (correlation coefficient of 0.68). Various segments of CFS scores were used as predictors in multiple models: CFS as a continuous predictor, CFS < 5 vs. CFS ≥ 5, [CFS ≤ 4 - not frail, CFS = 5– mild frailty, CFS = 6– moderate frailty, CFS ≥ 7– severe frailty], CFS < 6 vs. CFS ≥ 6 and the model with the least Akaike Information Criterion (AIC) was considered as the best explanatory model with least error.

The concordance correlation coefficient for inter-rater agreement between the two assessors was assessed by Bland Altman plot.

Results

Out of a total of 358 patients who got consecutively admitted to ICU during the one-year study period, 317 patients were recruited in the study. Seventeen patients were lost to follow-up further after ICU discharge, so hospital LOS, hospital and 30-day mortality could be assessed for 300 patients. (Fig. 1)

Amongst the demographic characteristics of the two groups, the frail patients (60.00, 46.25–68.75 years) were older than non-frail (32.00, 25.0-47.5 years) by a mean difference of 28 years ($p < 0.001$). Amongst the frail patients, two patients (10.5%) belonged to youngest age group (13–17 years), 20% of patients belonged to 18–65 years age group and 58.1% of patients aged more than 65 years were frail. The median monthly family income of frail patients in INR thousands per month (50.00, 20.50-71.25) was higher than non-frail patients (18.00,10.00–30.00) and this difference was statistically significant ($p < 0.001$). (Table 1)

The source of ICU admission for the study cohort are shown in Table 2.

The prevalence of frailty (i.e., CFS ≥ 5) was 24.6% (95% CI, 20 – 29.8%) ($n = 78$) in the study population with 239 non-frail patients (75.4%). The median CFS score as assessed at study enrolment was 2 [Inter Quartile Range, 2–4]. (Fig. 2).

Though there was no difference between the two groups regarding overall requirement of any one organ support ($p = 0.133$), a higher number of frail patients required vasoactive support than non-frail patients (RR 1.34, 95% CI 1.11–1.61) and this difference was statistically significant ($p = 0.006$). (Table 3) The two groups were also compared for the number of organ systems that were supported during ICU stay and the number of patients requiring support for more than one organ system was higher in frail patients (54 out of 78, 69.2%) as compared to non-frail patients (128 out of 239, 53.5%).

Amongst the clinical outcomes, the median ICU LOS was 7 days [IQR, 3–7] in frail compared to 6 days [IQR, 3–10] in non-frail group, $p = 0.051$. The median hospital LOS in frail patients was 18 days [IQR, 10–32] compared to 15 days [IQR, 8.25-26] in non-frail, $p = 0.005$. A total of 88 (27.8%) patients developed HAIs during the study period. The incidence of HAI in frail group was significantly higher (48.7%) as compared to non-frail group (20.9%) ($p < 0.001$). The most common HAI was ventilator associated pneumonia (46.5%) followed by catheter related blood stream infection (13.6%). Frail patients had

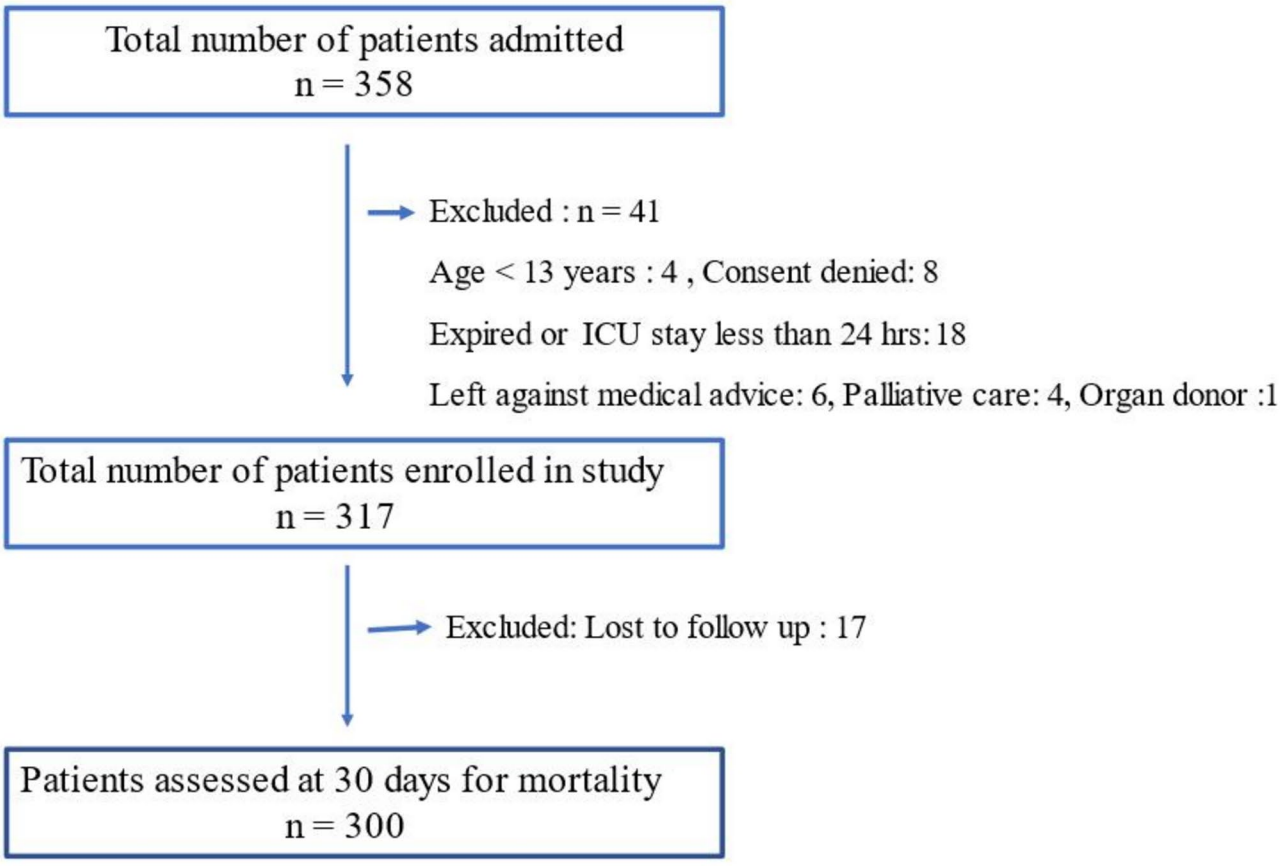

Fig. 1 Study flow diagram

a higher ICU, hospital and 30-day mortality as compared to non-frail group and these differences were statistically significant. (Table 4; Fig. 3)

Since only a small number of patients (10) were admitted with neurological events such as traumatic brain injury, infarction and haemorrhage etc., the GOS score was similar between the frail and non-frail group.

On univariable analysis frailty (CFS ≥ 5) was associated with 3.18 (95% CI, 1.86–5.45, $p < 0.001$) odds of mortality. When adjusted for APCAHE II score frailty this changed to 1.76 (95% CI, 0.93–3.31, $p = 0.081$). When CFS was used as a continuous predictor the APACHE II adjusted odds ratio for mortality was 1.22 (95%CI, 1.03–1.43, $p = 0.020$, Fig. 2C). Moderate or worse frailty (CFS ≥ 6) when compared to CFS < 6 was associated with 4.85 (2.43–9.95, $p < 0.001$) odds of mortality (Table 4).

As CFS is a judgement-based score, there was dual assessment of CFS score by a second assessor with similar level of training for all patients enrolled in the study. The concordance correlation coefficient for inter-rater agreement between the two assessors was 0.96 (CI 0.951–0.968), indicating substantial agreement. Out of 317, 264 (83.28%) agreed perfectly, with further 49 (15.45%) differing by only one point and 2 (0.63%) by two points. (Fig. 4)

Discussion

In this one-year prospective, observational study, the prevalence of frailty was 24.6% determined by CFS, in critically ill patients admitted in a mixed medical-surgical ICU of a tertiary care hospital. There is considerable variation in the reported prevalence of frailty in critically ill patients (10–40%) depending upon the age group of study population, the frailty assessment tool used and the socio-demographic variations. While Fisher et al. found a low frailty prevalence (13%) in an Australian ICU [11], Darvall et al. described 19% and 18.8% frailty prevalence in multiple ICUs of Australia and New Zealand in two different studies [7, 12]. Brummel et al. found a prevalence of 30% in five US centres [13] and Montgomery et al. reported 28% frailty prevalence [14]. Bagshaw et al. and Sanchez et al. reported a prevalence of 32.8% and 39.2%, respectively in patients aged more than 50 years [15, 16] Kizilarslanoglu et al. found frailty prevalence of 21.3% in patients aged 60 years and above, while Heyland et al. described frailty to be present in 31.6% of patients aged more than 80 years [17, 18]. In a systematic review by Falk Erhag et al., the prevalence of frailty varies from 14 to 91% across 29 studies [19].

Table 1 Demographics and baseline characteristics

Characteristic	Overall, *N* = 317 (100%)[1]	Frail, *N* = 78 (25%)[1]	Not Frail, *N* = 239 (75%)[1]	*p*-value[2]
Age in years	36 (26, 59)	60 (46.2, 68.7)	32 (25, 47.5)	< 0.001
Age group				< 0.001
13–17	19 (5.9%)	2 (2.6%)	17 (7.1%)	
18–65	255(80.4%)	51 (65.4%)	204 (85.4%)	
More than 65	43 (13.6%)	25 (32%)	18 (7.5%)	
Gender				0.017
Female	163 (51.4%)	31 (39.7%)	132 (55.2%)	
Male	154 (48.4%)	47 (60.3%)	107 (44.8%)	
Education level				0.2
Less than high school	147 (58.3%)	35 (55.6%)	112 (59.3%)	
Doctorate/Postgraduate	18 (7.1%)	8 (12.7%)	10 (5.3%)	
Undergraduate	87 (34.5%)	20 (31.7%)	67 (35.4%)	
Marital status				0.072
Married	254 (80.1%)	68 (87.2%)	186 (77.8%)	
Single	63 (19.9%)	10 (12.8%)	53 (22.2%)	
Family income in thousands of INR/month	20 (10, 50)	50 (20.5, 71.2)	18 (10, 30)	< 0.001
Comorbidities				
Hypertension	72 (22.7%)	45 (57.7%)	27 (11.3%)	< 0.001
Diabetes Mellitus	72 (22.7%)	38 (48.7%)	34 (14.2%)	< 0.001
Chronic Kidney Disease	17 (5.4%)	16 (20.5%)	1 (0.4%)	< 0.001
Coronary Artery Disease	11 (3.5%)	7 (8.9%)	4 (1.7%)	0.006
Cerebrovascular Accident	2 (0.6%)	1 (1.3%)	1 (0.4%)	0.4
Chronic Liver Disease	5 (1.6%)	3 (3.8%)	2 (0.8%)	0.10
Chronic Obstructive Pulmonary Disease	5 (1.6%)	2 (2.6%)	3 (1.3%)	0.6
Asthma	3 (0.9%)	2 (2.6%)	1 (0.4%)	0.2
Obesity	4 (1.3%)	3 (3.8%)	1 (0.4%)	0.047
Hypothyroidism	4 (1.3%)	2 (2.6%)	2 (0.8%)	0.3
Others	25 (7.9%)	13 (16.7%)	12 (5%)	< 0.001
Number of comorbidities	0 (0, 1)	2 (1, 2)	0 (0, 1)	< 0.001
Any comorbidities (Yes/No)	136 (42.9%)	70 (89.7%)	66 (27.6%)	< 0.001
APACHE II	12 (9, 17)	16 (12, 21)	11 (8, 15)	< 0.001
Diagnosis category				< 0.001
Cardiac	1 (0.32%)	1 (1.3%)	0 (0)	
COVID	55 (17.3%)	15 (19.2%)	40 (16.7%)	
Gastrointestinal	17 (5.3%)	2 (2.6%)	15 (6.3%)	
Miscellaneous	35 (11%)	10 (12.8%)	25 (10.5%)	
Neurological	40 (12.6%)	9 (11.5%)	31 (12.9%)	
Obstetric	41 (12.9%)	1 (1.3%)	40 (16.7%)	
Post operative	33 (10.4%)	7 (8.9%)	26 (10.9%)	
Self-harm	13 (4.1%)	1 (1.3%)	12 (5%)	
Sepsis	82 (25.9%)	32 (41%)	50 (20.9%)	

[1]Median (IQR); n (%); [2]Wilcoxon rank sum test; Fisher's exact test; Pearson's Chi-squared test

Quantitative and qualitative values are expressed as the mean ± SD and n (%) respectively

APACHE II Acute Physiology and Chronic Health Evaluation

IQR Inter quartile range

INR Indian Rupee

When considering the different types of frailty assessment tools, Le Maguet et al. reported a prevalence of 23% with CFS and 41% with frailty phenotype assessment tool [20]. While Zampieri et al. used modified frailty index, Mueller et al. applied 50 item frailty index and Shears at al used CFS [8, 21, 22]. A systematic review and meta-analysis of 10 observational studies showed that frailty was common, involving about 30% of the critically ill population [23].

We used CFS, a well validated ordinal scale to assess frailty in critically ill population as it is neither time consuming nor cumbersome. Since CFS is a

Table 2 Source of admission to ICU

Variable	Total (*n* = 317)	Frail (*n* = 78)	Non-frail (*n* = 239)
Source of Admission			
Emergency Department	123 (38.8)	30 (39.7)	93 (38.5)
Operation Theatre	34 (10.7)	4 (5.1)	30 (12.6)
Medical Wards	87 (27.4)	18 (23.1)	69 (28.9)
COVID ICU after COVID negative report	58 (18.3)	16 (20.5)	42 (17.6)
Other ICUs[#]	15 (4.7)	9 (11.5)	6 (2.5)

n (%)

Other ICU: Gastroenterology ICU, Hepatology ICU, Neurology ICU

Table 3 Organ support and mortality

	Frail (*n* = 78)	Non-Frail (*n* = 239)	Relative Risk (95% CI)	*p*-value
Any organ support	73 (93.6)	209 (87.4)	1.07(0.93–1.15)	0.133
Mechanical Ventilation	71 (91.0)	203 (84.9)	1.07 (0.98–1.62)	0.173
Vasoactive support	55 (70.5)	125 (52.5)	1.34 (1.11–1.61)	0.006
Renal Replacement Therapy	19 (24.4)	36 (15.1)	1.62 (0.98–2.62)	0.060
ICU mortality	39/78 (50.0)	54/239 (22.6)	2.21(1.60–3.06)	< 0.001
Hospital mortality	41/76 (53.9)	60/224 (26.8)	2.01(1.49–2.72)	< 0.001
30-day mortality	46/76 (60.5)	68/224 (30.4)	1.99(1.52–2.61)	< 0.01

*n(%)

judgement-based scale, to reduce the potential of single observer bias, a second assessor also assigned CFS score to each patient and there was a high level of agreement between the two (concordance correlation coefficient 0.96). The literature also shows good inter-rater agreement when using CFS as a tool to assess frailty [6, 7,

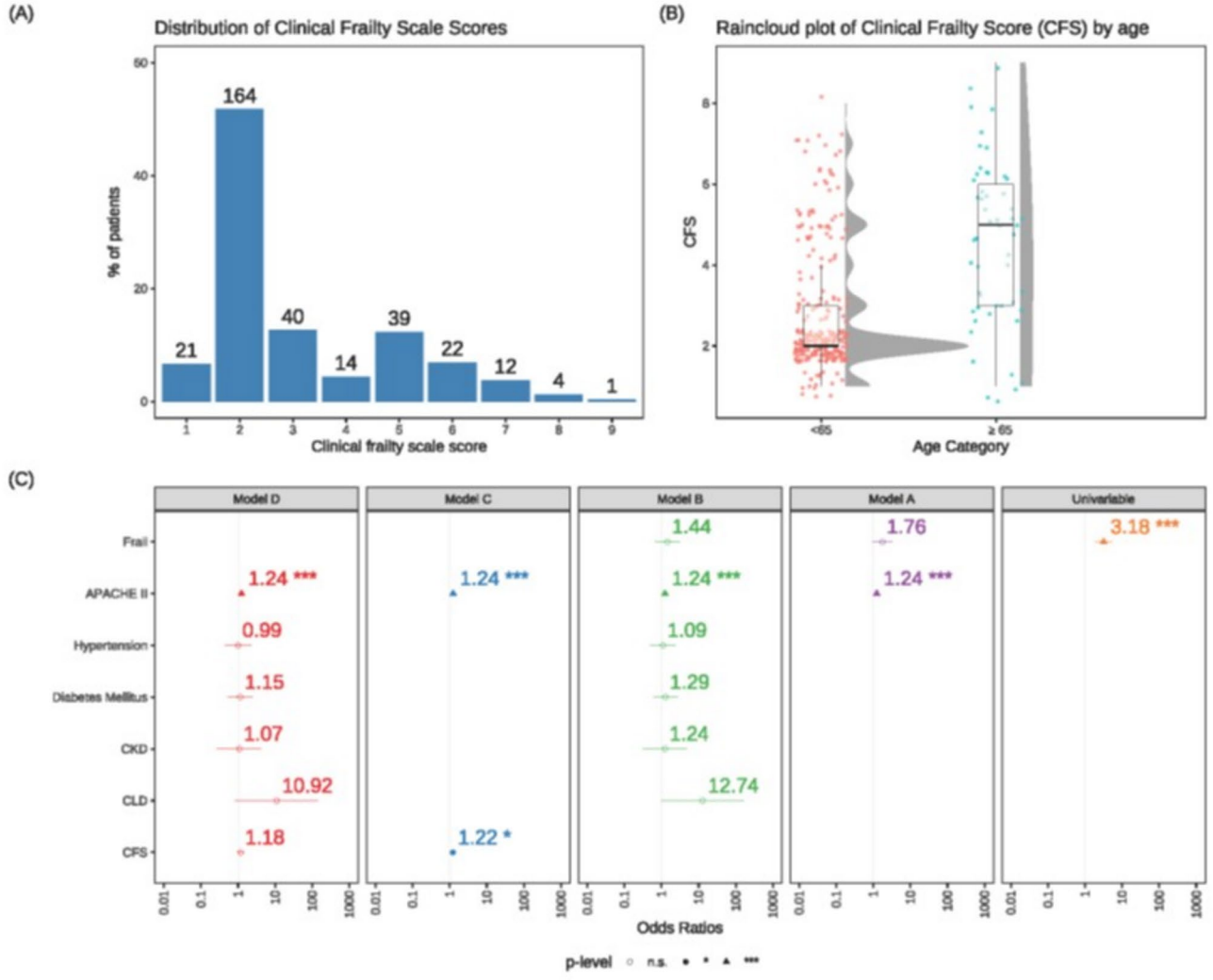

Fig. 2 (**A**) Distribution of Clinical Frailty Scores (CFS), numbers on bars represent counts; (**B**) Raincloud plots depicting distribution of CFS scores by age category; (**C**) Forest plot of odds ratios of various models involved in multivariable modelling of frailty (CFS ≥ 5 vs. CFS < 4) or CFS as a continuous independent variable (*** $p < 0.001$, ** $p < 0.05$, *$p < 0.1$, n.s.– $p > 0.1$)

Table 4 Multivariate analysis of CFS < 6 vs CFS ≥ 6

	Univariate		Model 1		Model 2		Model 3		Model 4	
Predictors	**OR**	***p***	**OR**	***p***	**OR**	***p***	**OR**	***p***	**OR**	***p***
(Intercept)	0.33 (0.25–0.43)	**< 0.001**	0.02 (0.01–0.04)	**< 0.001**	0.01 (0.01–0.04)	**< 0.001**	0.02 (0.01–0.04)	**< 0.001**	0.01 (0.00–0.02)	**< 0.001**
CFS < 6Vs CFS ≥ 6	4.85 (2.43–9.95)	**< 0.001**	2.56 (1.12–5.91)	**0.026**	1.99 (0.78–5.08)	0.149	2.49 (0.99–6.35)	0.053		
APACHE II			1.24 (1.17–1.31)	**< 0.001**	1.24 (1.17–1.31)	**< 0.001**	1.24 (1.17–1.31)	**< 0.001**	1.24 (1.17–1.31)	**< 0.001**
Hypertensive					1.11 (0.50–2.40)	0.785				
Diabetes Mellitus					1.25 (0.58–2.65)	0.568				
CKD					1.15 (0.30–4.65)	0.837				
CLD					11.15 (1.00–272.35)	0.068				
Number of comorbidities							1.02 (0.73–1.42)	0.891	0.87 (0.57–1.30)	0.509
CFS									1.28 (1.03–1.61)	**0.032**
R^2 Tjur	0.070		0.313		0.328		0.313		0.318	
AIC	367.525		290.681		294.291		292.663		291.685	

AIC– Akaike Information Criterion; APACHE– Acute Physiology and Chronic Health Evaluation; CFS - Clinical Frailty Scale; CKD– Chronic Kidney Disease; CLD– Chronic Liver Disease

22]. Since we used CFS as applicable to two weeks prior to the index hospital admission, the effect of current illness as confounding factor is nullified. Different group of investigators have chosen different time points to assess pre-admission frailty, varying from 1 week before ICU admission to a month or two [6–8, 22].

The median CFS score in our study (median 2, IQR 2–4) was slightly lower than that observed by majority of authors. Fisher et al. and Bagshaw et al. reported CFS score of 4 [11, 15]. Shears et al. (mean 4.66) and Pugh et al. (median 3.5) also reported high median CFS score in patients above 60 years of age [6, 22]. The source of ICU admission could be a plausible explanation for this difference.

We recruited all patients admitted to ICU above the age of 13 years, the average age of frail patients being 56 years with youngest 13 years and eldest 89 years old. The mean difference in age between frail and non-frail patients was about 30 years. Our data shows that frailty affects patients of all ages. The prehospital frailty is common even among the younger critically ill patients and it is associated with higher mortality as well as readmission [7, 24].

Several studies have shown higher prevalence of frailty in female patients [7, 14, 25] whereas there was a higher percentage of male patients (60%) in frail group in our study. The observed difference could be explained by the fact that the female patients in our study population were admitted to ICU following obstetric complications, were younger in age and did not have previous co-morbid illnesses.

It is well known that frail patients have poor physiological reserve, hence the homeostasis is not easily achieved after any external stress. The deranged physiology leads to greater degree of organ damage. We found more comorbidities (2 vs. 0) and higher median APACHE II score at 24 h of admission (16 vs. 11) in frail patients. About 40% of frail patients were admitted with the diagnosis of sepsis, similar to the findings of Bagshaw et al. (40%) and Fernando et al. (33%) [24, 26]. A recently published prospective cohort study by Lee et al. found that 52.6% of the patients with sepsis were frail [27].

Though we found a higher number of frail patients requiring vasoactive support (1.34 times), there was a marginal increase in requirement of MV and RRT even though the point estimate for the relative risk of RRT was the highest. A lack of effect of frailty on RRT may be due to the study being underpowered for this outcome and low RRT event rate. Similar to our results, Bagshaw et al., Montgomery et al. and Le Maguet et al. showed no increase in organ support requirement in frail patients [14, 15, 20]. In a systematic review and meta-analysis by Muscedere et al., many authors did not find any difference in requirement of organ support between frail and non-frail population [8, 15, 17, 18, 20, 23]. On the contrary, Zampieri et al., Hessey et al. and Darvall et al. reported higher requirement of organ support (vasoactive support, MV and RRT) in frail patients [8, 12, 25]. This difference could be attributed to large study

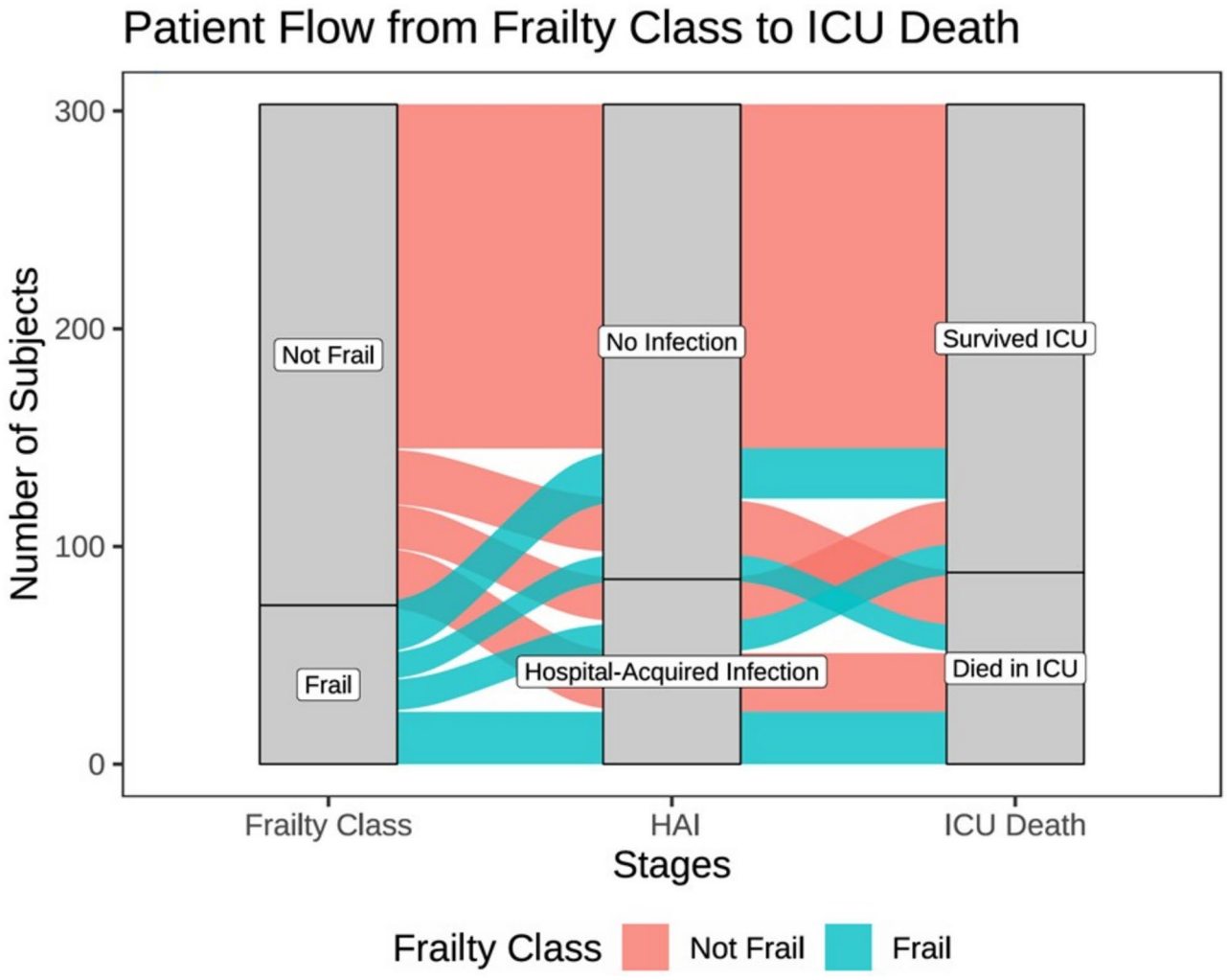

Fig. 3 Alluvial plot representing the trajectory of patients according to frailty class through hospital acquired infection status to ICU discharge/mortality

population in these studies and/or use of different frailty assessment tool. The study in surgical ICU also mentioned requirement of more than one organ support in frail patients [21]. Importantly, many studies reporting frailty in ICU population have not explored the association of frailty with requirement of organ support [6, 11–13, 22, 26, 28, 29].

We found marginally longer ICU and hospital LOS in frail patients, the median difference being 1 day and 3 days, respectively. Fischer et al. and Le Maguet et al. also did not find any difference in ICU LOS for frail patients [11, 20]. A lot of authors have found longer ICU as well as hospital LOS in frail population [7–8, 14–17, 21, 26]. Darvall et al. commented about tendency of ICU physicians to continue aggressive management for longer duration in younger frail patients, thereby, increasing ICU LOS [7]. We believe that longer hospital LOS is determined by multiple factors ranging from patient's clinical condition to availability of easy, appropriate and affordable domiciliary care facilities without which, the confidence of both family as well as treating team in discharging patients to home is limited.

Interestingly, we found a high incidence of HAIs in frail patients (50%) as compared to non-frail patients (21%) with two and a half times relative risk in frail patients. The most common HAI was ventilator associated pneumonia followed by catheter related blood stream infection. Although HAI are a major cause of morbidity and high healthcare cost, there is paucity of literature on association of frailty with HAI in ICU patients. Our data showed increased mortality, longer ICU and hospital LOS in frail patients who experienced HAI (supplementary file). Bagshaw et al. observed nosocomial infections, especially CLABSI only as one of the components of adverse events and found higher odd-ratio of adverse events in frail population [15].

In our study, the frail patients had almost double the risk of mortality (ICU/hospital/30-day). Several authors have reported higher unadjusted ICU or/and hospital mortality in frail patients [12, 17, 18, 21, 28]. Flaatten et

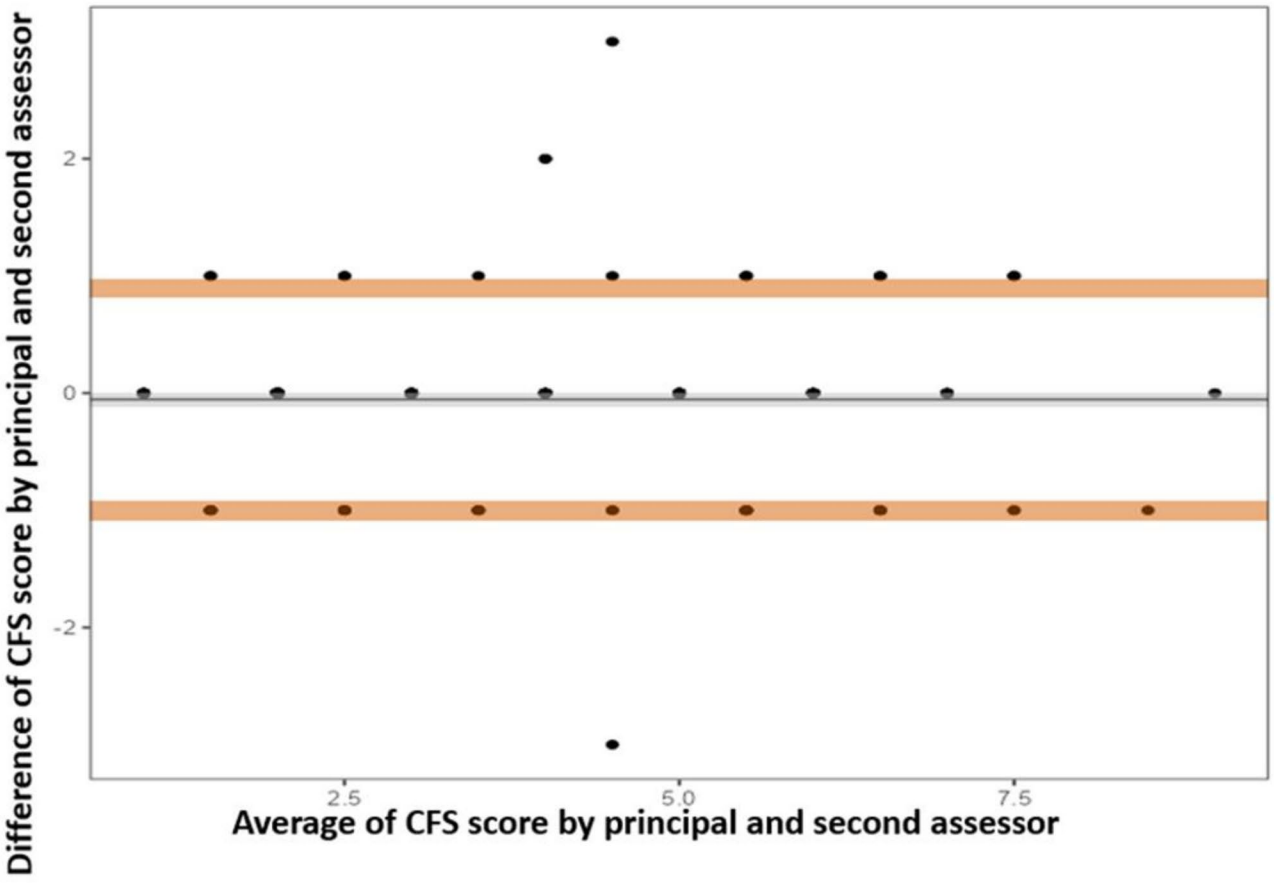

Fig. 4 Bland Altman plot for agreement of CFS score between principal investigator and second assessor

al. reported high 30-day mortality (32.6%) in frail, elderly patients, Falk Ehgar et al. reported a high all-cause mortality in frail patients, Le Maguet et al. concluded that incremental CFS was independently associated with ICU mortality and that at 6 months and Brummel et al. observed greater hazard of death at 3 and 12 months [13, 19–20, 28]. The systematic review and meta-analysis by Muscedere et al. showed an increased risk of both ICU and hospital mortality in frail patients (RR 1.51; 95% CI 1.31–1.75 & RR 1.71; 95% CI 1.43–2.05, respectively) [23]. Shears et al. demonstrated that each one-point increase in CFS was positively correlated with ICU and hospital mortality [22]. Thus, CFS score was found to be a strong, independent factor predicting mortality at 1, 3, 6 and 12-months [19]. However, several studies on critically ill frail patients have not mentioned any association between frailty and ICU mortality [8, 11–13, 26]. In the two studies by Bagshaw et al., though the authors did not report any difference in ICU mortality, both the studies concluded independent association of frailty with mortality at 1 year [15, 24].

Our cohort consisted comprised of patients belonging to 18–65-year age group. Moderate and higher degrees of frailty (CFS ≥ 6) appear to be associated with mortality in our cohort when adjusted for disease severity (APACHE II) while the conventional CFS ≥ 5 was not statistically associated with mortality compared to CFS < 5 when adjusted for APACHE II. This could be due to the higher proportion of patients with age < 65 years in our cohort. Future studies should explore the influence of newer cut-offs of CFS on mortality and other outcomes in this age group. Also, more robust methods of quantifying frailty may need to be developed for this age group.

Implications for practice, policy and research

Since frailty takes into account the clinical as well as socio-demographic parameters, it is evident from literature review that assessing frailty in critically ill patients in different study populations gives different results ranging from prevalence to the effects of frailty on clinical outcomes. However, as frailty could be associated with worsened outcomes, it is suggested to diagnose frailty at the time of ICU admission. Moreover, future studies are needed to prove the effect of various interventions like mobilization, infection prevention in frail patients on improvement in LOS, mortality of re-admission to ICUs.

Strengths and limitations

Our study cohort is representative of the general population admitted in mixed adult intensive care setting since we have done a complete sampling of all patients more than 13 years of age getting admitted to ICU consecutively. The excellent inter-observer reliability is reflective of accurate assessment of CFS. Also, missing data is limited only to 17 patients who were lost to follow up after discharge from ICU. However, a longer follow-up of patients could help determine outcomes like 6-month or 1-year mortality. Also, since the patients were recruited after Main ICU admission, this is not representing all critically ill patients presenting to the hospital. The single-center nature of the study limits generalizability. Also, the results of the study are hypothesis-generating as this is an observational study and does not demonstrate causality between frailty and poor outcomes and frailty may simply be a marker of more severe chronic illness.

Conclusion

The prevalence of frailty in ICU patients was 24.6% and a higher number of frail patients had requirement of vasopressor support and incidence of HAI. Frail patients also had longer hospital LOS and higher ICU, hospital and 30-day mortality.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions
D.K.S: literature search, data collection, statistical analysis, compilation of results. V.G.: result compilation, data analysis, manuscript preparation. N.S.: concept, design, literature search, manuscript preparation, definition of intellectual content. B.K.: data collection, compilation of results. V.S.: definition of intellectual content, manuscript review. Y.L.N.: design, statistical analysis, definition of intellectual content, manuscript review.

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Data availability
The complete de-identified dataset and code utilized in producing this manuscript is available upon reasonable request, pending local regulatory approval.

Declarations

Ethics approval and consent to participate
This study received approval from our Institutional Ethics Committee (INT/IEC/2021/SPL-240) on 13/02/2021, with registration in Clinical Trials Registry of India (CTRI) (CTRI/2021/04/032782) on 13/04/2021. Written informed consent was obtained from every patient by the investigators, and that this work was conducted in accordance with the Declaration of Helsinki.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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