

FRAILITY COULD PREDICT DEATH IN OLDER ADULTS AFTER ADMISSION AT EMERGENCY DEPARTMENT? A 6-MONTH PROSPECTIVE STUDY FROM A MIDDLE-INCOME COUNTRY

I. APRAHAMIAN, G.V. ARICÓ DE ALMEIDA, C.F. DE VASCONCELLOS ROMANIN, T. GOMES CALDAS, N.T. ANTUNES YOSHITAKE, L. BATAGLINI, S. MORI LIN, A. ALVES PEREIRA, L. NARA ALEGRINI LONGHI, R.L. MAMONI, J.E. MARTINELLI

Group of Investigation on Multimorbidity and Mental Health in Aging (GIMMA), Geriatrics division, Internal Medicine Department, Faculty of Medicine of Jundiaí, Jundiaí, Brazil. Corresponding author: Ivan Aprahamian, MD, MS, PhD, FACP. Group of Investigation on Multimorbidity and Mental Health in Aging (GIMMA), Geriatrics Division, Internal Medicine Department, Faculty of Medicine of Jundiaí, Jundiaí, Brazil. 250 Francisco Telles street. ZIP 13.202-550. E-mail: ivan.aprahamian@gmail.com

Abstract: *Background:* The number of older adults attending emergency department (ED) is increasing all over the world. Usually, those patients are potentially more complex due to their greater number of comorbidities, cognitive disorders, and functional or physical disabilities. Frailty is a vulnerable state that could predict adverse outcomes of those patients. There are very few studies that addressed this topic in the ED, and none of them used a simple instrument for frailty assessment. *Objectives:* The primary outcome was to evaluate the association between frailty identified through the FRAIL questionnaire at baseline and death after a 6-month follow-up period after hospital discharge from the ED. Secondary outcomes were readmission to the ED and disability after 6 months. *Methods:* A 6-month follow-up prospective study (FASES study) was conducted at a university-based trauma-center ED in Jundiaí, southwestern of Brazil. A total of 316 older adults aged 60 or older were randomly included based on a lottery of their medical record admission number. Frailty was evaluated through the FRAIL questionnaire. The association between frailty and death was estimated through a binary logistic regression adjusted for age, sex, and cognitive performance. *Results:* From the total sample, the mean age was 72.11±8.0 years, and 51.6% were women. Participants presented 2.28±1.4 comorbidities and 25.6% were frail. Mean hospital stay was 5.43±5.6 days. Death occurred in 52 participants, readmission to the emergency in 55, and new disability in 16 after 6 months. Frailty was associated with an odds ratio of 2.18 for death after 6 months (95% CI = 1.10–4.31; $p = 0.024$). This association lost significance after multivariate analysis taking into account cognitive performance. There was no association between frailty status at baseline and readmission to the ED or disability. *Conclusion:* The identification of frailty using the FRAIL at admission was not predictive of death after a 6-month period after discharge from the ED. Simple frailty assessment could identify patients at higher risk for death in the follow-up.

Key words: Frailty, adverse reactions, prognosis, emergency.

Introduction

Frailty can be defined as a state of vulnerability due to low homeostatic reserve and a trend to adverse health conditions (1). It is a very common condition seen among older adults, with a mean prevalence of 9.9% (2). The prevalence of frailty in low to middle-income countries is even higher with a pooled mean of 17.4% (3). At long-term at least, frail patients are at higher risks for hospitalization, emergency department (ED) visits, falls, fractures, functional disability, and death (1, 2, 4, 5). Especially concerning ED visits and acute medical scenarios, frail older adults are becoming more common as population progressively ages (6). Decades ago, before frailty operationalization was made, many older adults were seen as more resource-demanding and time-consuming when compared to younger adults (7). Nowadays, emergency physicians have less time to attend seniors with cognitive decline, multimorbidity, polypharmacy, and several disabilities (8). Nonetheless, many efforts and instruments have been validated to identify older adults with increased risk of adverse outcomes after ED admission (9-12). However, few are time or

operationally feasible or presented heterogeneous and modest findings. The identification of easy and time effective clinical or biological markers of increased risk for adverse outcomes is a matter of investigation.

Few studies accessed frailty status among older adults admitted or discharged from general ED settings. Generally, the majority of criteria or instruments to detect frailty are more complex to be implemented in the routine of emergency physicians, increasing their time of evaluation (13-15). All of these studies evaluated frailty using validated instruments in ED settings in high-income countries. Results from these studies were heterogeneous and only one presented a follow-up of at least 6 months. Death as an outcome measure was rare and with short follow-up period (16). Some instruments used on those studies were also more complex and more time-consuming to ED physicians, usually using specific equipment or requiring physical maneuvers that are frequently difficult for older adults with acute diseases to perform.

A feasible way to detect older adults in ED with high risk to adverse outcomes is needed. Frailty identification can be a marker of negative prediction in this setting. However,

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instruments to detect frailty should be brief, fast and friendly to emergency physicians. Finally, the aim of this prospective study was to evaluate if the presence of frailty identified through a simple and very fast screening instrument (FRAIL questionnaire) could predict death after 6 months of ED admission of older adults in a middle-income country. Secondarily, we evaluated its predictive value to readmission to the ED and functional disability after 6 months.

Methods

Design, setting, and participants

We conducted a prospective study (FASES study, Frailty and sarcopenia Assessment in Seniors at Emergency Setting) in an ED from a university-based trauma-center hospital located in Jundiá, Brazil, between May 2015 and June 2016. A follow-up evaluation was performed after 6 months of hospital discharge. The city of Jundiá has 397,965 inhabitants and is located at the southwestern of the state of São Paulo. The study followed ethical standards of the Committee on Human Experimentation as well as with the Declaration of Helsinki, and followed the standards established by the National Council of Health (resolution 466/12) in Brazil. All patients were oriented about the study and agreed to participate by signing an informed consent protocol approved by the national ethics committee (national protocol CAAE: 54389716.1.0000.5412).

Community-dwelling patients aged 60 years or older who were admitted to the ED according to the following inclusion criteria: clinically stable, admitted in the last 24h, collaborative with the study, and comprehended the study and signed a written consent. We excluded those who presented a diagnosis of dementia, severe mental disorder or terminal condition (expected survival less than 6 months), important disability, severe sensorial impairment, and those whose surgery would occur at the day of the interview. We also excluded patients that did not follow-up at our post-discharge outpatient unit. They should attend at this unit at least twice during the 6-month period after discharge.

Procedures

Each week during the study, the research team raffled patients to be interviewed. The patient lottery was performed using the electronic admission number, without knowing the diagnosis or any other information of the patient before the interview. A trained researcher invited the drafted patient to participate in the study. Patients who agreed to participate had an explanation about the study and were asked to read and sign a written consent. There was no impact or change in the treatment of patients that did not agree to participate. After that, during the interview, sociodemographic and clinical data were collected, measurements of dominant calf diameter and dominant hand-grip strength using a manual hydraulic dynamometer (3 trials with a final measure based on the mean of the trials; Saehan Corporation, 973, Yangdeok-Dong, Masan

630-728, Korea) were done, and validated, transculturally-adapted and translated instruments FRAIL questionnaire (17), SARC-F scale (18), Geriatric Depression Scale (GDS) 15-items (19), Functional Assessment Questionnaire (FAQ) (20), and the 10-point Cognitive Screener (10-CS) (21) were applied. This protocol has an average time to administer of 13.4 minutes. The research team followed the total time length of hospitalization, and medical diagnosis during the period of hospitalization. After 6 months, the research team monitored any hospitalization, loss of follow up at the outpatient post-discharge unit or death. Patients were interviewed once by phone call and the FRAIL questionnaire, a 4-item GDS and the FAQ were also applied. The FAQ was chosen because it is an easy and fast way to detect common functional impairment (a score of 5 to 30 points indicates impairment).

Frailty and other measurements

The frailty was evaluated using the FRAIL questionnaire (fatigue, resistance, ambulation, illnesses, and weight loss), which is regarded to be as effective in predicting poor outcomes as more complex frailty criteria, however, it is easier to administer (17, 22, 23). This instrument involves five simple questions to evaluate the presence of frailty components and takes approximately less than 1 minute. The scale is based on self-report without any objective measurement. Each question requires a “yes” or “no” answer, with one point for an affirmative response. Scores ranged from zero to five points, classifying patients as robust (0 points), prefrail (1 or 2 points), or frail (≥ 3 points). The scale assesses the presence of fatigue, muscle resistance, aerobic capacity, disease burden, and weight loss. Fatigue was evaluated by asking participants whether they felt tired most of the time; muscle resistance by participants’ report of his/ her capacity to climb a flight of stairs; aerobic reserve by participants’ report of his/her capacity to walk a block independently; disease burden by the presence of five or more of a total of 11 listed diseases; and loss of weight by a decline of $\geq 5\%$ within the past 6 months.

The SARC-F scale was used to screening for sarcopenia, which presents a good accuracy (18). GDS-15 items was used to identify depressive symptoms (19). The FAQ identifies loss of functional disability (20). It presents good accuracy especially for patients with cognitive decline. Finally, the 10-CS shows better sensitivity and specificity than the Mini Mental State Examination to detect mild cognitive impairments (21).

Outcomes

The primary outcome was death at 6 months after hospital discharge. Secondary outcomes were readmission to the ED by any cause and functional disability based at the FAQ and compared to the baseline evaluation.

Table 1
 Baseline characteristics of the participants according to frailty status

	Total (n=316)	Robust (n=67)	Prefrail (n=168)	Frail (n=81)	p
Age (years), mean (SD)	70.58 (7.92)	71.64 (7.96)	74.38 (7.99)	72.12 (8.06)	0.009a
Female, n (%)	153 (48.4%)	24 (35.8%)	75 (44.6%)	54 (66.7%)	0.000b
Income n (%)					0.137
Lower	310 (98.1%)	64 (95.5%)	165 (98.2%)	81 (100%)	
Higher	6 (1.9%)	3 (4.5%)	3 (1.8%)	0	
Education (years)					0.520
Informal	85 (28.1%)	16 (26.2%)	44 (26.8%)	25 (32.1%)	
1-3 years	137 (45.2%)	30 (49.2%)	70 (42.7%)	37 (47.4%)	
≥ 4 years	81 (26.7%)	15 (24.6%)	50 (30.5%)	16 (20.5%)	
Marital Status n (%)					0.075
Married	176 (55.7%)	33 (49.3%)	104 (61.9%)	38 (46.9%)	
Single	47 (14.9%)	13 (19.4%)	24 (14.3%)	10 (12.3%)	
Widow or others	93 (29.4%)	21 (31.3%)	40 (23.8%)	32 (39.5%)	
Ethnicity					0.215
White	249 (78.8%)	52 (77.6%)	127 (75.6%)	70 (86.4%)	
Brown	34 (10.8%)	9 (13.4%)	18 (10.7%)	7 (8.6%)	
Black	33 (10.4%)	6 (9%)	23 (13.7%)	4 (4.9%)	
Comorbidities, n (%)	2.48 (1.55)	1.87 (1.10)	2.43 (1.50)	3.09 (1.75)	0.000c
Diabetes	127 (40.2)	18 (26.9%)	73 (43.5%)	36 (44.4%)	0.043
Hypertension	244 (77.2%)	48 (71.6%)	130 (77.4%)	66 (81.5%)	0.364
Myocardial infarction	8 (2.2%)	0	6 (3.6%)	1 (1.2%)	0.192
Heart Failure	46 (14.6%)	9 (13.4%)	20 (11.9%)	17 (21%)	0.156
Arrhythmia	4 (1.3%)	2 (3%)	2 (1.2%)	0	0.268
CKD	37 (11.7%)	7 (10.4%)	21 (12.5%)	9 (11.1%)	0.890
Anemia	1 (0.3%)	0	1 (0.6%)	0	0.643
COPD	26 (8.2%)	2 (3%)	12 (7.1%)	12 (14.8%)	0.025
Cancer	4 (12.7%)	7 (10.4%)	15 (8.9%)	18 (22.2%)	0.011
Depression	(15.8%)	3 (4.5%)	28 (16.7%)	19 (23.5%)	0.006
Osteoporosis	16 (5.1%)	1 (1.5%)	6 (3.6%)	9 (11.1%)	0.13
Osteoarthritis	67 (21.2%)	11 (16.4%)	30 (17.9%)	26 (32.1%)	0.020
SARC-F	2.70 (2.69)	0.82 (1.21)	2.34 (2.31)	4.89 (2.80)	0.000d
Physical Activity	63 (19.9%)	23 (34.3%)	34 (20.2%)	6 (7.4%)	0.000
10-CS	5.93 (2.68)	6.71 (2.60)	5.88 (2.67)	5.44 (2.67)	0.020e
GDS-15	4.74 (2.89)	3.03 (1.71)	4.78 (2.84)	5.99 (3.08)	0.000f
FAQ	4.65 (6.59)	1.5 (3.62)	4.27 (6.32)	7.85 (7.55)	0.000g
Calf circumference (cm)	33.22 (4.01)	33.75 (3.85)	33.14 (3.93)	32.89 (4.32)	0.571
Handgrip strength (Kg)	16.58 (4.63)	17.30 (4.26)	16.90 (4.98)	15.42 (3.99)	0.25
In hospital stay (days)	5.43 (5.61)	4.94 (4.97)	5.46 (6.04)	3.09 (1.75)	0.663

Note: SD=standard deviation; CHD (coronary heart disease); CKD (chronic kidney disease); COPD (chronic obstructive pulmonary disease); 10-CS screener: uses temporal orientation, category fluency and word recall; GDS-15: Geriatric Depression Scale 15 items; FAQ (Functional Assessment Questionnaire): instrument to measure disability with scoring between 0 to 30, in which impairment is present above 4 points. a:robust ≠ frail=<0.001, prefrail ≠ frail=<0.030; b:robust ≠ prefrail=0.026, robust ≠ frail=0.004, prefrail ≠ frail=0.004; c:robust ≠ prefrail=0.026, robust ≠ frail=<0.001, prefrail ≠ frail=0.004; d:robust ≠ prefrail=<0.001, robust ≠ frail=<0.001, prefrail ≠ frail=<0.001; e:robust ≠ frail=0.015; f:robust ≠ prefrail=<0.001, robust ≠ frail=<0.001, prefrail ≠ frail=0.003; g:robust ≠ prefrail=0.009, robust ≠ frail=<0.001, prefrail ≠ frail=<0.001.

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Data analysis

Analyses were performed using the SPSS software (IBM SPSS Statistics for Mac, Version 21.0. Armonk, NY: IBM Corp.). Data presented normal distribution after the Kolmogorov-Smirnov test and analysis of skewness and kurtosis. Categorical variables were presented as number and percentages and continuous variables as mean and standard deviation (SD) when comparing frailty status (robust, pre-frail and frail groups). Baseline characteristics were compared according to frailty status (robust, pre-frail and frail participants) using the independent samples t-test for interval variables and the chi-squared test for categorical variables. The FRAIL questionnaire was correlated with SARC-F score, GDS-15, FAQ, 10-CS, calf circumference, and handgrip strength using Pearson correlation test. The association between frailty and primary or secondary outcomes was analyzed through a binary logistic regression adjusted for covariates in two models. Model 1 adjusted for age and sex; model 2 additionally adjusted for cognitive performance. Models 1 and 2 were applied if unadjusted model was significant. All statistical tests were two-tailed, with an alpha level of 0.05, and confidence interval was established at 95%.

Results

Figure 1 illustrates the study's flow diagram. A total of 367 patients were raffled, and 51 denied participation or had exclusion criteria, totalizing 316 patients at baseline. During the follow-up, 94 patients were unable to be contacted by phone after several trials or did not attend to the post-discharge outpatient unit and follow-up at another medical service. After 6 months of hospital discharge, 52 patients died, 55 were readmitted to ED, and 16 presented new functional disability. Baseline characteristics, described in Table 1, showed mean age of 70.5 ± 7.92 , 48.4% of female, 98.1% had a low income characterized by less than 4 minimum wages, 26.7% had 4 or more years of schooling. The majority was white 78.8% and had $2.48 \pm (1.55)$ comorbidities. Regarding frailty status, 21.2% were robust, 53.2% were prefrail and 25.6% were frail. SARC-F had significantly higher scores in prefrail and frail individuals compared to robust ($p < 0.001$), as well as GDS-15, FAQ and 10-CS.

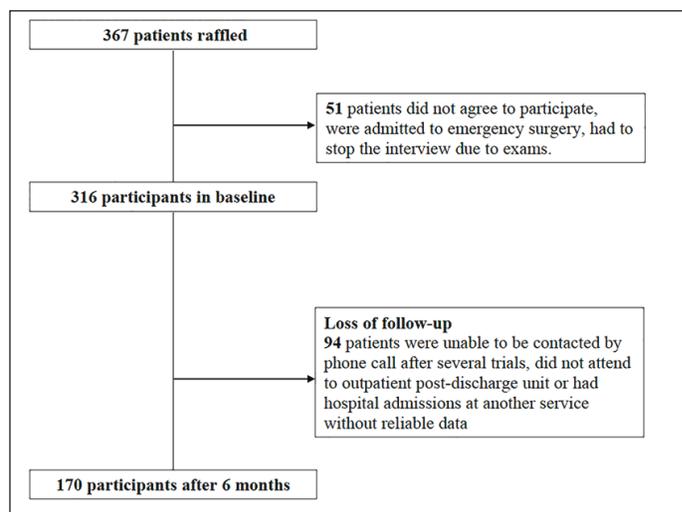
Moderate significant positive correlations were observed between the SARC-F scores and the FRAIL, the GDS-15 items and FAQ (Table 2). Additionally, the FAQ and 10-CS also presented moderate and significant negative correlation. Other significant but weaker correlations can be seen in Table 2.

Mean hospital stay was 5.43 ± 5.6 days, and death occurred in 52 (16.5%) participants, readmission to the ED in 55 (17.4%), and new disability in 16 (9.5%) after 6 months of follow-up. Frailty was associated with an odds ratio of 2.18 for death after 6 months (95% CI = 1.10–4.31; $p = 0.024$) even when adjusted for age and sex. However, this significant association was lost after adjustment the cognitive performance. There was no

association between frailty status at baseline and readmission to the ED or disability, as shown in Table 3. Even when prefrail and frail were taken together for risk prediction (e.g. FRAIL between 1 and 5), no significant association was observed (Table 3).

Figure 1

Study flowchart of the participants



Discussion

We conducted a prospective study to evaluate if frailty, or even prefrailty, could predict death, hospital readmission or functional disability to older adults admitted to an ED from a middle-income country. We used a simple and friendly instrument, such as the FRAIL, to identify frailty in this setting. In initial unadjusted and after adjustments for age and sex, frailty consisted of a good predictor to death, but not new hospital admission neither disability after 6 months of follow-up. However, after adjusting for cognitive performance, frailty was not associated with death. Secondly, we observed a moderate correlation between SARC-F, a screening instrument to detect sarcopenia, and depressive symptoms, frailty and disability. Finally, functional disability (measured by FAQ) was correlated with cognitive performance.

Previously, few studies evaluated the predictive value of frailty to adverse health reactions between a total of 90 to 7,532 older adults (mostly under 75 years) admitted to general ED (not only trauma or surgical patients) (14, 16, 24-27). Frailty was identified using an adapted Fried's phenotype criteria, the Clinical Frailty Scale, the Deficit Accumulation Index (aka Frailty Index), the Identification of Seniors At Risk (ISAR), Rothman's scale, Ávila-Funes' scale, and the Study of Osteoporotic Fracture frailty index (SOF). Four of those studies were prospective with follow-up ranging from 30 days to 6 months (16, 24-27). One of them did not clearly state the time of follow-up (26). Outcomes also varied with death been

Table 2

Correlation between the FRAIL questionnaire, calf circumference, Geriatric Depression Scale-15 items, Functional Assessment Questionnaire (FAQ), SARC-F scale, 10-Cognitive Screening, and handgrip strength

	Calf Circumference	GDS-15	FAQ score	FRAIL	SARC-F	10-CS	Handgrip strength
Calf Circumference	1	-0.093	-0.205**	-0.073	-0.158**	0.167**	0.007
GDS-15		1	0.397**	0.373**	0.414**	-0.229**	-0.045
FAQ score			1	0.339**	0.618**	-0.414**	-0.166**
FRAIL				1	0.511**	-0.138**	-0.154**
SARC-F					1	-0.239**	-0.165**
10-CS						1	0.108
Handgrip strength							1

Note: **significant Pearson's linear correlation for two-tale $p < 0.05$.

Table 3

Association between frailty and pre-frailty identified through the FRAIL questionnaire and death, readmission to ED and functional disability after 6 months of hospital discharge

Variables	Odds Ratio (95% confidence interval)					
	Unadjusted Model	p ^a	Adjusted Model 1*	p ^a	Adjusted Model 2**	p ^a
Death						
Robust	1 (ref.)	-	1 (ref.)	-	1 (ref.)	-
Prefrailty	1.63 (0.62-4.31)	0.324	1.48 (0.55-3.96)	0.436	1.39 (0.51-3.76)	0.520
Frailty	3.93 (1.41-10.89)	0.009	2.90 (1.01-8.34)	0.049	2.73 (0.94-7.95)	0.066
Prefrail + Frail	2.24 (0.895-6.4)	0.088	1.85 (0.72-4.77)	0.201	1.74 (0.66-4.54)	0.257
Readmission to ED						
Robust	1 (ref.)	-	N/A	-	N/A	-
Prefrailty	1.23 (0.54-2.80)	0.612				
Frailty	1.63 (0.61-4.35)	0.327				
Prefrail + Frail	1.33 (0.60-2.92)	0.472				
Functional disability						
Robust	1 (ref.)	-	N/A	-	N/A	-
Prefrailty	4.64 (0.57-37.55)	0.150				
Frailty	6.72 (0.74-60.70)	0.090				
Prefrail + Frail	5.17 (0.66-40.49)	0.117				

Note: a)binary logistic regression model; *adjusted for age and sex; **adjusted for cognitive performance in 10-CS instrument. N/A=analyses not applied since unadjusted model not significant.

considered in only two studies after 30 days of observation in one and the other without presenting the time of follow-up (16, 26). Disability was evaluated in two studies (after 3 and 6 months). Results from these studies were heterogeneous with mixed findings regarding frailty as a predictive factor for death, hospital admission, ED visit or disability. In general, despite this, most studies tend to favor the use of frailty to better prediction of negative outcomes. Only one study compared the ability to predict disability between the SOF instrument and ED physicians' evaluation (25). In this study, SOF presented better accuracy. One study compared 5 frailty instruments (27).

Outcomes were mortality, institutionalization (new admission to a care home or a move to a new care home), new hospital readmission and disability after 90 days. All instruments (Fried's phenotype, frailty index, SOF, Rothman's, and Ávila-Funes') were associated with an increased risk of death, but with poor predictive properties. Most of the studies presented several methodological limitations. From this overview, we can depict the idea that evidence of using frailty identification to predict adverse events in ED patients are still controversial and deserves more attention in research. No randomized trial was found in this topic of interest, lacking the highest degree of

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scientific evidence.

Currently, there is no gold standard to measure frailty (1). Recently, 35 frailty instruments were compared in a large community-based European study (28). These instruments presented a wide range and different degrees of agreement between them for diagnosis of frailty (Cohen's $\kappa = 0.10$ – 0.83). Frailty status classification (i.e. robust, prefrailty and frailty) also showed a wide range of agreement. In this study, the highest agreement was seen in accumulation of deficits model (i.e. Frailty Index), while better accuracy was seen in multidimensional instruments. In ED setting, as shown above, most instruments were derived from the accumulation of deficits or phenotype models (as we can assume for the SOF). Two potential problems can be assumed when using these models: both are time-consuming and require training. This can be problematic in ED settings indeed. Even with SOF, a short and fast instrument, the necessity of seating and standing 5 times may be hard for some older adults admitted to the ED. The FRAIL questionnaire is also a simple and friendly instrument, takes less than 1 minute to administer and do not require any physical evaluation. It could be easily implemented by ED physicians. This instrument is also multidimensional, assuming both characteristics from the phenotype and accumulated deficits. This latter is present in the FRAIL through the presence of multimorbidity of 5 or more chronic diseases. We observed a moderate correlation between the FRAIL and the SARC-F, which can estimate the presence of sarcopenia with good accuracy. Sarcopenia is one cornerstone in the biological model of the physical frailty phenotype model.

Frailty lost its predictive value for death after adjusted for cognitive performance measured using the 10-CS, which is a rapid instrument for detecting mild impairments and is recommended by important consensus (29). Cognitive status at admission to ED can be a major predictor for negative outcomes in acute medical conditions. Recently, we evaluated the potential improvement in death prediction after adding 10-CS to the FRAIL questionnaire (13). Secondary outcomes were new functional disability and falls. A sample of 701 older adults with an acute or decompensated disease was evaluated at an intermediate care unit. Frail patients with both normal (hazard risk [HR] 4.0, 95% confidence interval [CI], 1.73–9.25) and impaired cognitive performance had a higher risk of death (HR 4.38, 95% CI, 1.95–9.87) than robusts. The presence of cognitive impairment increased the risk of death also in prefrail (HR 3.60, 95% CI, 1.55–8.34) and robust patients (HR 3.49, 95% CI, 1.22–9.96). The predictive accuracy of the FRAIL scale was lower than expected (between 0.58 and 0.69). In the study that compared 5 frailty instruments, those that included cognitive evaluation have demonstrated better predictive accuracy for negative outcomes (27). A possible explanation is that neither frailty nor cognitive impairment could be independent markers for negative outcomes (30).

Our study presents some limitations that must be pointed out. First, a larger sample could have contributed to a higher

significant association between frailty and death prediction. Additionally, we had a high rate of drop outs which may also reduce the power of our findings. Our results came from a single general trauma-reference ED center. So, our findings cannot be generalized to specific populations with acute diseases admitted to ED (e.g. surgical patients). However, our study had a prospective design with the longest follow-up to date. Our data are original since it is the first study coming from a middle-income country, and the first using a simple and highly recommended frailty instrument such as the FRAIL. In conclusion, frailty can be a predictive factor to death after ED discharge, but it can be influenced by cognitive performance. It appears, along with previous evidence, that frailty and cognitive impairment are two main components in the prognosis of older adults admitted to ED settings. More studies, especially randomized controlled trials, have to explore important and common geriatric conditions such as frailty in acute care units.

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