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Frailty and mortality: Utility of Frail-VIG index in ED short-stay units for older adults

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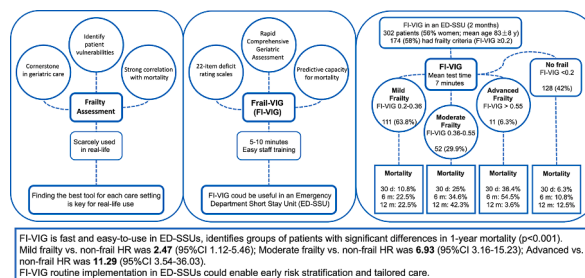
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HIGHLIGHTS

- Frailty assessment is useful to individualize diagnostic and therapeutic intensity.
- Selecting the most appropriate frailty scale for each setting is highly relevant.
- ED short-stay units should progressively implement frailty assessment.
- Frail-VIG takes 7 min by trained staff and is strongly related to mortality.
- Frail-VIG allows identifying a high-risk group of patients in ED short-stay units.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Frailty assessment allows the identification of patients at risk of death. The aim here was to study the ability of Frail-VIG Index (FI-VIG) in order to discriminate frailty groups of older adults and garner its correlation with mortality in an Emergency-Department Short-Stay Unit (ED-SSU).

Methods: Our observational, single-center, prospective study consecutively included patients over 65-years-old admitted between March 1, 2021, and April 30, 2021.

Results: 302 patients were included (56 % women), mean age 83 ± 8 years, and 39.1 % of them had a functional disability whilst 16.5 % of them had dementia. A total of 174 patients (58 %) met the frailty criteria (FI-VIG ≥ 0.2): 111 (63.8 %) had mild frailty (FI-VIG 0.2–0.36), 52 (29.9 %) had moderate frailty (FI-VIG 0.36–0.55), and 11 (6.3 %) had advanced frailty (FI-VIG > 0.55). Mortality at 30 days, 6 months, and 1 year was analyzed: no frailty was 6.3 %, 10.8 %, and 12.5 %, respectively; mild frailty was 10.8 %, 22.5 %, and 22.5 %, respectively; moderate frailty was 25 %, 34.6 %, and 42.3 %, respectively; advanced frailty was 36.4 %, 54.5 %, and 3.6 %, respectively. This shows the significant differences between the groups (1-year mortality $p < 0.001$). Mild frailty vs. non-frail HR was 2.47 (95 %CI 1.12–5.46), moderate frailty vs. non-frail HR was 6.93 (95 %CI 3.16–15.23), and advanced frailty vs. non-frail HR was 11.29 (95 %CI 3.54–36.03). The mean test time was 7 min.

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Conclusions: There was a strong correlation between frailty degree and mortality at 1, 6, and 12 months. FI-VIG is fast and easy-to-use in this setting. Its routine implementation in ED-SSUs could enable early risk stratification.

1. Introduction

Aging of the global population is increasing. In 2030, one in six people in the world will be over 65 years old. By 2050, two billion people are expected to be older than 65 years, and the number of people over 80 will have tripled, reaching 426 million. (United Nations Population, Division; WHO. Health & Ageing, 2022) This has several implications for health and social care planning (Clegg et al., 2013).

Frailty is the most complex expression of aging, and it is defined as a state of vulnerability and having a poor recovery rate following a stressful event, which leads to an increased risk of delirium, disability, hospitalization, and death. (Clegg et al., 2013; Song, Mititski & Rockwood, 2010; Theou, Campbell, Malone & Rockwood, 2018) Frail patients usually have high health care needs, (Blumenthal, Chernof, Fulmer & Lumpkin, 2016) and are a growing group in the emergency departments (ED) of hospitals. (Blumenthal, Chernof, Fulmer & Lumpkin, 2016; Brousseau, Dent & Hubbard, 2018)

Frailty assessment is a keystone in geriatric care. It is common in older patients in both hospital wards and in EDs, with reported prevalence rates between 21 and 62 %. (Ji, Michal Jazwinski & Kim, 2021; Turner & Clegg, 2014; Boreskie et al., 2022; Amblàs-Novellas, Martori & Espauella, 2018) In these two settings, frailty assessment is helpful for identifying the needs of patients and providing specific, tailored, and effective care. (Simon, Jauslin, Bingisser & Nickel, 2022; Djärv, Castrén, Martenson & Kurland, 2015; Fehlmann et al., 2022; Lucke, Mooijaart & Heeren, 2022) A large number of tools have been proposed for frailty assessment, each with different characteristics and limitations, and they have all been validated in different healthcare setting. (Boreskie et al., 2022; Amblàs-Novellas, Martori & Espauella, 2018) Despite this, frailty assessment is not routinely performed in ED. (Elliott, Taub & Banerjee, 2021; Kaeppli, Rueegg & Dreher-Hummel, 2020; O’Caoimh et al., 2020; Jørgensen & Brabrand, 2017; Elliott, Phelps, Regen & Conroy, 2017; Lewis, Dent & Alkhoury, 2019; O’Caoimh, Costello & Small, 2019) Barriers include the lack of ED clinical guidelines on frailty as well as the unfeasibility of conducting the assessment in a stressed setting.

Short Stay Units (SSU) are emergency support hospitalization units, which are useful for avoiding or reducing admissions. (Cosco, Best & Davis, 2021; Puig-Campmany, Blázquez-Andión, & Ris-Romeu, 2020; Alonso & Escudero, 2010) The admission criteria includes patients with medical pathology, a clear diagnosis, or a stable condition that does not require close monitoring or invasive treatment, and with an expected length of stay under 72 h. (Puig-Campmany, Blázquez-Andión, & Ris-Romeu, 2020; Alonso & Escudero, 2010; Sánchez-Marcos, Jacob & Llorens, 2022; González Armengol, Fernández Alonso & Martín Sánchez, 2009) Over the years, the clinical profile of patients admitted to SSUs has changed significantly as a result of a change in the age demographic. (Sánchez-Marcos, Jacob & Llorens, 2022) Patients admitted to an SSU are now older, and they have more comorbidities and polypharmacy. Frailty assessment in an SSU may now be useful, then, but it is not routinely used, and, indeed, we did not find any work in which frailty has been explored in this setting. SSU-EDs are units with a heavy workload, and there are no recommendations on the best tools to assess frailty in this particular setting.

The Frail-VIG index (FI-VIG (VIG is the Spanish/Catalan abbreviation for Comprehensive Geriatric Assessment)) is a frailty index (FI) developed by Amblàs et al. (C3RG, Chronicity Research Group of Central Catalonia), which offers the possibility of conducting a rapid CGA of individuals as well as calculating their grade of frailty, and which was initially validated in a cohort of patients over 85 years of age in an Acute Geriatric Unit (UGA) (Amblàs-Novellas, Martori & Espauella, 2018).

The index consists of a 22-item deficit rating scale. As the authors have noted, the results describe a simple and quick tool (it is completed in 5–10 min) with an excellent discriminative and predictive capacity in relation to mortality, and it performs a multidimensional assessment of the patient.

The scale has subsequently been validated in the context of intermediate care or health care hospitals (Amblàs Novellas et al., 2022; Amblàs-Novellas et al., 2017) as well as in the community setting with the same results. The authors keep it available in different languages and free of charge at <https://www.c3rg.com/index-fragil-vig>.

We think that this tool, which addresses more dimensions than other shorter tools recommended in ED, even though it requires a little more time, is applicable in SSUs and can provide significant clinical value. The aim of our study is to analyze the utility of FI-VIG in a new scenario— an ED-SSU.

2. Materials and methods

An observational, single-center, prospective cohort study was conducted in the SSU of the ED of the Hospital de la Santa Creu i Sant Pau (Barcelona, Spain), a tertiary and university urban hospital with a 550-bed center. The SSU in this hospital has 36 beds, reporting to the ED, and it had 2243 admissions in 2021.

The admission criteria in the SSU includes patients with a medical pathology but with a stable condition that does not require close monitoring or invasive treatment, and the expected length of stay should be under 72 h. The most frequent diagnoses are heart failure, acute chronic lung disease, urinary tract infection, respiratory infections, pyelonephritis, contusions, and non-surgical fractures of the elderly, among others.

The study was approved by the Clinical Research Ethics Committee under sponsor code IIBSP-FRA-2020–74. The CEIC considered the request for informed consent unnecessary because it was a registry of a validated scale and a non-interventional study. All patients admitted to the SSU were over 65 years old between March 1, 2021 and April 30, 2021, and they were consecutively included. Due to the characteristics of the study, and since it was an preliminary exploratory trial, with the aim of obtaining an overview of the population and collecting baseline data, a specific sample size was not established due to the lack of previous information or the novel nature of the research topic. Patients were included consecutively for 2 months, which was considered a reasonable period to obtain a representative sample based on the availability and accessibility of the participants. Only patients admitted for end-of-life care treatment were excluded from the study. After admission, patients were followed up for one year. Follow-up was performed by consultation with the Shared Health Record of Catalonia (HC3) and comprised a telephone call to the patient or carer after 12 months. There was no loss to follow-up.

The research team consisted of two attending physicians from the ED, the SSU chief nurse, and four nurses. FI-VIG support was used (available at <https://en.c3rg.com/index-fragil-vig>). After initial training by the principal investigator, one of the nurses assessed FI-VIG within the first 24 h of admission, taking into account, as determined by the index, the patient’s situation in the 30 days prior to admission.

Based on the FI-VIG <https://en.c3rg.com/index-fragil-vig>, patients were categorized into non-frail (< 0.2), mild frailty (0.2–0.36), moderate frailty (0.36–0.55), and advanced frailty (> 0.55).

The study variables were demographic and administrative data (date of birth, sex, date of admission to the short-stay unit, discharge date from the unit, and reason for discharge) as well as clinical data

(comorbidities, functional and cognitive status, social status, polypharmacy, and geriatric syndromes).

Following the methodology recommended by the authors of the scale, the binary variables were scored as "0" for absence and "1" for presence of deficits. Money management, telephone use, and medication management were assessed as instrumental activities of daily living. Weight loss of more than 5 % in 6 months was assessed as a nutritional marker; the presence of depressive syndrome, insomnia, and anxiety were assessed as emotional markers; and the presence of social vulnerability was assessed as a social marker. The presence of pain and dyspnea were considered as symptoms that met the severity criteria. Delirium, falls, ulcers, polypharmacy, and dysphagia were assessed as geriatric syndromes. Finally, the existence of chronic diseases was recorded as "1", and in the case of advanced chronic disease, according to the NECPAL Test (*NECesidades PALiativas* in Spanish, palliative needs), (Gómez-Batiste, Martínez & Blay, 2013) 2 points were assigned. In relation to ordinary variables, the Barthel index (Mahoney & Barthel, 1965) was used in four categories according to the absence of dependence or mild, moderate–severe, or severe dependence. Cognitive impairment was classified as 0 points with no impairment, 1 point was classed as mild/moderate impairment, and 2 points classed as severe/very severe impairment. Mortality was monitored at admission, at 1 month and 6 months, and then, finally, at 1 year through HC3 and telephone calls.

The result of the FI-VIG of each patient was not communicated to the healthcare team in order not to modify clinical practice or perform any intervention at this stage of the study.

Categorical variables were described as the frequency and the percentage of the available data while quantitative variables were described as the mean and standard deviation (SD). Descriptive statistics of the variables analyzed were performed using SPSS. Statistical significance (95 % confidence interval/ $p < 0.05$) for the variables between patients alive/dead was determined by means of mean contrasts (for quantitative variables) and proportion contrasts (for qualitative variables). For survival analysis, the log-rank test was used to compare survival curves according to the FI-VIG value and ROC curve analysis in order to determine the prognostic capacity of FI-VIG for 12-month mortality.

3. Results

3.1. Descriptive analysis of the cohort

- Of the 501 patients admitted to the SSU during the study period, 323 were over 65 years old. Of these, 21 had been admitted for end-of-life care and were excluded. A total of 302 patients were included in the study, whose mean age was 83 years (range 65–101), and 56 % of them were women ($n = 169$). A total of 5 % of the patients ($n = 15$) lived in a nursing home.
- A total of 60.9 % of the patients had independence regarding the basic activities of daily living (ADLs, $n = 184$). Mild–moderate dependence for ADLs was observed in 23.5 % ($n = 71$), moderate–severe in 10.3 % of patients ($n = 31$), and absolute dependence in 5.3 % ($n = 16$). Mild–moderate cognitive impairment $GDS < 5$ ($n = 44$) and moderate–severe cognitive impairment $GDS > 6$ ($n = 6$) accounted for 14.6 % of patients.
- In-hospital mortality of the cohort was 3 % ($n = 9$), and at 1 month it was 12.3 % ($n = 37$), at 6 months it was 20.6 % ($n = 62$), and at 1 year it was 23.2 % ($n = 70$).

3.2. Frailty assessment

- Characteristics of patients admitted to the SSU according to their frailty are presented in Table 1 and Table 2.
- Of the 302 patients included, 128 (42.4 %) were categorized as non-frail and 174 (57.6 %) were categorized as frail. Of these, 111 (36.8

Table 1

Characteristics of patients admitted to the SSU.

Total population	Non-frail N = 128 (42 %)	Frail N = 174 (58 %)
Mean age (years, mean \pm SD)	80 \pm 7	85 \pm 7
Women (n,%)	63 (20.9 %)	106 (35.1 %)
Men (n,%)	65 (21.5 %)	68 (22.5 %)
Barthel	86 \pm 12	50 \pm 14
Dementia (n,%)	3 (1 %)	47 (15.6 %)
Dementia GDS > 6 (n,%)	0	6 (2 %)

^cNon-frailty: Frail-VIG Index < 0.2; Frailty: Frail-VIG Index \geq 0.2. GDS: global deterioration scale.

Table 2

Patient's characteristics.

	Total (N = 302)	Frail (N = 174)	No Frail (N = 128)	p
Comorbidities N (%)				
Depression	63 (20.9)	51 (29.3)	12 (9.4)	0.001
Cognitive impairment	50 (16.6)	47 (27)	3 (2.3)	0.001
Delirium	21 (7)	21 (100)	0	0.001
Polipharmacy	230 (76.2)	156 (89.7)	74 (57.8)	0.001
Malnutrition	35 (11.6)	26 (14.9)	9 (7)	0,029
Cardiovascular disease	162 (53.6)	109 (62.6)	53 (41.5)	0.005
Respiratory disease	100 (33.1)	71 (40.8)	29 (22.7)	0.013
Neurological disease	53 (17.5)	46 (26.4)	7 (5.5)	0.001
Kidney disease	114 (37.7)	93 (53.4)	21 (16.4)	0.001
Digestive disease	34 (11,3)	29 (16.7)	5 (3.9)	0.001
Neoplastic disease	25 (8.3)	18 (10.3)	7 (5.3)	0.179
Barthel Index N (%)				
Mild dependence	71 (23.5)	60 (34.5)	11 (8.6)	0.001
Moderate dependence	31 (10.3)	31 (17.8)	0	0.001
Severe dependence	16 (5.3)	16 (5.3)	0	0.001

%) had mild frailty, 52 (17.2 %) had moderate frailty, and 11 (3.6 %) had advanced frailty.

3.3. Time of test execution

- The mean running time of the index was 7 min per patient.

3.4. Mortality analysis

- Table 3 shows the differences in the percentage of mortality between the frailty groups.

Table 3

Mortality of patients according to frailty degree.

	Non-frail	Mild frailty	Moderate Frailty	Advanced Frailty	p
Women N (%)	63 (49.2 %)	65 (58.6 %)	33 (63.5 %)	8 (72.7 %)	0.584
Age	80 \pm 7	84 \pm 7	86 \pm 7	87 \pm 6	0.256
In-hospital Mortality	0 (0)	2 (1.8 %)	5 (9.6 %)	2 (18.2 %)	0.024
30-day Mortality	8 (6.3 %)	12 (10.8 %)	13 (25 %)	4 (36.4 %)	0.020
6-month Mortality	13 (10.2 %)	25 (22.5 %)	18 (34.6 %)	5 (54.5 %)	0.045
12-month Mortality	16 (12.5 %)	25 (22.5 %)	22 (42.3 %)	7 (63.6 %)	0.003

Table 3. Based on the Frail-VIG index, patients were classified into non-frail (< 0.2), mild frailty (0.2–0.36), moderate frailty (0.36–0.55), and advanced frailty (0.55–0.7).

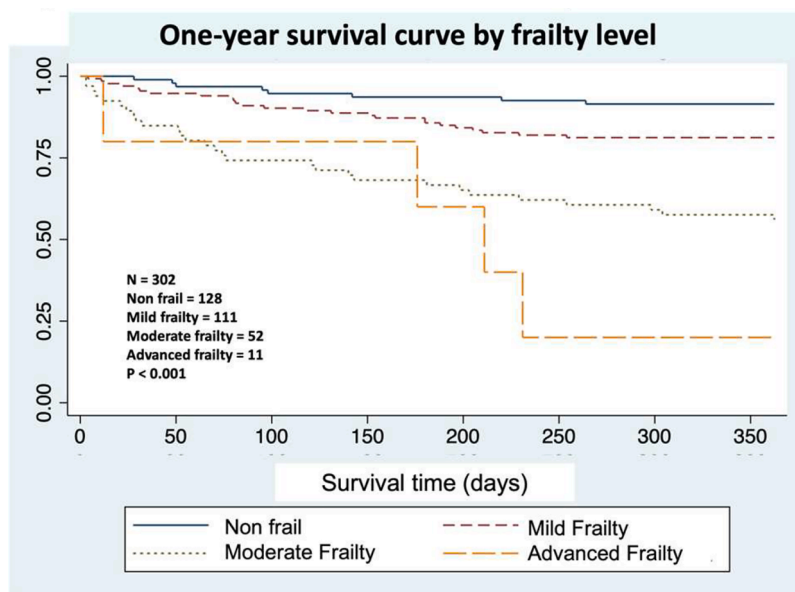


Fig. 1. Correlation between one-year survival and different degrees of frailty. One-year survival curve by frailty level. Different frailty groups present significant differences in mortality at one year (Hazard Ratio Mild Frailty vs. Non-Frail HR 2.47 CI95 % 1.12–5.46; Moderate Frailty vs Non-Frail HR 6.93 CI95 % 3.16–15.23; Advanced Frailty vs Non-Frail HR 11.29 CI95 % 3.54–36.03).

- Fig. 1 shows the correlation between mortality at 1 year and FI-VIG using the log-rank test, comparing the survival curves according to the value of FI-VIG, and discretized by the previously described intervals.

3.5. Model usefulness

- A ROC analysis was performed at 12 months to check the usefulness of the model in the population studied (Fig. 2). The ROC area under the curve was 0.7120 (95 %CI 0.6423–0.7816).
- Hazard Ratio in relation to degrees of frailty is shown in Table 4.

4. Discussion

Our work shows that FI-VIG is a reliable and accurate tool for frailty

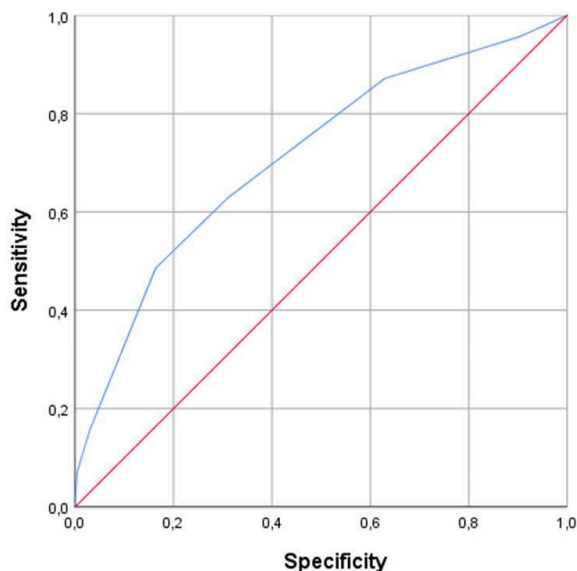


Fig. 2. ROC curve analysis to determine the prognostic capacity of FI-VIG for 12-month mortality. The Area under ROC curve was 0,71 (IC95 % 0,64–0,78).

Table 4
Hazard Ratio in relation to degrees of frailty.

	Hazard Ratio
Mild frailty vs No-Frail	2,47 IC95 % 1.12–5.46
Moderate frailty vs No-Frail	6,93 IC95 % 3.16–15.23
Advanced frailty vs No-Frail	11,29 IC95 % 3.54–36.03

Table 4. Based on the Frail-VIG index, patients were classified into non-frail (< 0.2), mild frailty (0.2–0.36), moderate frailty (0.36–0.55), and advanced frailty (0.55–0.7).

screening in SSU, with a similar performance to that already demonstrated in other settings. Although FI-VIG has been validated in other healthcare settings, it's essential to validate its performance specifically in the SSU setting to ensure its relevance and accuracy in this context. FI-VIG correlates frailty status with mortality, and our study shows that this correlation is also valid for an SSU setting. Moreover, the performance mean time was 7 min, which confirms that it is a feasible and easy-to-use scale in this unit.

It is well known that frailty status leads to progressively higher mortalities during hospital admission, as well as at 30 days, 6 months, and 1 year after discharge. Although the patients admitted to the SSU showed different characteristics compared with the population in which the FI-VIG was initially validated, the results of this study demonstrate that the FI-VIG is also applicable in an SSU setting. Although the ROC curve results are slightly lower than those obtained in the pivotal study, in this patient cohort, FI-VIG value is accurate for predicting 12-month mortality.

In our study, the mean cohort age was 83 years old, and almost 40 % of the patients had some degree of disability and 16.5 % had dementia. As in other SSUs in our country, the population is selected a priori by the criteria that determine the decision of admission to this unit, and the demographic characteristics of our cohort are similar to those reported in the recent literature. (Amblàs-Novellas, Murray & Espauella, 2016) Through FI-VIG application, we were able to determine that 57.6 % of the patients in our SSU had some degree of frailty, given that most classified as mild (63.8 %) or moderately (29.9 %) frail. These data are relevant since we have not found similar studies describing frailty features in an SSU. Despite being a previously selected population with an expected short hospital stay, our study revealed that in our SSU, there

was a large group of frail individuals in whom FI-VIG performance could offer a great opportunity for tailored interventions.

Systematically measuring frailty is undoubtedly useful in patient management (Amblàs Novellas et al., 2022). Different tools have been validated in different scenarios. The ED and the SSU are related settings, but the population served has different demographic, emergency level and disease characteristics. For this reason, ED recommendations about frailty assessment cannot simply be extrapolated to SSU. We haven't found any works that analyze or provide recommendations on frailty assessment in SSU.

In the SSU, FI-VIG turned out to be an accurate tool that should be incorporated in clinical practice. FI-VIG assigns to each patient a numerical score, allowing its categorization into different frailty degrees, which, in turn, correlate well with mortality. Its implementation time, which may be too long for an emergency situation, is very well adapted to the SSU setting. In addition, as it is a multidimensional scale, it is able to detect several deficits in frail patients that could be used as the base of a reglementary Comprehensive Geriatric Assessment (CGA) in a second step. (Amblàs-Novellas, Martori & Espauella, 2018; Sánchez-Marcos, Jacob & Llorens, 2022). This would allow prompt patient referral to expert teams in order to initiate interventions focused on reversing or preventing secondary risks. By doing this, it improves the prevention of incidental geriatric syndromes during admission in frail individuals, as a specific care plan can be designed early (i.e., early mobilization, identification and correct management of delirium, prevention of constipation and falls, careful pain management, avoidance of medication-related risks, and initiation of pharmaceutical care programs, among others). Finally, by frailty stratification, FI-VIG offers the chance for tailored interventions and therapeutic intensity for these patients. (Van Dam, Hoogendijk & Mooijaart, 2021; Juanes, Garin & Mangues, 2018; Amblàs-Novellas, Murray & Espauella, 2016)

The lack of clinical guidelines or consensus documents for frailty assessment in ED and SSU is a barrier. The busy environment, the short length of stay, and the emergency situation are difficulties for frailty assessment, which, combined with the lack of clear evidence on useful tools and their impact, are delaying the implementation of frailty assessment strategies in these settings. It is reasonable to assume that finding evidence on the best valid tool to use, will allow implementation of frailty assessment in the daily routine in this complex environments, improving patient's care, and our work sheds light on this issue.

Although is a pilot study, and further, multicenter, and more robust studies are needed, our work suggest that in an SSU, where stays are short and there is only a level degree of urgency, FI-VIG is adequate because it assesses several dimensions and has a reasonable test time. In other settings as ED, other scales that require less time and training as Clinical Frailty Scale (CSF), are appropriate for establishing rapid assessments although it values fewer dimensions (Fehlmann et al., 2022; Lucke, Mooijaart & Heeren, 2022; Elliott, Taub & Banerjee, 2021; Kaeppli, Rueegg & Dreher-Hummel, 2020). FI-VIG needs more time than CFS, but its execution time is reasonable and allows its inclusion in the SSU as a routine, involving a high value-added care. First, it could promote the prescription of simple interventions such as early mobilization, identification and correct management of delirium, prevention of constipation and falls, careful management of pain, prevention of medication-related risks that have an impact on patient health. Second, more complex and more targeted interventions would be possible, opening up a wide scope of possibilities.

Our study has some notable limitations. It is an exploratory single-center study, and contains a low number of patients with advanced frailty, probably due to the narrow admission criteria in an SSU. The consecutive inclusion of patients may introduce selection bias, although the number of frail patients is quite high, as the only exclusion criteria was that patient was admitted for end-of-life care. No descriptive analysis of associated diseases beyond the clinical data necessary to answer the items contained in FI-VIG, nor discharge destination, or length of stay were performed. However, frailty assessment with FI-VIG includes

several dimensions, including chronic and oncologic diseases, and, thus, these diseases that can impact on mortality are included in the frailty assessment itself. Our study is limited to frailty and mortality evaluation, and the absence of any analysis of the length of stay or the discharge destination is an obvious limitation. However, the study does have several strengths: it was designed as a prospective study, we recruited a large number of patients, and, lastly, frailty assessment was performed by a small and highly-trained research team.

Future research is needed for improving the findings generalizability, with multi-center studies with larger and randomized samples, and including patients with varying degrees of frailty. Also, longitudinal studies assessing the effectiveness of tailored interventions based on FI-VIG scores in improving patient outcomes and healthcare resource utilization could provide valuable insights into the practical application of the scale in clinical practice.

Finally, given the growing importance of frailty as an expanding public health problem, we believe that consensus documents on frailty assessment in ED and SSUs should be developed as soon as possible. The stay of older adults in these units is a window of opportunity for frailty assessment, in order to deliver an integrated care.

5. Conclusions

In conclusion, there is a strong correlation between the frailty degree measured with FI-VIG and mortality at 1, 6, and 12 months, and FI-VIG is a valid tool for systematic frailty identification in an ED SSU. It is a feasible and easy-to-use scale in this setting.

Its routine implementation in the SSU could enable early risk stratification to detect vulnerable patients with specific needs. Future research is need to strengthen of the utility of FI-VIG in guiding interventions and care plans for vulnerable patients in the SSU setting.

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Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee Clinical Research Ethics Committee of the IIB Sant Pau, code IIBSP-FRA-2020-74.

Informed consent statement

Patient consent was obtained in all cases, as requested by the Ethics Committee.

CRedit authorship contribution statement

Marta Blázquez-Andión : Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Josep Anton Montiel-Dacosta** : Writing – original draft, Validation, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Miguel Rizzi-Bordigoni** : Writing – original draft, Validation, Methodology, Formal analysis, Data curation. **Belen Acosta-Mejuto** : Writing – original draft, Validation, Supervision, Methodology, Investigation, Data curation. **Antoni Moliné-Pareja** : Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Formal analysis, Data curation. **Josep Ris-Romeu** : Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Mireia Puig-Campmany** : Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Funding

acquisition, Formal analysis, Conceptualization. Other contributors are Elena Gonzalez, Rosario Fraile, David Figueroa, Sergio Herrera, J.Leopoldo Higa, Gastón Fernández, data curation.

Declaration of Competing Interest

The authors declare no conflict of interest.

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