



Original Article

# Prevalence and Prognosis Impact of Frailty Among Older Adults in Cardiac Intensive Care Units

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## ABSTRACT

**Background:** Whether frailty, defined as a biological syndrome that reflects a state of decreased physiological reserve and vulnerability to stressors, may impact the outcomes of elderly patients admitted to a cardiac intensive care unit (CICU) remains unclear. We aimed to determine the prevalence of frailty and its impact on mortality in patients aged  $\geq 80$  years admitted to a CICU.

**Methods:** This prospective single-centre observational study was conducted among patients aged  $\geq 80$  years admitted to a CICU in a tertiary centre. Frailty was assessed using the Edmonton Frail Scale (EFS), which provides a score ranging from 0 (not frail) to 17 (very frail). The population was divided into 3 classes: EFS-score of 0-3, EFS-score of 4-6, and EFS-score  $> 7$ .

## RÉSUMÉ

**Contexte :** On ignore si la fragilité, définie comme un syndrome biologique reflétant une diminution des réserves physiologique et une vulnérabilité au stress, impacte le pronostic des sujets âgés admis en unité de soins intensifs cardiologiques (USIC). Notre objectif était de déterminer la prévalence de la fragilité et son impact sur la mortalité chez les sujets âgés de 80 ans ou plus admis en USIC.

**Méthodologie :** Il s'agit d'une étude prospective monocentrique observationnelle conduite sur les patients de 80 ans ou plus admis en USIC dans un centre tertiaire. La fragilité a été évaluée par l'échelle de fragilité d'Edmonton (EFS) qui donne un score allant de 0 (pas fragile) à 17 (très fragile). La population a été divisée en 3 classes : score EFS de 0 à 3, score EFS de 4 à 6, et score EFS de  $> 7$ .

Life expectancy is increasing, and with this advancement, the prevalence of cardiovascular disease (CVD) rises in association:  $> 85\%$  of patients aged  $> 85$  years live with some form of CVD.<sup>1</sup> In France, according to the national health insurance data, around 43% of men and 28% of women aged  $\geq 75$  years have some form of CVD.<sup>2</sup> As a result, the prevalence of older patients in cardiac intensive care units (CICUs) is high: according to French Registry of Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI) data, 29% of patients admitted to a CICU in 2015 for acute coronary syndrome were aged  $\geq 75$  years.<sup>3</sup> Octogenarians, and nonagenarians, are therefore frequently admitted to CICUs.<sup>4</sup> This proportion of elderly people in CICUs is

predicted to increase in the next decades, as analyses by the French National Institute for Statistical and Economic Studies (INSEE) predict for France that the proportion of the population aged  $\geq 75$  years—which represented 9.3% of the population on January 1st 2019—will double by 2080.

Age represents a strong prognostic factor for poor short- and long-term clinical outcomes for patients admitted to the ICU.<sup>5</sup> However, aside from comorbidities that vary from patient to patient, age alone is a poor indicator of physiological reserve, owing to interindividual variability in aging. To help determine the level of reserve, an assessment of frailty in older people could be beneficial. The concept of frailty, defined as a biological syndrome that reflects a state of declined physiological reserve and vulnerability to stressors,<sup>6,7</sup> has become more familiar to cardiologists over the past few years. Well respected European and North American cardiac societies recently published position papers focusing on elderly patients presenting with acute CVD.<sup>8,9</sup> They suggest that frailty be assessed in the CICU, but there is no consensus on what is the best tool for this evaluation, which is even more difficult to conduct in the setting of acute CVD. The

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**Ethics Statement:** The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

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See page 1017 for disclosure information.

**Results:** A total of 199 patients were included, and median follow-up duration was 365 days. The mean age was 84.8 years, and 50 patients (25.1%) died during the follow-up period. In all, 45 (22.6%), 60 (30.2%), and 94 patients (47.2%) had an EFS-score of 0-3, 4-6, and  $\geq 7$ , respectively. The all-cause mortality rate was 4.4%, 27.1%, and 37.2% in the 0-3, 4-6, and  $\geq 7$  EFS-score groups, respectively ( $P < 0.001$ ). After multivariate analysis, frailty status remained associated with all-cause mortality: hazard ratio was 2.60 (95% confidence interval 0.54-12.45) within the 4-6 EFS-score group, and 5.46 (95% confidence interval 1.23-24.08) within the  $\geq 7$  EFS-score group.

**Conclusions:** Frailty is highly prevalent in older adults admitted to the population hospitalized in a CICU and represents a strong prognostic factor for 1-year all-cause mortality.

Edmonton Frail Scale (EFS) is a simple tool based on series of basic questions or tasks that gives a global evaluation of frailty,<sup>10,11</sup> and previous data suggest that it could be suitable and relevant in the setting of hospitalization in a CICU, in particular in those admitted with acute coronary syndrome.<sup>12</sup>

The aim of the present analysis was to assess the prevalence of frailty, using the EFS, and its impact on all-cause mortality at 1-year follow-up among patients aged  $\geq 80$  years admitted to a CICU in a tertiary centre.

## Materials and Methods

### Population

From November 2018 to November 2019, we prospectively and consecutively recruited 199 patients aged  $\geq 80$  years who were referred to our tertiary care centre at the University Hospital of Toulouse and admitted to the CICU. We did not include patients who were admitted for monitoring after a scheduled interventional procedure (eg, post-transcatheter aortic valve implantation, post-Mitraclip (Abbott, Abbott Park, Illinois) implantation, post-pacemaker extraction). The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

### Data collection

Age, socioeconomic variables, and cardiovascular risk factors were obtained through standardized face-to-face interviews conducted by a cardiologist. For smoking status, patients were classified as either smokers (current or past) or nonsmokers. The final diagnosis of the pathology responsible for the index hospitalization was recorded from the medical file at admission, or later if initially unclear. Medical history was obtained through a standardized questionnaire and through checking of the patient's file. The history included the following: coronary heart disease, heart failure, atrial fibrillation, pacemaker implantation, implanted cardioverter defibrillator, valvular heart disease, peripheral vascular disease, transient ischemic attack or stroke, severe chronic kidney disease (defined as an estimated glomerular filtration rate  $< 30$  mL/min per  $1.73$  m<sup>2</sup>), chronic obstructive pulmonary disease, history of cancer (past or current), and dementia.

**Résultats :** Cent quatre-vingt-dix-neuf patients ont été inclus avec un suivi médian de 365 jours. L'âge moyen était de 84,8 ans. Cinquante patients (25,1 %) sont décédés au cours de la période de suivi. Quarante-cinq patients (22,6 %) avaient un score EFS de 0 à 3, 60 patients (30,2 %) avaient un score EFS de 4 à 6 et 94 patients (47,2 %) avaient un score EFS de  $\geq 7$ . Les taux de mortalité toutes causes étaient de 4,4 % dans la classe de score EFS de 0 à 3, 27,1 % dans la classe de score EFS de 4 à 6 et 37,2 % dans la classe de score EFS de  $\geq 7$ , ( $p < 0.001$ ). En analyse multivariée, la fragilité demeurait associée avec la mortalité toutes causes : le rapport de risques instantanés (RRI) était à 2,60 (intervalle de confiance [IC] à 95 % [0,54 - 12,45]) dans la classe de score EFS de 4 à 6, et le RRI était à 5,46 (IC à 95 % [1,23 - 24,08]) dans la classe de score EFS de  $\geq 7$ .

**Conclusion :** La fragilité est fortement prévalente dans la population des sujets âgés admis en USIC et constitue un facteur pronostique fort de mortalité toutes causes à un an.

Cardiovascular drugs at admission and discharge were also recorded. Body mass index was calculated using the standard formula: weight divided by height squared (kg/m<sup>2</sup>). New York Heart Association class, heart rate, and blood pressure were assessed at admission.

At admission to the CICU, an electrocardiogram and transthoracic echocardiography were performed. The left ventricular ejection fraction was then measured by transthoracic echocardiography using the biplane Simpson method. Right ventricular dysfunction (TAPSE) was defined by a tricuspid annular plane systolic excursion (systolic excursion of the tricuspid ring) of  $< 14$  mm. Severe aortic stenosis was defined by a mean gradient  $\geq 40$  mm Hg and/or an aortic valve area  $\leq 0.6$  cm<sup>2</sup>/m<sup>2</sup>. A blood sample was taken systematically at admission to determine hemoglobin, NT pro-brain natriuretic peptide, C-reactive protein, and creatinine levels. Estimated glomerular filtration rate was determined using the Cockcroft and Gault formula. An acute renal failure episode during hospitalization was defined as an increase of at least 50% in the creatinine serum level, as compared to baseline measure.

### The EFS

The EFS (Table 1) is a validated tool used to determine a patient's level of frailty as a score ranging from 0 (not frail) to 17 (very frail) based on a series of basic questions or tasks that provides a global evaluation.<sup>10,11</sup> Obtaining the score is fast ( $< 5$  minutes) and can be done by a non-geriatric specialist. The EFS was performed by a physician as soon as possible after admission into our centre. Given that strict bedrest is systematically prescribed at arrival, the timed "get up and go" test was performed to assess a patient's mobility when this restriction was removed. As described in a previous study using this test in the setting of acute coronary syndrome,<sup>12,13</sup> 3 categories were established based on the calculated EFS score: 0-3 points, 4-6 points, and  $\geq 7$  points.

### Primary endpoint

Our primary endpoint was all-cause mortality. Patients' vital status was obtained at the 1-year follow-up. Vital status (and date of death, when applicable) was obtained by

**Table 1. Edmonton Frail Scale**

Frailty domain	Item	0 points	1 point	2 points
Cognition	Imagine that this pre-drawn circle is a clock. I would like you to place the numbers in the correct position then place the hands to indicate a time of “ten after eleven”	No errors	Minor spacing errors	Other errors
General health status	In the past year, how many times have you been admitted to a hospital?	0	1-2	> 2
	In general, how would you describe your health?	Excellent, very good, good	Fair	Poor
Functional independence	With how many of the following activities do you require help? (meal preparation, shopping, transportation, dialling telephone, housekeeping, laundry, managing money, taking medications)	0-1	2-4	5-8
Social support	When you need help, can you count on someone who is willing and able to meet your needs?	Always	Sometimes	Never
Medication use	Do you use five or more different prescription medications on a regular basis?	No	Yes	
	At times, do you forget to take your prescription medications?	No	Yes	
Nutrition	Have you recently lost weight such that your clothing has become looser?	No	Yes	
Mood	Do you often feel sad and depressed?	No	Yes	
Continence	Do you have a problem with losing control of urine when you don't want to?	No	Yes	
Functional performance (timed get up and go test)	I would like you to sit in this chair with your back and arms resting. Then, when I say “GO,” please stand up and walk at a safe and comfortable pace to the mark on the floor (3 meters away), return to the chair, and sit down.	0-10 s	11-20 s	> 20 s, patient unwilling or requires assistance
Totals				/17 points

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contacting patients, their families, their general practitioners, their cardiologists, and the town hall in their place of birth.

### Statistical analyses

Statistical analysis was performed on STATA statistical software, release 14.1 (Stata Corporation, College Station, TX). Continuous variables are summarized as means and standard deviations for normal distributions, and as medians and interquartile ranges when distributions were not normally distributed. Categorical variables are presented as proportions. In univariate analysis, categorical variables were compared with  $\chi^2$  test results (or results of Fischer's exact test when necessary). The Student *t* test or an analysis of variance were used to compare the distribution of continuous normally distributed data according to categorical variables. The Mann-Whitney and Kruskal-Wallis tests were used to compare ranges of continuous non-normally distributed variables according to categorical variables. A *P* value of < 0.05 was considered statistically significant.

Cumulative survival of patients with EFS scores of 0-3, 4-6, and  $\geq 7$  was determined by the Kaplan-Meier method and compared using the log rank test. Univariate and multivariate Cox regression models were used to investigate the association between variables and mortality during the follow-up, and to determine hazard ratios with 95% confidence intervals (CIs) for mortality.

The impact of the EFS score on mortality was initially assessed by determining a crude hazard ratio using a Cox model; then a model adding age and gender to the EFS score was built; and, last, all variables associated with a *P*-value < 0.20 in univariate analysis were introduced in a multivariate Cox model to obtain a complete model.

Afterward, a backward procedure was applied to assess the variables that were significantly and independently associated with high mortality (*P* < 0.05). However, diabetes, diagnosis at admission, hemoglobin, and severe renal failure—which were not significantly associated with mortality—were kept in the multivariate Cox analysis, as these variables are well described prognostic factors in the literature. The proportional-hazard assumption was tested for each covariate by the

**Table 2. Population baseline characteristics**

Characteristic	All (n = 199)	EFS score 1-3 (n = 45)	EFS score 4-6 (n = 60)	EFS score ≥ 7 (n = 94)	P
Age, y (mean ± SD)	84.8 ± 3.8	83.5 ± 3	85.2 ± 3.7	85.8 ± 3.6	<b>0.001</b>
Male	116 (58.3)	33 (73.3)	34 (56.7)	49 (52.1)	0.06
Marital status					
Married	120 (60.3)	31 (68.9)	40 (66.7)	49 (52.1)	0.08
Widowed	55 (27.6)	10 (22.2)	17 (28.3)	28 (29.8)	
Single	24 (12.1)	4 (8.9)	3 (5.0)	17 (18.1)	
Place of residence					
At home	191 (96.0)	44 (97.8)	59 (98.3)	88 (93.6)	0.27
In Institution	8 (4.0)	1 (2.2)	1 (1.7)	6 (6.4)	
Assistance at home	93 (47.9)	13 (28.9)	26 (43.3)	54 (60.7)	<b>0.002</b>
Cardiovascular risk factors					
Tobacco (past or current)	52 (26.1)	16 (35.6)	17 (28.3)	19 (20.2)	0.14
Dyslipidaemia	80 (40.2)	17 (35.8)	21 (35.0)	42 (44.7)	0.45
Diabetes	61 (30.7)	8 (17.8)	17 (28.3)	36 (38.3)	<b>0.04</b>
Hypertension	154 (77.4)	30 (66.7)	47 (78.3)	77 (81.9)	0.13
Cardiovascular past medical history					
Previous CHD	54 (27.1)	9 (20.0)	13 (21.7)	32 (34.0)	0.11
Previous HF	32 (16.1)	4 (8.9)	9 (15.0)	19 (20.2)	0.22
Previous AF	64 (32.2)	6 (13.3)	17 (28.3)	41 (43.6)	<b>&lt; 0.001</b>
Previous pacemaker	15 (7.5)	2 (4.4)	2 (3.3)	11 (11.7)	0.10
Previous ICD	3 (1.5)	1 (2.2)	0 (0.0)	2 (2.1)	0.51
Previous VHD	31 (15.6)	5 (11.1)	7 (11.7)	19 (20.2)	0.23
Previous PVD	18 (9.1)	1 (2.2)	9 (15.0)	8 (8.5)	0.07
Noncardiovascular past medical history					
Stroke/TIA	22 (11.1)	4 (8.9)	7 (11.7)	11 (11.7)	0.87
CKD	27 (13.6)	4 (8.9)	3 (5.0)	20 (21.3)	<b>0.009</b>
COPD	18 (9.1)	2 (4.4)	8 (13.3)	8 (8.5)	0.28
Neoplasia	29 (14.6)	7 (15.6)	9 (15.0)	13 (13.8)	0.95
Dementia	4 (2.0)	0 (0.0)	0 (0.0)	4 (4.3)	0.14
Cardiovascular drugs at admission					
Antiplatelet therapy	85 (42.7)	19 (42.2)	26 (43.3)	40 (42.6)	0.99
Anticoagulant	54 (27.3)	5 (11.4)	15 (25.0)	34 (36.2)	<b>0.009</b>
β-blockers	80 (40.2)	12 (26.7)	20 (33.3)	48 (51.1)	<b>0.01</b>
Statin	76 (38.9)	14 (31.8)	26 (43.3)	36 (38.3)	0.49
ACEIs or ARBs	100 (50.3)	25 (55.6)	31 (51.7)	44 (46.8)	0.60
Aldosterone blockers	10 (5.0)	0 (0)	5 (8.3)	5 (5.3)	0.15
Calcium blockers	74 (37.2)	18 (40.0)	19 (31.7)	37 (39.4)	0.57
Amiodarone	26 (13.1)	2 (4.4)	7 (11.7)	17 (18.1)	0.07
Thiazide diuretics	25 (12.6)	2 (4.4)	8 (13.3)	15 (16.0)	0.15
Loop diuretics	69 (34.7)	6 (13.3)	18 (30.0)	45 (47.9)	<b>&lt; 0.001</b>

Values are n (%), unless otherwise indicated. Boldface indicates significance.

ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; CHD, coronary heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; EFS, Edmonton Frail Scale; HF, heart failure; ICD, implanted cardioverter defibrillator; PVD, peripheral vascular disease; SD, standard deviation; TIA, transient ischemic attack; VHD, valvular heart disease.

“log-log” method, plotting  $(-\ln[-\ln\{\text{survival}\}])$  for each category of a nominal covariate, vs  $\ln(\text{analysis time})$ .

## Results

A total of 199 patients aged  $\geq 80$  years were included in our 12-month study (November 2, 2018 to November 2, 2019). The median duration of follow-up was 365 days (interquartile range: 318-365 days). During the follow-up period, 50 patients died (25.1%).

The mean age was 84.8 (+/-3.8) years. Among the 199 patients, 45 (22.6%), 60 (30.2%), and 94 (47.2%) had an EFS score of 0-3, 4-6, and  $\geq 7$ , respectively. The patients' baseline characteristics according to their frailty level are presented in Table 2. Patients with the highest frailty scores were older and had more comorbidities (diabetes, atrial fibrillation, chronic kidney disease). They were more likely to be treated with β-blockers, loop diuretics, and anticoagulant therapy. There tended to be a higher prevalence of

women among the frailest groups. Logically, frail patients were more likely to benefit from assistance at home via daily nurse visits or a regular home help service ( $P = 0.002$ ). No significant differences were observed regarding marital status or residence location.

The main reasons for admission were acute coronary syndrome (41.7%), conductive disorders (19.6%), and acute heart failure (14.6%); 24.1% of patients had other pathologies. No differences were observed regarding the mode of arrival at the hospital (ambulance, emergency medical assistance service, or patients' own means) or diagnosis at admission. Hemodynamic presentation (heart rate, blood pressure, New York Heart Association classification) and echocardiographic data did not differ among the 3 frailty-level groups. Frail patients were more likely to present a non-sinus rhythm (ie, supra-ventricular;  $P = 0.005$ ) and had worse renal function at admission. Clinical and paraclinical data recorded at admission are listed in Table 3.

**Table 3. Clinical and paraclinical data at admission**

Admission data	All (n = 199)	EFS score 1-3 (n = 45)	EFS score 4-6 (n = 60)	EFS score $\geq$ 7 (n = 94)	P
Origin at admission					0.50
Medical ambulance service	35 (17.6)	12 (26.7)	8 (13.3)	15 (16.0)	
Emergency department	71 (35.7)	12 (26.7)	23 (38.3)	36 (38.3)	
Non-PCI capable hospital	58 (29.2)	15 (33.3)	18 (30.0)	25 (26.6)	
Direct CICU admission	35 (17.6)	6 (13.3)	11 (18.3)	18 (19.1)	
Diagnostic at admission					0.056
Acute coronary syndrome	83 (41.7)	27 (60.0)	24 (40.0)	32 (34.0)	
Pulmonary oedema	29 (14.6)	3 (6.7)	6 (10.0)	20 (21.3)	
Conduction disturbance	39 (19.6)	7 (15.6)	13 (21.7)	19 (20.2)	
Other	48 (24.1)	8 (17.8)	17 (28.3)	23 (24.5)	
Clinical presentation at admission					
Heart rate (bpm)	73 $\pm$ 22	74 $\pm$ 20	73 $\pm$ 21	74 $\pm$ 24	0.96
Systolic blood pressure (mm Hg)	131 $\pm$ 25	137 $\pm$ 21	129 $\pm$ 26	128 $\pm$ 25	0.17
Diastolic blood pressure (mm Hg)	74 $\pm$ 14	78 $\pm$ 12	74 $\pm$ 12	73 $\pm$ 16	0.13
Body mass index (kg/m <sup>2</sup> )	25.5 $\pm$ 3.7	25.3 $\pm$ 3.5	26 $\pm$ 3.5	25.4 $\pm$ 4	0.48
Sinus rhythm	137 (68.8)	39 (86.7)	42 (70.0)	56 (59.6)	<b>0.005</b>
NYHA stage					0.11
1	120 (60.3)	32 (71.1)	37 (61.7)	51 (54.3)	
2	14 (7.0)	1 (2.2)	4 (6.7)	9 (9.6)	
3	35 (17.6)	10 (22.2)	7 (11.7)	18 (18.2)	
4	30 (15.1)	2 (4.4)	12 (20.0)	16 (17.0)	
Biology					
Hemoglobin (g/dL)	12.3 $\pm$ 1.9	12.6 $\pm$ 1.9	12.6 $\pm$ 1.8	12 $\pm$ 2	0.09
CRP (mg/l)	12 (3-53)	9 (3-27)	8 (2-52)	22 (4-62)	0.11
NT pro-BNP (pg/mL)	3577 (1598-9650)	3244 (999-7547)	3245 (806-5444)	4680 (2800-13,000)	0.07
eGFR (Cockcroft & Gault)	47 $\pm$ 22	46 $\pm$ 19	54 $\pm$ 24	44 $\pm$ 22	0.02
Echocardiographic data					
LVEF	50 $\pm$ 13	52 $\pm$ 13	49 $\pm$ 12	49 $\pm$ 13	0.37
LVEF > 50%	124 (62.3)	29 (64.4)	37 (61.7)	58 (61.7)	0.62
LVEF 35%-50%	49 (24.6)	13 (28.9)	13 (21.7)	23 (24.5)	
LVEF < 35%	26 (13.1)	3 (6.7)	10 (16.7)	13 (13.8)	
Right ventricular systolic dysfunction	22 (11.1)	2 (4.4)	9 (15)	11 (11.7)	0.22
Severe aortic stenosis	21 (10.6)	2 (4.4)	7 (11.7)	12 (12.8)	0.31

Values are n (%), mean  $\pm$  standard deviation, or median (interquartile range), unless otherwise indicated. Boldface indicates significance.

EFS, Edmonton Frail Scale; CICU: Intensive Care Unit; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LVEF, left ventricular ejection fraction; NT pro-BNP, NT pro-brain natriuretic peptide; NYHA, New York Heart Association Classification; PCI, percutaneous coronary intervention; SD, standard deviation.

Sixteen (8%) and 1 (0.5%) patients died or had a stroke, respectively, during the hospitalization period. Mortality and stroke occurrence did not significantly differ among the frailty groups ( $P = 0.26$  and  $P = 0.56$ , respectively). During the same period, noncardiovascular complications were frequent: 59 patients (29.7%) had acute renal failure, 19 (9.6%) had sepsis, 12 (6.0%) had significant bleeding (Bleeding Academic Research Consortium (BARC) scale  $\geq$  3), and 5 (2.5%) presented delirium. Acute renal failure and sepsis were more frequent among the frailest patients ( $P = 0.04$  and  $P = 0.02$ , respectively). However, length of stay did not differ among the 3 frailty-level groups. In-hospital outcomes are summarized in [Table 4](#).

At discharge, cardiovascular medications did not differ among the 3 frailty-level groups, but the frailest patients tended to be prescribed a loop diuretic more frequently ( $P = 0.06$ ). Destination at discharge significantly differed among the 3 groups: frail patients were less likely to be discharged to home (55.6%, 51.9%, and 22.4% in the 0-3, 4-6, and  $\geq$  7 EFS-score groups, respectively,  $P < 0.001$ ; [Table 5](#)). The frailest patients were thus most often transferred at discharge to the cardiology department of a primary care hospital (close to their place of residence), a geriatric ward, or post-acute care and rehabilitation.

At the end of the follow-up period, the global survival rate was 74.9%. The survival rate was 95.6%, 78.3%, and 62.8%, respectively, in the 0-3, 4-6, and  $\geq$  7 EFS-score groups (log rank test,  $P < 0.001$ ; [Table 6](#)). The Kaplan-Meier survival curves according to frailty level are presented in [Figure 1](#).

On univariate Cox regression analysis, the variables associated with the occurrence of death were: marital status, diabetes, higher score on the Edmonton Frail scale, left ventricular ejection fraction, right ventricular dysfunction, low hemoglobin level, and the occurrence of delirium.

In multivariate analysis after the backward procedure, the Cox proportional hazard model was adjusted for age, diabetes, diagnosis at admission, hemoglobin level, C-reactive protein level, severe renal failure, left ventricular ejection fraction level, and any occurrence of delirium. Discrimination performance of our model was acceptable, with an area under the curve of 0.81 ( $\pm 0.04$ ) for the receiver operating characteristic curve. Frailty remained significantly and independently associated with a significant increase in the risk of all-cause death, as patients with a 4-6 EFS-score had a hazard ratio of 2.60 (95% CI 0.54 to 12.45,  $P = 0.23$ ), and patients with a  $\geq$  7 EFS-score had a hazard ratio of 5.46 (95% CI 1.23 to 24.08,  $P = 0.02$ ; [Table 7](#)).

**Table 4. In-hospital outcomes**

Outcome	All (n = 199)	EFS score 1-3 (n = 45)	EFS score 4-6 (n = 60)	EFS score ≥ 7 (n = 94)	P
In-hospital cardiovascular outcomes					
Death	16 (8.0)	1 (2.2)	6 (10.0)	9 (9.6)	0.26
Stroke	1 (0.5)	0 (0.0)	0 (0.0)	1 (1.1)	0.56
In-hospital noncardiovascular complications					
Acute renal failure	59 (29.7)	13 (28.9)	11 (18.3)	35 (37.2)	<b>0.04</b>
Sepsis	19 (9.6)	2 (4.4)	2 (3.3)	15 (16.0)	<b>0.02</b>
Bleeding (BARC ≥ 3)	12 (6.0)	1 (2.2)	3 (5.0)	8 (8.5)	0.31
Delirium	5 (2.5)	0 (0.0)	0 (0.0)	5 (5.3)	0.08
Length of stay, d	4 (2-7)	4 (2-8)	4 (2-6)	4 (1-7)	0.47

Values are n (%) or median (interquartile range). Boldface indicates significance.  
BARC, Bleeding Academic Research Consortium; EFS, Edmonton Frail Scale.

**Table 5. Cardiovascular medications and destinations at discharge**

Medication/destination	All (n = 199)	EFS score 1-3 (n = 45)	EFS score 4-6 (n = 60)	EFS score ≥ 7 (n = 94)	P
Cardiovascular drugs at discharge					
Antiplatelet therapy	117 (63.6)	34 (77.3)	33 (61.1)	50 (58.8)	0.10
Anticoagulant	75 (40.4)	16 (36.4)	23 (42.6)	35 (41.2)	0.81
β-blockers	100 (54.6)	29 (65.9)	29 (53.7)	42 (49.4)	0.20
Statin	111 (60.7)	31 (70.5)	36 (66.7)	44 (51.8)	0.07
ACEI or ARB	90 (49.2)	23 (52.3)	29 (53.7)	38 (44.7)	0.52
Aldosterone blockers	8 (4.4)	1 (2.3)	2 (3.7)	5 (5.9)	0.61
Calcium blockers	56 (30.6)	11 (25.0)	14 (25.9)	31 (36.5)	0.27
Amiodarone	28 (15.3)	3 (6.8)	7 (13.0)	18 (21.2)	0.09
Thiazide diuretics	11 (6.0)	0 (0.0)	3 (5.6)	8 (9.4)	0.10
Loop diuretics	101 (54.6)	19 (43.2)	27 (50.0)	54 (63.5)	0.06
Destination at discharge					
Home	71 (38.8)	24 (55.6)	28 (51.9)	19 (22.4)	<b>&lt; 0.001</b>
Other	112 (61.2)	20 (45.5)	26 (48.1)	66 (77.6)	

Values are n (%), unless otherwise indicated. Boldface indicates significance.  
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; EFS, Edmonton Frail Scale.

**Discussion**

This study aimed to evaluate the prevalence of frailty in subjects aged ≥ 80 years admitted to the CICU of a single tertiary centre and its potential impact on all-cause mortality at 1 year. We observed that nearly half of patients (47%) aged > 80 years had an EFS score ≥ 7 and therefore a significant state of frailty. In addition, we demonstrated that an EFS score ≥ 7 is an independent factor for all-cause mortality at 1-year follow-up.

Despite the high quality of medical cardiovascular care provided, the CICU environment represents a significant challenge for older adults where they encounter many stressors: invasive procedures (eg, intravenous lines, urinary catheter); introduction of new medications; forced bedrest, isolation from family; malnourishment; and sleep deprivation. As a result, delirium is frequently reported in CICU patients, in particular in those with baseline cognitive and sensory limitations.<sup>14</sup> Delirium episodes complicate the management of

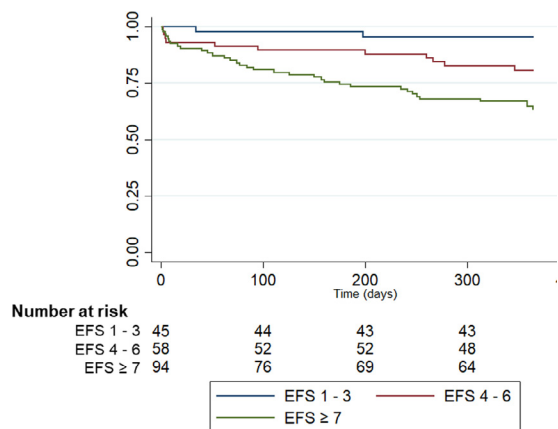
these patients and worsen their clinical outcomes: mortality rates range between 17% and 33% in this situation.<sup>14</sup> Patients' ability to endure the CICU stay is thus related to their frailty status, as by definition, it reflects an increased vulnerability to stressors due to loss of physiological reserve. This finding highlights the importance of assessing frailty in the CICU, which, unfortunately, is often perceived as a lower priority compared to specific cardiovascular management.

Frailty is often underestimated by clinicians. The simple "eyeball test" alone is insufficient to detect frailty.<sup>15</sup> Moreover, frailty is not a dichotomous condition but a continuum; specific tools are thus needed to properly detect and evaluate this condition. Moreover, geriatricians are not necessarily available to perform these assessments in the CICU, so cardiologists should use simple validated tools, accessible to nonspecialists. The question then arises—how should frailty be assessed in the CICU by non-geriatricians? No consensus exists as to the best method of evaluation. The EFS presents, in our opinion,

**Table 6. One-year outcomes**

Outcome	All (n = 199)	EFS score 1-3 (n = 45)	EFS score 4-6 (n = 60)	EFS score ≥ 7 (n = 94)	P
Death	50 (25.1)	2 (4.4)	13 (21.7)	35 (37.2)	< 0.001
Living in institution (n = 149)	9/149 (6.0)	0/42 (0)	1/47 (2.1)	8/60 (13.3)	< 0.001

Values are n (%), unless otherwise indicated.  
EFS, Edmonton Frail Scale.



**Figure 1.** Survival according to the Edmonton Frail Scale (EFS) score group (log rank test  $P < 0.001$ ).

significant advantages in that frailty evaluation can be performed within only 5 minutes and can be made by a nonspecialist. Although the “get up and go” test—which is a part of the EFS—cannot be done at admission (patients are systematically prescribed strict bedrest upon arrival), it can be performed when this restriction is removed. Moreover, a severe state of frailty can be detected even without this part of the EFS. In the SHARE Study<sup>16</sup> (Survey of Heart and Ageing and Retirement in Europe), which included 27,527 subjects

from 17 countries and compared 8 frailty scales, the EFS showed the best performance, along with the Frailty Index, in midterm mortality prediction. This multi-domain score presents good statistical parameters such as a small interoperator variability ( $\kappa = 0.77, P = 0.001$ ) and good internal coherence (Cronbach’s  $\alpha = 0.62$ ). These factors, added to the fact that it can be executed quickly, make the EFS a good test for daily practice. Moreover, a revised version of the EFS—the Reported EFS—that is particularly interesting in the setting of CICU hospitalization, has been proposed as an alternative to the EFS.<sup>10</sup> This version overcomes a limitation of the original EFS, as the timed “get up and go” test, which is impossible to perform in the CICU, has been replaced by a patient self-reported measure of ability to walk 2 weeks earlier.

The prevalence of frailty among CVD patients is reported to be between 4% and 59%<sup>17</sup>; our study, which identifies 47% of patients as having an EFS  $\geq 7$  (ie, being significantly frail) is thus concordant with previous works.

In the setting of acute coronary syndrome<sup>12,13,18,19</sup> (especially in non-ST elevation myocardial infarction), heart failure,<sup>20-22</sup> or cardiac surgery,<sup>23</sup> the independent impact of frailty on clinical hard outcomes has been demonstrated in previous surveys. In our study, we observed that an EFS score  $\geq 7$  is independently related to all-cause mortality occurrence at 1-year follow-up. This result is thus not surprising, as many patients included in our cohort had pathologies for which the impact of frailty on prognosis is known. However, our work underlines

**Table 7.** Univariate and multivariate analyses identifying parameters related to the occurrence of death at 1-year follow-up

Parameter	Univariate analysis			Multivariate analysis		
	HR	95% CI	<i>P</i>	HR	95% CI	<i>P</i>
EFS score						
0-3	1 (ref)			1 (ref)		
4-6	4.66	1.03-21.03	<b>0.04</b>	2.60	0.54-12.45	0.23
$\geq 7$	9.96	2.39-41.45	<b>0.002</b>	5.46	1.23-24.08	<b>0.02</b>
Age (for 1 year more)	1.06	0.99-1.13	0.08	1.1	[1.01-1.20]	<b>0.02</b>
Marital status						
Married	1 (ref)			—		
Widowed	1.24	0.63-2.44	0.51	—	—	—
Single	2.24	1.07-4.68	<b>0.03</b>	—	—	—
Dyslipidemia	0.56	0.30-1.05	0.07	—	—	—
Diabetes	2.03	1.14-3.61	<b>0.01</b>	1.54	0.73-3.22	0.25
Hypertension	1.46	0.68-3.12	0.32	—	—	—
Diagnosis at admission						
Acute coronary syndrome	1 (ref)			1 (ref)		
Pulmonary oedema	1.27	0.58-2.79	0.54	0.77	0.29-1.99	0.59
Conduction disturbance	0.64	0.27-1.52	0.32	0.39	0.12-1.28	0.12
Other	0.88	0.42-1.84	0.74	1.26	0.50-3.19	0.61
Heart rate at admission	1.01	0.99-1.02	0.09	—	—	—
Biology						
Hemoglobin (for 1 dg/L more)	0.83	0.72-0.97	<b>0.02</b>	0.87	0.74-1.02	0.11
CRP (for 10 mg/L more)	1.01	0.99-1.02	0.1	1.01	1.00-1.02	<b>0.04</b>
Renal failure (eGFR < 30 mL/min)	1.56	0.85-2.86	0.15	1.55	0.76-3.12	0.22
LVEF, %						
> 50	1 (ref)			1 (ref)		
35-50	1.54	0.78-3.05	0.21	1.84	0.75-4.46	0.17
< 35	3.06	1.51-6.20	<b>0.002</b>	3.40	1.36-8.45	<b>0.008</b>
Right ventricular systolic dysfunction	2.56	1.27-5.15	<b>0.008</b>	—	—	—
In-hospital noncardiovascular complications						
Sepsis	1.93	0.90-4.15	0.08	—	—	—
Delirium	6.89	2.44-19.45	<b>&lt; 0.001</b>	4.74	1.46-15.38	<b>0.009</b>

Boldface indicates significance.

CI, confidence interval; CRP, C-reactive protein; EFS, Edmonton Frail Scale; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LVEF, left ventricular ejection fraction; ref, referent.

the importance of this impact by showing that frailty is the parameter that most impacts 1-year mortality—hazard ratio was 5.46 (95% CI 1.23–24.08) within the  $\geq 7$  EFS-score group. This result should encourage clinicians to assess frailty among elderly patients on a regular basis. Given the impact of frailty on prognosis, it appears relevant to take this parameter into account in medical decision and management.

### Limitations

Our study has some limitations. Our findings result from a single-centre experience, and so their generalizability needs to be demonstrated. Moreover, there is no consensus on what constitutes the best tool to assess frailty in an acute situation. We decided to focus on the EFS because of its simplicity and feasibility in the acute context. This simplicity may also be a drawback, as the EFS omits some frailty determination parameters.

Finally, we defined our primary endpoint as all-cause mortality instead of cardiovascular mortality only. However, it is always difficult to determine the exact cause of death, as multiple causes are frequently entangled in the geriatric population.

### Conclusion

Our study emphasizes the high prevalence of frailty among elderly patients admitted to a CICU, regardless of the initial reason for admission. We demonstrate here that frailty in this context is a strong and vital prognostic factor. The EFS appears to be a suitable tool for frailty assessment in the CICU setting, and its systematic utilization in the elderly population may help clinicians with their therapeutic decisions and management.

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### References

1. members Writing Group, D Mozaffarian, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation* 2016;133:e38–360.
2. Tuppin P, Riviere S, Rigault A, et al. Prevalence and economic burden of cardiovascular diseases in France in 2013 according to the national health insurance scheme database. *Arch Cardiovasc Dis* 2016;109:399–411.
3. Belle L, Cayla G, Cottin Y, et al. French Registry on Acute ST-elevation and non-ST-elevation Myocardial Infarction 2015 (FAST-MI 2015). Design and baseline data. *Arch Cardiovasc Dis* 2017;110:366–78.
4. Kochly F, Haddad C, Harbaoui B, et al. Therapeutic management and outcome of nonagenarians versus octogenarians admitted to an intensive care unit for acute coronary syndromes. *Arch Cardiovasc Dis* 2020;113:780–90.
5. Bagshaw SM, Webb SA, Delaney A, et al. Very old patients admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis. *Crit Care* 2009;13:R45.
6. Walston J, Robinson TN, Ziemann S, et al. Integrating frailty research into the medical specialties—report from a U13 conference. *J Am Geriatr Soc* 2017;65:2134–9.
7. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet* 2013;381:752–62.
8. Damluji AA, Forman DE, van Diepen S, et al. Older adults in the cardiac intensive care unit: factoring geriatric syndromes in the management, prognosis, and process of care: a scientific statement From the American Heart Association. *Circulation* 2020;141:e6–32.
9. Walker DM, Gale CP, Lip G, et al. Editor's choice—frailty and the management of patients with acute cardiovascular disease: a position paper from the Acute Cardiovascular Care Association. *Eur Heart J Acute Cardiovasc Care* 2018;7:176–93.
10. Hilmer SN, Perera V, Mitchell S, et al. The assessment of frailty in older people in acute care. *Australas J Ageing* 2009;28:182–8.
11. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. *Age Ageing* 2006;35:526–9.
12. Blanco S, Ferrieres J, Bongard V, et al. Prognosis impact of frailty assessed by the Edmonton Frail Scale in the setting of acute coronary syndrome in the elderly. *Can J Cardiol* 2017;33:933–9.
13. Graham MM, Galbraith PD, O'Neill D, et al. Frailty and outcome in elderly patients with acute coronary syndrome. *Can J Cardiol* 2013;29:1610–5.
14. Ibrahim K, McCarthy CP, McCarthy KJ, et al. Delirium in the cardiac intensive care unit. *J Am Heart Assoc* 2018;7:e008568.
15. George EL, Kashikar A, Rothenberg KA, et al. Comparison of surgeon assessment to frailty measurement in abdominal aortic aneurysm repair. *J Surg Res* 2020;248:38–44.
16. Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc* 2013;61:1537–51.
17. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc* 2012;60:1487–92.
18. Ekerstad N, Swahn E, Janzon M, et al. Frailty is independently associated with 1-year mortality for elderly patients with non-ST-segment elevation myocardial infarction. *Eur J Prev Cardiol* 2014;21:1216–24.
19. Sanchis J, Bonanad C, Ruiz V, et al. Frailty and other geriatric conditions for risk stratification of older patients with acute coronary syndrome. *Am Heart J* 2014;168:784–91.



20. Rodriguez-Pascual C, Vilches-Moraga A, Paredes-Galan E, et al. Comprehensive geriatric assessment and hospital mortality among older adults with decompensated heart failure. *Am Heart J* 2012;164:756–62.
21. Rodriguez-Pascual C, Paredes-Galan E, Vilches-Moraga A, et al. Comprehensive geriatric assessment and 2-year mortality in elderly patients hospitalized for heart failure. *Circ Cardiovasc Qual Outcomes* 2014;7:251–8.
22. Martin-Sanchez FJ, Rodriguez-Adrada E, Mueller C, et al. The effect of frailty on 30-day mortality risk in older patients with acute heart failure attended in the emergency department. *Acad Emerg Med* 2017;24:298–307.
23. Yanagawa B, Graham MM, Afilalo J, Hassan A, Arora RC. Frailty as a risk predictor in cardiac surgery: beyond the eyeball test. *J Thorac Cardiovasc Surg* 2019;157:1905–9.