Journal of Geriatric Cardiology | JGC
RESEARCH ARTICLE
J Geriatr Cardiol 2026; 23(9): 565–575

The geriatric syndromes in elderly patients with infective endocarditis: impact on in-hospital mortality

Maria Fernandez-Regueras[1], Patricia Muñoz García[2], Ane Josune Goikoetxea Agirre[3], Mª José Blanco Vidal[3], Mikel del Alamo Martínez de Lagos[3], Miguel Ángel Goenaga Sánchez[4], María Jesús Bustinduy Odriozola[4], Xabier Camino Barrón[4], Martha Kestler Hernández[5], Andrea Kallmeyer Mayor[6], Manuel Martínez-Sellés[7], Jose-Angel Perez-Rivera[8,✉]. The researchers from the GAMES cohort are listed as collaborators. The full list of collaborators is provided in the Appendix.

1. Infectious Diseases Unit, Department of Internal Medicine, Hospital Universitario de Burgos, Instituto de Investigación Biosanitaria de Burgos (IBioBurgos), Spain; 2. Department of Clinical Microbiology and Infectious Diseases, Hospital General Universitario Gregorio Marañón, Madrid, Instituto de Investigación Sanitaria Gregorio Marañón, CIBER Enfermedades Respiratorias-CIBERES (CB06/06/0058), Faculty of Medicine, Universidad Complutense de Madrid, Spain; 3. Department of Infectious Diseases, Hospital Universitario de Cruces, Bilbao, Spain; 4. IIS Biogipuzkoa, Infectious Diseases Area, Research Group on Infectious Diseases and Global Health; Osakidetza, Hospital Universitario Donostia, Department of Infectious Diseases, San Sebastián, Spain; 5. Department of Clinical Microbiology and Infectious Diseases, Hospital General Universitario Gregorio Marañón, Madrid, Instituto de Investigación Sanitaria Gregorio Marañón, Faculty of Medicine, Universidad Complutense de Madrid, Spain; 6. Department of Cardiology, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; 7. Cardiology Department, Hospital General, Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón, CIBERCV, School of Biomedical Sciences and Health, Universidad Europea, School of Medicine, Universidad Complutense, Madrid, Spain; 8. Department of Cardiology, Hospital Universitario de Burgos, Instituto de Investigación Biosanitaria de Burgos (IBioBurgos), Faculty of Health Sciences, Universidad Isabel I, Burgos, Spain

✉ Correspondence to: japerezr@saludcastillayleon.es
https://doi.org/10.26599/1671-5411.2026.09.006

ABSTRACT

Background Infective endocarditis (IE) is associated with high morbidity and mortality. However, the impact of geriatric syndromes on clinical outcomes in elderly patients with IE remains insufficiently characterized. The aim was to assess the prevalence of geriatric syndromes; focusing on frailty, functional dependence, comorbidity and malnutrition; and their association with in-hospital mortality in advanced-age patients with infective endocarditis.

Methods This prospective multicenter observational registry included patients aged ≥ 75 years with possible or definitive IE. Comprehensive geriatric assessment was performed after IE diagnosis using the Clinical Frailty Scale (CFS), FRAIL scale, Mini Nutritional Assessment Short Form (MNA-SF), Barthel index, and age-adjusted Charlson comorbidity index. Patients were classified as frail (CFS ≥ 4) or non-frail (CFS < 4).

Results Among 115 patients (median age 81 [78–85] years, 70.4% male), 52 (45.2%) were classified as frail. Despite similar surgical indications, frail patients underwent surgery less frequently than non-frail patients (10 (19.2%) *vs.* 30 (47.6%), $P = 0.001$) and presented higher in-hospital mortality (19 (36.5%) *vs.* 10 (15.9%), $P = 0.011$). Multivariate analysis identified malnutrition risk (MNA-SF: OR = 0.712, 95% CI: 0.516–0.983, $P = 0.039$) and comorbidity (adjusted Charlson: OR = 1.623, 95% CI: 1.108–2.379, $P = 0.013$) as independent predictors of in-hospital mortality. Frailty was significantly associated with mortality in a separate model excluding malnutrition, suggesting overlap between both constructs.

Conclusions Geriatric syndromes, particularly comorbidity and malnutrition, are highly prevalent in elderly patients with IE and independently predict in-hospital mortality. Comprehensive geriatric assessment should be integrated into clinical decision-making for this population.

© 2026 JGC All rights reserved; www.jgc301.com

Infective endocarditis (IE) remains a condition with high morbidity and mortality.[1,2] Its incidence is rising, particularly among older adults, driven by population aging, increased use of cardiovascular devices and prosthetic valves,[3] and healthcare-associated infections.[4,5] As a result, IE in elderly patients is associated with poorer prognosis and greater functional decline.[6]

Frailty is characterized by reduced physiological reserve and increased vulnerability to stressors, and is associated with worse outcomes, including in cardiac surgery. Functional dependence, however, refers to the need for assistance in daily activities and represents a distinct domain of geriatric assessment.[7,8] Frailty and dependence assessment is increasingly incorporated into preoperative evaluation before valve replacement procedures.[9,10]

Malnutrition is common among hospitalized older adults and is associated with worse short-term outcomes, including in patients with IE, possibly due to chronic inflammation and a predominance of catabolic pathways.[11] Comorbidity is also highly prevalent in elderly patients with IE and has been linked to increased short- and long-term adverse events, likely reflecting reduced physiological reserve and greater vulnerability to infection-related complications.[5,12]

Previous studies have shown that frailty is associated with worse outcomes in IE. However, most have assessed frailty without any specific screening validated scale[6] or using a single instrument,[13] focused on surgical patients,[9] or evaluated isolated geriatric domains rather than a multidimensional approach. Comprehensive assessment integrating different frailty scales together with malnutrition, functional dependence, and comorbidity specifically in older IE patients remains limited. Moreover, current clinical guidelines[14] do not provide specific recommendations regarding systematic multidimensional geriatric assessment in this setting.

Our aim was to assess the prevalence of frailty, comorbidity, functional independence, and malnutrition and their independent association with in-hospital mortality in advanced-age patients with IE.

METHODS

Study Oversight

This prospective observational registry included patients older than 75 years with a definitive or possible diagnosis of IE according to modified Duke criteria[14] at 5 hospitals between February 2023 and June 2025. Epidemiological, clinical, analytical, microbiological, and cardiac imaging data were collected during hospitalization according to the our group protocol,[2] including cardiological or infectious complications occurring during admission, both before and after surgery. The protocol of this study was performed in accordance with the Declaration of Helsinki and was reviewed and approved by the Institutional Ethics Committee at all participating hospitals, according to local standards.

Throughout the study period, consecutive patients meeting inclusion criteria (admission for possible or definitive IE and age over 75 years) underwent geriatric assessment at the moment of IE diagnosis after signing informed consent. No exclusion criteria were specified, and efforts were made to consecutively include all patients without exclusion based on clinical severity or functional status.

Patient management was conducted at the treating physician's discretion, and prescribed antibiotic treatment, surgical indication, and whether surgery was performed were recorded. In-hospital all-cause mortality was recorded as the primary outcome variable.

Geriatric Assessment

Geriatric assessment (supplementary Tables S1-S5) was performed at the moment of IE diagnosis by adequately trained physicians responsible for patient care. This assessment included frailty screening using the Fatigue, Resistance, Ambulation, Illnesses and Loss of weight scale (FRAIL)[15] and the Clinical Frailty Scale (CFS).[16] These both instruments were selected because they represent complementary approaches to frailty assessment: CFS is a clinician-judgment-based global measure of vulnerability integrating comorbidity, cognition and functional status, whereas FRAIL is a questionnaire-based screening tool focused on physical frailty domains. The use of both scales aimed to explore the robustness of frailty assessment across different operational definitions. Both scores were performed at the time of IE diagnosis, but particular attention was paid to reconstructing the patient's baseline functional status prior to the acute event. The assessment integrated information provided by both patients and relatives regarding pre-admission functional capacity and clinical condition.

Furtheremore, nutritional risk analysis using the Mini Nutritional Assessment Short Form (MNA-SF),[17] and dependence assessment using the Barthel index.[18] Ad-

ditionally, comorbidity was evaluated using the age-adjusted Charlson scale.[19]

Statistical Analysis

No formal a priori sample size calculation was performed given the exploratory, registry-based design; however, based on an estimated eligible population of approximately 150 patients across the five centres, a sample of 114 was calculated to achieve 95% confidence with a 5% margin of error. Continuous variables were expressed as median (interquartile range [IQR]) and categorical variables as percentages. Initially, the sample was divided into frail (CFS ≥ 4) and non-frail (CFS < 4) patients, and main characteristics were compared between both groups using Chi-square and Mann-Whitney *U* tests. Subsequently, factors associated with in-hospital mortality were analyzed using Chi-square and Mann-Whitney *U* tests; additionally, geriatric variables showing statistical significance with in-hospital mortality were represented using survival curves. Finally, logistic regression was performed with all variables showing statistical significance in univariate mortality analysis, excluding those demonstrating overlap. A backward stepwise conditional procedure ("Conditional steps backward") was applied for variable selection, and the Hosmer–Lemeshow goodness-of-fit test was also included. Odds Ratio (OR) for continuous variables represent the effect per 1-point increase in the corresponding scale.

RESULTS

Baseline Patients' Characteristics

During the study period, a total of 203 IE cases were registered across the five participating centres, of which 130 were aged ≥ 75 years and therefore potentially eligible. A total of 15 patients were not enrolled, 3 died before geriatric assessment could be performed; the remaining 12 were missed due to logistical constraints inherent to consecutive prospective recruitment (Supplementary Figure S1). Finally, 115 patients with IE (102 definite and 13 possible IE) were included. There were no missing data in the dataset; data completeness was a primary objective of the study's quality control process. The median age was 81 (78–85) years and there were 81 (70.4%) men (Table 1). Most registered IE cases were enterococcal (35 cases, 30.4%), involving the aortic valve (72

Table 1 Key clinical features of infective endocarditis.

Demographic characteristics	*N* = 115
Age, yrs	81 (78–85)
Male	81 (70.4%)
Comorbidity – Age-adjusted Charlson Index	Median 5.7 (IQR 5–7)
Community-acquired	80 (69.6%)
Nosocomial	24 (20.9%)
Healthcare-associated	11 (9.6%)
Location	
Aortic	72 (62.6%)
Mitral	51 (44.3%)
Tricuspid	1 (0.9%)
Pulmonary	1 (0.9%)
Native valve	60 (52.2%)
Prosthetic valve	50 (43.5%)
Cardiac device-related (pacemaker/ICD) infection	6 (5.2%)
Etiology	
Staphylococcus aureus	23 (20.0%)
Enterococcus spp	35 (30.4%)
Streptococcus spp	30 (26.1%)
Coagulase-negative staphylococci	12 (10.4%)
Candida spp	1 (0.9%)
No identified etiology	3 (2.6%)
Polymicrobial	2 (1.7%)
Gram-negative bacilli	3 (2.6%)
Complications	
Cardiac Complications	21 (18.3%)
Perforation or rupture	7 (6.1%)
Pseudoaneurysm	7 (6.1%)
Abscess	11 (9.6%)
Intracardiac fistula	2 (1.7%)
Heart Failure	40 (34.8%)
Central Nervous System involvement	20 (17.4%)
Embolic Events	25 (21.7%)
Acute Kidney Injury	24 (20.9%)
Septic Shock	9 (7.8%)
In-hospital mortality	29 (25.2%)
Management	
Surgery Indicated	74 (64.3%)
Surgery Performed	40 (34.8%)
Antibiotic Duration, day	42 (28–48)

Data are presented as Median (IQR) or *n* (%). ICD: implantable cardiac defibrillator; IQR: interquartile range.

cases, 62.6%), and community-acquired (80 cases, 69.6%).

Regarding nutritional status, 71 patients (61.7%) were at risk of malnutrition (MNA-SF 7–11) and 13 (11.3%) were malnourished (MNA-SF < 7). Functional dependence, defined as a Barthel Index < 60, was present in 20 patients (17.3%). Frailty according to FRAIL scale (≥ 3 points) was identified in 93 patients (80.9%). Fifty-two patients (45.2%) were classified as frail according to CFS (≥ 4 points). Analysis of responses to each item of the applied geriatric scales is presented in table S6 of the supplementary material.

Frail patients were older (82 ± 5.1 *vs.* 80 ± 4.1, P = 0.014) than non-frail patients, with no statistical significance detected in other clinical and microbiological characteristics (Table 2). As expected, they presented a more unfavorable geriatric profile with greater comorbidity and higher prevalence of all analyzed geriatric syndromes.

Despite no significant differences in surgical indication between frail and non-frail patients, surgery was performed less frequently in frail patients (10 [19.2%] *vs.* 30 [47.6%], P = 0.001) (Table 2). Accordingly, surgery indicated but not performed was more common among patients with CFS ≥4 compared to those with CFS < 4 (46.2% *vs.* 17.4%, P < 0.01). Although the reasons for not performing surgery were not systematically recorded in all cases, the available data suggest that the main reasons were prohibitive operative risk and a multidisciplinary decision by the Endocarditis Team against surgical intervention. The median EuroSCORE was similar between groups, with 30 (IQR 20–55) in patients with CFS < 4 and 32 (IQR 24–58) in those with CFS ≥ 4 (P = 0.510). In-hospital mortality in the overall sample was 29 cases (25.2%), being higher in frail patients (19 deaths (36.5%) *vs.* 10 (15.9%), P = 0.011) (Table 2).

In-hospital Mortality Analysis

Univariate analysis of in-hospital mortality is presented in Table 3. Mortality was higher in women and in patients with healthcare-associated endocarditis. The presence of intracardiac complications, specifically paravalvular abscess, and the development of heart failure and septic shock were similarly associated with higher mortality. Surgery was a protective factor, as was longer duration of antibiotic treatment, although the latter variable showed clear collinearity with length of hospital stay, which was longer in patients who survived.

Although scores on all geriatric assessment scales were more unfavorable in patients who died, significant differences were only found in CFS scores (Figure 1A), MNA-SF scale (Figure 1B) and Charlson index (Figure 1C).

Multivariate mortality analysis is presented in Table 4. Variables included in the analysis were: age, sex (male), age-adjusted Charlson index, healthcare-associated acquisition, intracardiac abscess, septic shock, heart failure, surgery performance, CFS, and MNA-SF scale. Antibiotic treatment duration was excluded from the multivariable model due to its tautological relationship with survival time: patients who died earlier received shorter antibiotic courses by definition (median antibiotic duration in non-survivors: 21 days [IQR 11–34]; median time to in-hospital death: 26 days [IQR 14–34]), and its inclusion would therefore not constitute an independent clinical predictor.

Factors independently associated with mortality were the occurrence of complications such as septic shock and healthcare-associated acquisition. Cardiac surgery was a protective factor. Regarding geriatric syndromes, both greater comorbidity measured by the Charlson scale (OR = 1.623, 95% CI: 1.108–2.379, P = 0.013) and higher malnutrition risk assessed by the MNA-SF scale (OR = 0.712, 95% CI: 0.516-0.983, P = 0.039) were associated with increased mortality.

Although formal collinearity was not detected (Variance Inflation Factor <1.2; Spearman ρ = 0.529), a sensitivity multivariable model excluding MNA-SF was performed (Table 4) given the recognized clinical and pathophysiological overlap between malnutrition and frailty as partially overlapping geriatric constructs sharing common biological pathways. We detected in this analysis an independent effect of frailty measured by CFS on in-hospital mortality (OR = 1.709, 95% CI: 1.205–2.425, P = 0.003).

DISCUSSION

The main findings of this study are: (1) the prevalence of geriatric syndromes in elderly patients hospitalized for IE is high, (2) despite similar surgical indication, frail patients underwent surgery less frequently, and (3) malnutrition, comorbidities and frailty are associated with higher in-hospital mortality rates in our sample (Figure 2).

In the present study, the frailty rate determined by a CFS score ≥ 4 was 45.2%. Frailer patients were older and had higher rates of complex comorbidity, as well as

Table 2 Comparison between frail and non-frail patients.

Variables	CFS < 4, *n* = 63	CFS ≥ 4, *n* = 52	*P*
Age, yrs	80 (77–83)	82 (78–87)	0.014
Male	48 (76.2%)	33 (63.5%)	0.132
Location			
Aortic	44 (69.8%)	28 (53.8%)	0.078
Mitral	23 (36.5%)	28 (53.8%)	0.063
Tricuspid	1 (1.6%)	0	-
Pulmonary	1 (1.6%)	0	-
Native IE	32 (50.8%)	28 (53.8%)	0.744
Prosthetic IE	26 (41.3%)	24 (46.2%)	0.599
PM/ICD	4 (6.3%)	2 (3.8%)	0.548
Comorbidities			
Age-adjusted Charlson. Median (IQR)	5 (4–6)	6 (5–7)	0.029
Etiology			
Staphylococcus aureus	11 (17.4%)	12 (23.0%)	0.454
CNS	6 (9.5%)	6 (11.5%)	0.725
Enterococcus spp	19 (30.1%)	16 (30.8%)	0.944
Streptococcus spp	19 (30.1%)	11 (21.2%)	0.274
Candida spp	1 (1.5%)	0	-
No etiology	2 (3.2%)	1 (1.9%)	0.675
Polymicrobial	2 (3.2%)	0	-
Gram-Negative Bacilli	2 (3.2%)	1 (1.9%)	0.675
Clinical Course			
Site of acquisition			
Community-acquired	45 (71.4%)	35 (67.3%)	0.633
Nosocomial	12 (19.0%)	12 (23.1%)	0.597
Healthcare-associated	6 (9.5%)	5 (9.6%)	0.987
Intracardiac complications	14 (22.2%)	7 (13.4%)	0.226
Perforation or rupture	7 (11.1%)	0	-
Pseudoaneurysm	3 (4.7%)	4 (7.6%)	0.513
Abscess	6 (9.5%)	5 (9.6%)	0.987
Intracardiac fistula	1 (1.5%)	1 (1.9%)	0.891
Heart failure	24 (38.1%)	16 (30.7%)	0.412
Central Nervous System involvement	11 (17.5%)	9 (17.3%)	0.915
Embolization	18 (28.5%)	7 (13.4%)	0.051
New/Worsening renal failure	15 (23.8%)	9 (17.3%)	0.393
Septic Shock	7 (11.1%)	2 (3.8%)	0.149
Sepsis	10 (15.8%)	4 (7.6%)	0.182
Surgical indication	40 (63.4%)	34 (65.3%)	0.833
Surgery	30 (47.6%)	10 (19.2%)	0.001
Antibiotic treatment duration	42 (31–51)	52 (21–46)	0.060
In-hospital mortality	10 (15.9%)	19 (36.5%)	0.011
FRAIL Scale. Median (IQR) (maximum 5 points)	1 (0–2)	3 (1–4)	<0.01
MNA-SF Test. Median (IQR) (maximum 14 points)	11 (9–12)	9 (7–10)	<0.01
Barthel index. Median (IQR) (0-100 points)	100 (95–100)	70 (55–95)	<0.01

Data are presented as Median (IQR) or *n* (%). CFS: Clinical Frailty Scale; CNS: Coagulase-Negative Staphylococci; FRAIL: Fatigue, Resistance, Ambulation, Illnesses and Loss of weight; ICD: Implantable Cardioverter Defibrillator; IE: Infective Endocarditis; IQR: Interquartile Range; MNA-SF: Mini Nutritional Assessment Short Form; PM: Pacemaker.

Table 3 Univariate in-hospital mortality analysis.

Variables	Survivors (86)	Deaths (29)	*P*
Age, yrs	80 (77–83)	83 (79–86)	0.218
Male	65 (75.6%)	16 (55.2%)	0.037
Location			
Aortic	54 (62.8%)	18 (62.1%)	0.945
Mitral	36 (41.9%)	15 (51.7%)	0.355
Tricuspid	1 (1.2%)	0	-
Pulmonary	0	1 (3.4%)	-
Native IE	46 (53.5%)	14 (48.3%)	0.627
Prosthetic IE	34 (39.5%)	16 (55.2%)	0.142
PM/ICD	6 (7.0%)	0	-
Comorbidities			
Age-adjusted Charlson	5 (4–6)	7 (5–8)	0.006
Etiology			
Staphylococcus aureus	15 (17.4%)	8 (27.6%)	0.238
CNS	7 (8.1%)	5 (17.2%)	0.166
Enterococcus spp	26 (30.2%)	9 (31.0%)	0.935
Streptococcus spp	26 (30.2%)	4 (13.8%)	0.081
Candida spp	1 (1.2%)	0	-
No etiology	3 (3.5%)	0	-
Polymicrobial	0	2 (6.9%)	-
Gram-Negative Bacilli	2 (2.3%)	1 (3.4%)	0.743
Clinical Course			
Site of acquisition			
Community-acquired	67 (77.9%)	13 (44.8%)	0.001
Nosocomial	12 (14.0%)	12 (41.4%)	0.002
Healthcare-associated	7 (8.1%)	4 (13.8%)	0.371
Intracardiac complications	12 (13.9%)	9 (31.0%)	0.040
Perforation or rupture	5 (5.8%)	2 (6.8%)	0.833
Pseudoaneurysm	4 (4.6%)	3 (10.3%)	0.267
Abscess	4 (4.6%)	7 (24.1%)	0.002
Intracardiac fistula	0	2 (6.8%)	-
Heart failure	24 (28.2%)	16 (55.2%)	0.009
Central Nervous System involvement	14 (16.2%)	6 (20.7%)	0.588
Embolization	19 (22.0%)	6 (20.7%)	0.874
New/Worsening renal failure	15 (17.4%)	9 (31.0%)	0.119
Septic Shock	3 (3.4%)	6 (20.7%)	0.003
Sepsis	9 (10.4%)	5 (17.2%)	0.335
Surgical indication	52 (60.4%)	22 (75.8%)	0.134
Surgery	36 (41.8%)	4 (13.8%)	0.006
Antibiotic treatment duration	42 (34–51)	21 (11–34)	< 0.01
FRAIL Scale. Median (IQR) (maximum 5 points)	1 (0-3)	2 (1–3)	0.215
MNA-SF Test. Median (IQR) (maximum 14 points)	10 (9–12)	9 (6–10)	0.005
Barthel index. Median (IQR) (0-100 points)	100 (80–100)	87 (60–100)	0.091
CFS. Median (IQR) (maximum 9 points)	3 (3–4)	5 (3–6)	0.008

Data are presented as Median (IQR) or *n* (%). CFS: Clinical Frailty Scale; CNS: Coagulase-Negative Staphylococci; FRAIL: Fatigue, Resistance, Ambulation, Illnesses and Loss of weight; ICD: Implantable Cardioverter Defibrillator; IE: Infective Endocarditis; IQR: Interquartile Range; MNA-SF: Mini Nutritional Assessment Short Form; PM: Pacemaker.

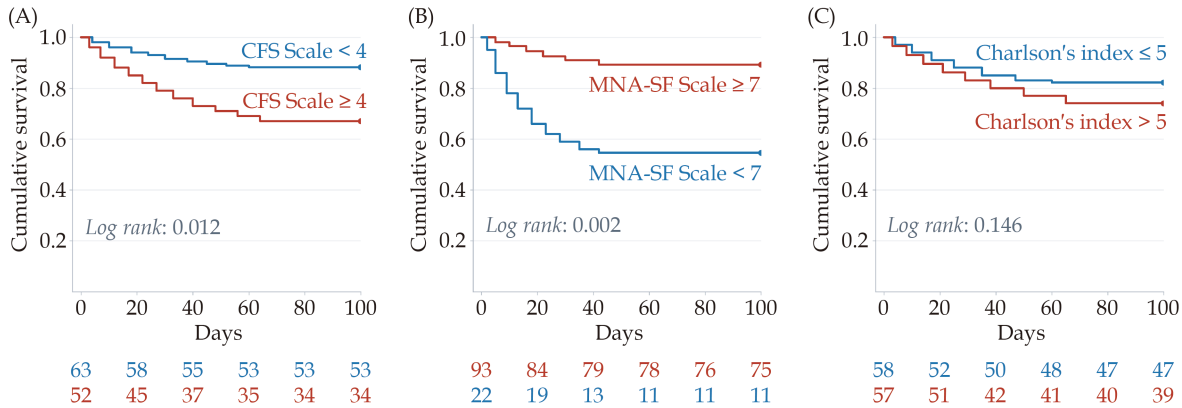


Figure 1 Kaplan-Meier Survival Curves for In-Hospital Mortality. (A): In-hospital mortality according to Clinical Frailty Scale; (B): in-hospital mortality according to MNA-SF scale; (C): in-hospital mortality according to age-adjusted Charlson index. MNA-SF: Mini Nutritional Assessment Short Form.

Table 4 Multivariate in-hospital mortality analysis.

Variable	Model 1 (with MNA-SF)			Model 2 (without MNA-SF)		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	0.961	0.847–1.089	0.529	0.988	0.879–1.111	0.838
CFS	1.291	0.843–1.977	0.240	1.709	1.205–2.425	0.003
MNA-SF Scale	0.712	0.516–0.983	0.039	-	-	-
Male sex	0.269	0.063–1.153	0.077	0.538	0.151–1.917	0.339
Age-adjusted Charlson Index	1.623	1.108–2.379	0.013	2.745	0.765–9.854	0.122
Nosocomial acquisition	8.527	1.999–36.366	0.004	9.786	2.308–41.500	0.002
Abscess	5.783	0.835–40.048	0.075	7.148	1.119–45.644	0.038
Heart failure	1.967	0.583–6.636	0.275	2.726	0.871–8.534	0.085
Septic shock	35.958	4.009–322.560	0.001	33.202	3.779–291.677	0.002
Surgery	0.091	0.012–0.722	0.023	0.108	0.016–0.752	0.025

CFS: Clinical Frailty Scale; MNA-SF: Mini Nutritional Assessment Short Form. OR for continuous variables represent the effect per 1-point increase in the corresponding scale. Hosmer-Lemeshow: 0.773. Model 1 includes all variables that showed significance in univariant survival analysis (excluding antibiotic duration for collinearity with mortality). Model 2 excludes MNA-SF to assess the independent effect of CFS.

greater prevalence of other geriatric syndromes. In this group, almost one third of the IE cases were healthcare-associated or nosocomial and caused by *Enterococcus spp*, similar to comparable studies.[13,20]

Comparison of geriatric assessment between our sample and previous studies is complex given the heterogeneity of scales used and populations included. In a French cohort of patients > 75 years with IE,[6] approximately 40% of patients were at risk of malnutrition and, although no specific frailty scale was employed, included patients had significant functional impairment at admission, with only 35.5% of patients able to walk. In another Spanish cohort of IE patients not selected by age,[13] dependence was less frequent than in our sample, but only 40.1% of patients were considered robust, similar to our findings.

To our knowledge, this is the first prospective study evaluating frailty in elderly patients hospitalized for IE using the CFS. This scale is a validated tool in advanced-age populations with both acute and chronic heart disease and has consistently demonstrated an association with adverse outcomes.[7] Its main strengths are its simplicity and rapid applicability, as it can be based on clinical judgment and information from the patient or relatives, making it suitable for use in acute settings. However, it remains partly subjective and may be less accurate in certain subgroups, such as patients with significant cognitive impairment.

In our cohort, frailty assessed by CFS was independently associated with in-hospital mortality, whereas the

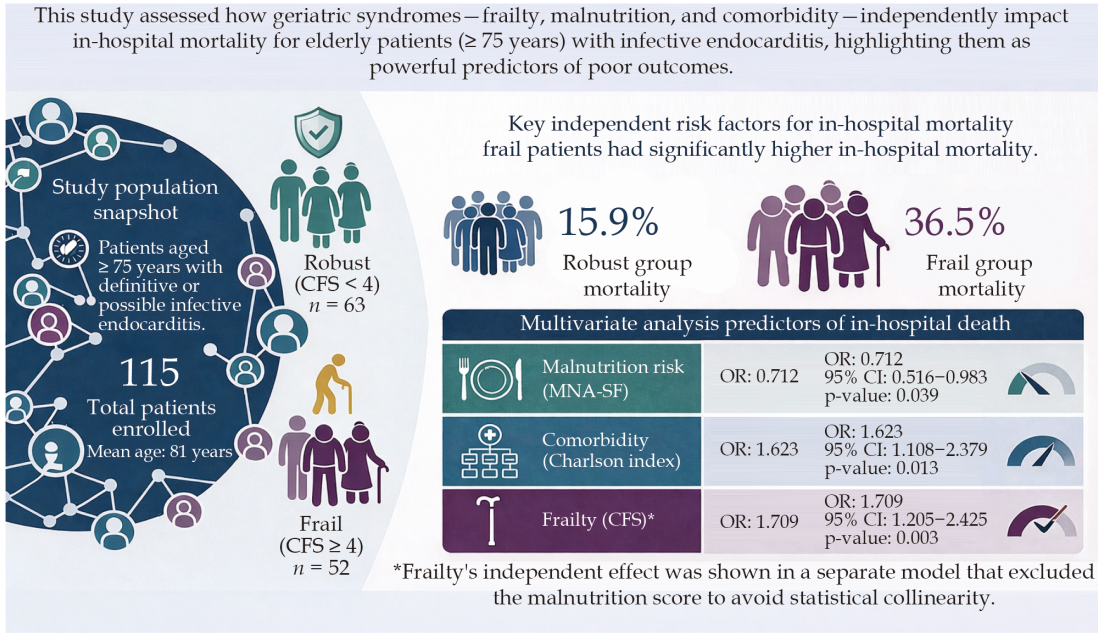


Figure 2 Geriatric syndromes as mortality predictors in elderly patients with infective endocarditis.

FRAIL scale was not. This difference may be explained by the distinct constructs captured by each instrument: CFS reflects global vulnerability, integrating functional, cognitive, and comorbidity domains, while FRAIL focuses primarily on physical frailty. Therefore, the association observed between CFS and in-hospital mortality should be interpreted as reflecting global multidimensional vulnerability rather than frailty per se. This broader construct may account for the greater prognostic discriminatory capacity of CFS compared with scales centered on physical frailty dimensions alone.

A recent prospective study demonstrated the prognostic value of the FRAIL scale at 1 year in an age-unselected population with IE.[13] The absence of an independent association in our study may relate to the exclusive inclusion of advanced-age patients, among whom baseline physical frailty is highly prevalent and therefore less discriminatory. In contrast, global vulnerability assessed by CFS, together with nutritional status, provided greater prognostic stratification, suggesting that multidimensional vulnerability rather than physical frailty alone may better capture risk in this elderly population.

In our study, we detected a high prevalence of patients at risk of malnutrition according to the MNA-SF scale. The prevalence of malnutrition or risk of developing it has not been sufficiently studied in this context. A prospective study identifies the long version of the MNA scale as a predictor of events in the first three months following an IE episode.[6] Another recent study evaluates nutritional status using the CONUT scale[13] without finding prognostic impact. This may be because this scale is based on analytical parameters, including total lymphocyte count, which may be altered by the IE episode itself.

However, our study is the first to use the short version of the MNA, which has similar value to the long version but has the main advantage of simplicity and requiring little time for assessment.[17] Based on questionnaire responses, most patients reported weight loss, decreased appetite, or coexistence of other stressful medical or emotional situations. Therefore, there may be some overlap between patients identified as at risk of malnutrition using the MNA-SF and frail patients identified with specific frailty scales.[21,22]

There is a clear bidirectional relationship between malnutrition and frailty. Malnourished patients typically develop muscular alterations due to reduced protein intake and impaired protein synthesis, leading to sarcopenia, physical inactivity, and, in advanced stages, cachexia. These changes are key components of the frailty phenotype and functional dependence, which in turn promote further inactivity, anorexia, and weight loss, creating a self-perpetuating cycle of declining physiological reserve.[23]

Moreover, frail and malnourished patients exhibit a marked proinflammatory state[24] associated with immune dysfunction, impaired tissue repair, and reduced

resilience to acute stressors. During an episode of IE, this diminished physiological reserve may limit the ability to cope with the severe inflammatory and metabolic burden imposed by infection, contributing to organ dysfunction and increased mortality. Additionally, frail and malnourished patients typically present greater comorbidity and higher healthcare utilization,[25,26] factors that further increase vulnerability and may partly explain the adverse prognosis observed in our cohort. In line with this, we also found higher in-hospital mortality among patients with a greater Charlson comorbidity index, as previously reported by our group.[3,5]

Finally, elderly patients with higher prevalence of geriatric syndromes undergo surgery less frequently even when presenting similar surgical indication. In our sample, only 19.2% of frail patients underwent surgery, compared with 47.6% of non-frail patients. This lower rate of performed surgery has been previously evidenced based on age,[20] comorbidity,[5] or frailty status.[9] This may be due to significant weight given to patients' geriatric and functional status in collegial decisions by IE teams. However, inclusion of these variables in main perioperative risk assessment scales is infrequent,[27,28] and geriatricians are not commonly found as part of these multidisciplinary teams. This is particularly striking when evidence already exists that IE surgery performed in frail patients is associated with worse outcomes than that performed in robust patients.[9]

Studies like ours highlight the need for specialized assessment of these syndromes as they are potentially reversible states. Treatment through nutritional counseling and supplementation and motor rehabilitation has already proven capable of improving nutritional status and functional status in patients with other heart diseases.[29,30] Therefore, early implementation of this approach could improve the prognosis of these patients and even make them suitable for surgical intervention for which they may not initially be candidates.

Based on our findings, we propose that comprehensive geriatric assessment should be systematically integrated into the initial evaluation of all IE patients aged ≥ 75 years at the time of diagnosis. A pragmatic three-domain workflow could include: (1) frailty screening using the CFS (≥ 4 points indicating frailty); (2) nutritional risk assessment using the MNA-SF (≤ 11 points indicating risk of malnutrition); and (3) functional assessment using the Barthel index (< 60 points indicating significant dependence). Charlson index might be also estimated by reviewing clinical registries. This assessment can be completed in under 15 minutes by trained physicians, especially geriatricians, and provides actionable risk stratification to guide multidisciplinary Endocarditis Team decisions regarding surgical candidacy, intensity of monitoring, and early referral for nutritional support and physical rehabilitation.

One limitation of our study is the relatively small sample size, with a total of 29 in-hospital deaths. Given this limited number of events, the multivariable logistic regression analyses should be interpreted with caution, as the estimates may lack statistical stability and the risk of overfitting cannot be excluded. Accordingly, the multivariable findings should not be considered definitive, and replication in larger prospective cohorts is warranted. The geriatric assessment was incomplete not including dimensions such as cognitive impairment and in some cases was performed by physicians trained in its application but not by dedicated geriatricians. Furthermore, CFS was assessed at the time of IE diagnosis rather than prior to the acute episode. In the context of acute illness — particularly in patients presenting with heart failure, sepsis, or septic shock — CFS scores may partly reflect acute disease severity rather than pre-existing frailty status what may lead to overestimation of baseline frailty. Although we attempted not to exclude the most severely ill patients, those who died before the geriatric assessment could be performed were not included, which may introduce a potential selection bias. Finally, post-discharge follow-up data were unavailable.

As a conclusion, geriatric syndromes, particularly comorbidities and malnutrition, emerge as highly prevalent conditions in elderly patients with IE, affecting outcomes independently of traditional risk factors. Given these observations, comprehensive geriatric assessment should be systematically integrated into the evaluation and management of elderly patients with IE.

DECLARATIONS

Author Contributions

All authors listed have contributed significantly to study conception and design and/or data acquisition and/or analysis and interpretation of the data. All authors were involved in the manuscript's preparation, revision, and final approval of version to be published. Study concept and design: JA Perez Rivera, M Martinez-

Selles. Acquisition of subjects and/or data: M Fernandez Regueras, P Munoz, MJ Goikoetxea-Agirre, MJ Blanco-Vidal, M del Alamo-Martinez de Lagos, MA Goenaga-Sanchez, MJ Bustinduy-Odriozola, X Camino-Barron, M Kestler-Hernandez, A. Kallmeyer-Mayor., Analysis and interpretation of data: JA Perez Rivera, M. Fernández-Regueras. Preparation of manuscript: JA Perez-Rivera, M Fernandez-Regueras, M Martinez-Selles.

Conflicts of Interest

None.

Acknowledgments

The Spanish Society of Cardiovascular Infections and the Geriatric Cardiology Section of the Spanish Society of Cardiology supported the conduct of this research. They had no role in the study design, data collection, data analysis, interpretation of results, manuscript preparation, or decision to submit the manuscript for publication. No financial support was provided.

Informed Consent

All participants provided written informed consent prior to participation.

Ethical Approval

The protocol of this study approved by the Institutional Ethics Committee of Hospital Universitario de Burgos (CEIm 2786) and ratified at all participating hospitals, according to local standards.

REFERENCES

[1] Ambrosioni J, Hernández-Meneses M, Durante-Mangoni E, *et al.* Epidemiological Changes and Improvement in Outcomes of Infective Endocarditis in Europe in the Twenty-First Century: An International Collaboration on Endocarditis (ICE) Prospective Cohort Study (2000-2012). *Infect Dis Ther* 2023; 12: 1083–1101.

[2] Muñoz P, Kestler M, De Alarcon A, *et al.* Current epidemiology and outcome of infective endocarditis: a multicenter, prospective, cohort study. *Medicine (Baltimore)* 2015; 94: e1816.

[3] Armiñanzas C, Fariñas-Alvarez C, Zarauza J, *et al.* Role of age and comorbidities in mortality of patients with infective endocarditis. *Eur J Intern Med* 2019; 64: 63–71.

[4] Bea C, Vela S, García-Blas S, *et al.* Infective Endocarditis in the Elderly: Challenges and Strategies. *J Cardiovasc Dev Dis.* 2022; 9: 192.

[5] Perez-Rivera J-A, Armiñanzas C, Muñoz P, *et al.* Comorbidity and Prognosis in Octogenarians with Infective Endocarditis. *J Clin Med.* 2022; 11: 3774.

[6] Forestier E, Roubaud-Baudron C, Fraisse T, *et al.* Comprehensive geriatric assessment in older patients suffering from infective endocarditis. A prospective multicentric cohort study. *Clin Microbiol Infect* 2019; 25: 1246–1252.

[7] Díez-Villanueva P, Arizá-Solé A, Vidán MT, *et al.* Recommendations of the Geriatric Cardiology Section of the Spanish Society of Cardiology for the Assessment of Frailty in Elderly Patients With Heart Disease. *Rev Esp Cardiol (Engl Ed)* 2019; 72: 63–71.

[8] Kim DH, Rockwood K. Frailty in Older Adults. *N Engl J Med* 2024; 391: 538–548.

[9] Graversen PL, Østergaard L, Smerup MH, *et al.* Surgery in patients with infective endocarditis and prognostic importance of patient frailty. *Infection* 2024; 52: 1953–1963.

[10] Diaz-Arocutipa C, Moreno G, Vicent L. Impact of valvular surgery according to frailty risk in patients with infective endocarditis. *Clin Cardiol* 2024; 47: e24268.

[11] Saito Y, Aizawa Y, Iida K, *et al.* Clinical Significance of the Controlling Nutritional Status (CONUT) Score in Patients with Infective Endocarditis. *Int Heart J* 2020; 61: 531–538.

[12] Lu KJ, Kearney LG, Ord M, *et al.* Age adjusted Charlson Co-morbidity Index is an independent predictor of mortality over long-term follow-up in infective endocarditis. *Int J Cardiol* 2013; 168: 5243–5248.

[13] Pérez-García CN, Olmos C, García-Arribas D, *et al.* Frailty predicts in-hospital and 1-year outcomes in patients with infective endocarditis. *Clin Microbiol Infect* 2026; 32: 118–127.

[14] Delgado V, Ajmone Marsan N, de Waha S, *et al.* 2023 ESC Guidelines for the management of endocarditis. *Eur Heart J* 2023; 44: 3948–4042.

[15] Abellan van Kan G, Rolland YM, Morley JE, Vellas B. Frailty: toward a clinical definition. *J Am Med Dir Assoc* 2008; 9: 71–72.

[16] Rockwood K, Song X, MacKnight C, *et al.* A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005; 173: 489–495.

[17] Rubenstein LZ, Harker JO, Salvà A, *et al.* Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci* 2001; 56: M366–M372.

[18] Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. *Md State Med J* 1965; 14: 61–65.

[19] Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987; 40: 373–383.

[20] Pazdernik M, Iung B, Mutlu B, *et al.* Surgery and outcome of infective endocarditis in octogenarians: prospective data from the ESC EORP EURO-ENDO registry. *Infection* 2022; 50: 1191–1202.

[21] Medeiros MMD de, Figueredo OMC de, Pinheiro MA, *et al.* Factors associated with the overlap of frailty and nutrition in institutionalized older adults: A multicenter study. *Arch Gerontol Geriatr* 2020; 90: 104150.

[22] Abe T, Jujo K, Fujimoto Y, *et al.* Overlap of frailty and malnutrition as prognosticators in older patients with heart failure. *Am Heart J Plus.* 2024; 46: 100467.

[23] Ligthart-Melis GC, Luiking YC, Kakourou A, *et al.* Frailty,

Sarcopenia, and Malnutrition Frequently (Co-)occur in Hospitalized Older Adults: A Systematic Review and Meta-analysis. *J Am Med Dir Assoc* 2020; 21: 1216–1228.
[24] Arosio B, Ferri E, Mari D, *et al*. The influence of inflammation and frailty in the aging continuum. *Mech Ageing Dev* 2023; 215: 111872.
[25] Esteban-Fernández A, Villar-Taibo R, Alejo M, *et al*. Diagnosis and management of malnutrition in patients with heart failure. *JCM* 2023; 12: 3320.
[26] Jiménez-Méndez C, Díez-Villanueva P, Bonanad C, *et al*. Fragilidad y pronóstico de los pacientes mayores con insuficiencia cardiaca. *Revista Españ ola de Cardiología* 2022; 75: 1011–1019.
[27] Martínez-Sellés M, Muñoz P, Arnáiz A, *et al*. Valve surgery in active infective endocarditis: A simple score to predict in-hospital prognosis. *Int J Cardiol* 2014; 175: 133–137.
[28] Fernández-Hidalgo N, Ferreria-González I, Marsal JR, *et al*. A pragmatic approach for mortality prediction after surgery in infective endocarditis: optimizing and refining EuroSCORE. *Clin Microbiol Infect* 2018; 24: 1102. e7–1102. e15.
[29] Bonilla-Palomas JL, Gámez-López AL, Castillo-Domínguez JC, *et al*. Nutritional Intervention in Malnourished Hospitalized Patients with Heart Failure. *Arch Med Res* 2016; 47: 535–540.
[30] Kitzman DW, Whellan DJ, Duncan P, *et al*. Physical Rehabilitation for Older Patients Hospitalized for Heart Failure. *N Engl J Med* 2021; 385: 203–216.

Please cite this article as: Fernandez-Regueras M, Muñoz García P, Goikoetxea Agirre AJ, Blanco Vidal MJ, del Alamo Martínez de Lagos M, Goenaga Sánchez MA, Bustinduy Odriozola MJ, Camino Barrón X, Kestler Hernández M, Kallmeyer Mayor A, Martínez-Sellés M, Perez-Rivera JA. The geriatric syndromes in elderly patients with infective endocarditis: impact on in-hospital mortality. *J Geriatr Cardiol* 2026; 23(9): 565–575. DOI: 10.26599/1671-5411.2026.09.006