



# Prognostic impact of muscle ultrasound-guided diagnosis of sarcopenia in older adults with severe aortic stenosis

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## Key summary points

**Aim** This study is the first to explore the implications of diagnosing sarcopenia through ultrasound in older adults with severe aortic stenosis, introducing an ultrasound-guided assessment that adheres to the recommendations of the European Working Group on Sarcopenia in Older People.

**Findings** 1) Symptomatic severe aortic stenosis is a heart valve disease with a poor prognosis that often leads to serious clinical complications in older patients, with a highly invasive treatment of choice. 2) The existence of other conditioning factors, such as sarcopenia, that worsen the prognosis is frequent and produces greater uncertainty regarding the outcomes of these patients. 3) Sarcopenia assessment using ultrasound has not been previously explored in this clinical context, despite the technique being increasingly used, noninvasive, and relatively simple. 4) In our sample, the diagnosis of sarcopenia was associated with an independent increase in the risk of hospital admission and mortality due to cardiological causes after six months.

**Message** Given its potential usefulness in planning follow-up and treatment, ultrasound-guided sarcopenia assessment is highly recommended for older adults with aortic stenosis who are candidates for aortic valve replacement.

## Abstract

**Background** Muscle ultrasound is increasingly popular thanks to its advantages over other techniques. However, its usefulness in the diagnosis of sarcopenia in older adults with aortic stenosis (AS) has not been studied to date. Objectives: to analyze the prevalence of sarcopenia using muscle ultrasound and its impact on the health outcomes in older patients with AS.

**Methods** The single-center FRESAS (FRailty-Evaluation-in-Severe-Aortic-Stenosis) registry was used to study patients over 75 years with severe AS susceptible to valve replacement. Sarcopenia was suspected in those individuals with diminished grip strength, and the diagnosis was confirmed in the presence of reduced ultrasound quadriceps muscle thickness, following the recommendations of the EWGSOP2 (European-Working-Group-on-Sarcopenia-in-Older-People). The primary composite endpoint was urgent hospital admission and mortality of cardiac cause 6 months after the diagnosis.

**Results** Of the 150 patients studied, 55.3% were females, and only 17.3% were frail; the mean age was 83.4 years. Sarcopenia was diagnosed in 42 patients (28%). The overall survival rate at 6 months was 92%. The primary endpoint was recorded in 23.2% of the cases and was more frequent in the sarcopenic patients (33.3%) than in the non-sarcopenic individuals (17.6%) ( $p=0.01$ ). The regression analysis found that sarcopenia was associated with an increased risk of the primary endpoint (HR: 2.25; 95% CI 1.19–4.45;  $p=0.02$ ), adjusting for potential confounding factors.

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**Conclusions** The incidence of serious cardiac complications in older patients with sarcopenia and severe AS is significant. The present study describes a noninvasive, ultrasound-guided diagnostic technique that may prove efficient in its predictive capacity.

**Keywords** Sarcopenia · Ultrasonography · Frailty · Aortic valve stenosis · Aortic valve replacement

## Introduction

Aortic stenosis (AS) has high morbidity and mortality among older adults [1]. In severe and symptomatic presentations, the prognosis of AS is poor, with mortality rates that may even exceed those of metastatic cancer [2]. The typical symptoms of AS (dyspnea, chest pain, and syncope) define it as a highly disabling disease with a significant impact on quality of life [3]. In addition, its prevalence is high and increases exponentially with age. In individuals over 75 years, the estimated prevalence is 3.4% [4], and reaches 10% in those over 80 years of age [5].

The definitive treatment for AS is invasive and involves surgical or percutaneous aortic valve replacement (AVR); though in some cases, this is not feasible, and conservative management is chosen [6]. Careful evaluation by a subspecialized Heart Team is recommended to adequately estimate the risk–benefit balance of AVR and define the AS treatment modality best suited to each patient [7].

The progressive aging of the population and the advances in interventional procedures for treating AS have resulted in a progressive increase in the number of older patients undergoing AVR in recent years [8]. An increasing number of Heart Teams are incorporating geriatric specialists to perform a Comprehensive Geriatric Assessment (CGA) [9] to optimize decision-making and patient health through specific planning, with a view to eventual AVR [10]. In this regard, a thorough assessment of the patient's functional capacity is required, including the evaluation of frailty [11], which becomes increasingly common with advancing age and is characterized by reduced physiological capacity and stress response. This situation of increased vulnerability has been shown to have a negative impact on the health outcomes of older patients subjected to AVR, with increased dependency, readmissions, and mortality [12].

One of the main biological factors underlying frailty is sarcopenia [13], which is characterized by a multifactorial decrease in muscle capacity that raises the risk of adverse health events [14], and has also been associated with increased mortality, specifically in patients undergoing AVR [15]. The diagnosis requires the confirmation of a decrease in both muscle strength (which would imply probable sarcopenia) and in the muscle mass or quality (which would confirm the diagnosis) [16].

The main limitation to incorporating sarcopenia assessment into clinical practice generally refers to the evaluation of muscle mass, which requires techniques that are not widely available and consume significant resources and time. Despite the significant health implications of sarcopenia for older adults, it is often underdiagnosed [17]. However, the increasing accessibility of muscle ultrasound could change this situation, as it offers several significant advantages over other imaging techniques in the evaluation of sarcopenia: non-invasiveness, real-time imaging, greater portability and accessibility, and a relatively simple learning curve. In addition, it allows a valid, reproducible, and dynamic assessment of muscle quantity and quality [16, 18].

Considering the above, the present study was carried out in a cohort of older adults with symptomatic severe AS amenable to valve replacement to assess: (i) the prevalence of sarcopenia based on ultrasound-guided diagnosis, (ii) the relationship between sarcopenia and other clinical, functional, mental, and biological variables, and (iii) the relationship between sarcopenia and patient mortality and hospital admission after 6 months.

## Methods

### Study design

A prospective study was carried out in patients over 75 years of age with severe AS and amenable to AVR from the FRESAS (FRailty-Evaluation-in-Severe-Aortic-Stenosis) [19] cohort and who were consecutively assisted by the only cardiac valve Heart Team in the region (Spanish Autonomous Community) where the study was conducted.

Before the procedure, a CGA was performed in a monographic frailty and prehabilitation clinic for older patients with AS eligible for AVR. The inclusion criteria were being 75 years of age or older, having been diagnosed with severe AS, agreeing to undergo the CGA, and providing written informed consent for participation in the study. Failure to meet any one of these criteria resulted in exclusion from the study. All patients signed the corresponding informed consent document. The study flowchart is shown in [Supplementary Figure S1]. The study adhered to the principles of the Helsinki Declaration and was approved by the local Research Ethics Committee.

## Study variables

Demographic, clinical, nutritional, functional, and mental health variables were studied. Regarding the study endpoints, the analysis focused on survival and urgent hospital admissions 6 months after CGA. The primary composite endpoint was urgent hospital admission and mortality from cardiac causes. This same endpoint was secondarily evaluated, referring to all-cause mortality. The definition of cardiovascular and non-cardiovascular events adhered to the recommendations of the Standardized Data Collection for Cardiovascular Trials Initiative [20]. We differentiated non-cardiovascular from cardiovascular causes due to the anticipated substantial rate of non-cardiological complications within our cohort, as documented in previous studies of patients with similar characteristics [21]. Medical record reviews were meticulously conducted and supplemented by telephone follow-ups. There were no follow-up losses.

## Identification of sarcopenia

A sarcopenia case was defined following the recommendations of the EWGSOP2 (European-Working-Group-on-Sarcopenia-in-Older-People) [16]. Grip strength was determined using a Smedley-SHAHAN hand dynamometer, recording the highest of three measurements in the dominant hand, with the patient seated, shoulders neutrally rotated, wrists in a neutral position, and elbows flexed at 90°. Muscle mass was estimated by measuring muscle thickness using a Vscan Extend handheld ultrasound system. In all cases, the assessment of muscle mass was carried out by the same investigator, who had previously been trained in muscle ultrasound. The examination was conducted at the level of the quadriceps femoris muscle, with the patient in a sitting position, hips and knees flexed at 90°, muscles relaxed, and after 10–15 min of rest. This position for ultrasound imaging was chosen as it best adapted to the functioning, professionals, and patients of the clinic; being one of the recommended positions for measuring muscle thickness in the lower extremity via ultrasound. The linear probe was positioned equidistantly between the proximal portion of the patella and the greater trochanter, applying minimal pressure to the skin. Muscle thickness was determined by measuring the distance from the deep muscle aponeurosis to the superficial aponeurosis, including the rectus femoris and vastus intermedius muscles, in a transverse ultrasound capture. The same chair was consistently used for all sarcopenia measurements. This sarcopenia assessment protocol was designed following major recommendations to achieve the greatest accuracy possible and to facilitate comparisons with other studies measuring grip strength using a dynamometer [22] and/or muscle thickness via ultrasound [23].

## Statistical analysis

A descriptive analysis of the baseline characteristics of the sample was carried out. Data were expressed as the mean  $\pm$  standard deviation (SD) for continuous quantitative variables and as percentages or frequencies for qualitative variables. Muscle mass was analyzed as a qualitative variable based on tertiles of muscle thickness (low, intermediate, and high). The Chi-square test or Fisher's exact test was used to compare qualitative variables between groups, while quantitative variables were compared using the Student's *t*-test or analysis of variance. The follow-up analysis was based on the Kaplan–Meier method and log-rank test. Multivariate logistic regression analysis explored differences in the study endpoints among groups, adjusting for potential confounders using the backward-stepwise method. As potential confounding factors, the multivariate regression analysis included patient age, sex, body mass index (BMI), the EuroSCORE-II, the New York Heart Association functional class, the short-form Charlson index, the degree of functional dependency (based on the Barthel index), and frailty (according to the Essential Frailty Toolset or EFT).

## Results

### General characteristics

The study comprised 150 patients (83 females [55.3%]) aged  $83.4 \pm 4.3$  years and with an estimated cardiological risk score (EuroSCORE-II) of  $3.1 \pm 2.5$ . Fifty-nine patients (39.3%) presented comorbidities, the most frequent of which were arterial hypertension (111 patients [74%]), anemia (56 patients [37.3%]), atrial fibrillation (48 patients [32%]), heart failure (43 patients [28.7%]), diabetes mellitus (43 patients [28.7%]), and chronic kidney disease (38 patients [25.3%]). The mean EFT score was  $1.4 \pm 1.0$ , with 26 patients (17.3%) being frail (score  $\geq 3$ ).

### Morphofunctional assessment

The morphofunctional assessment [Supplementary Table S1] recorded a grip strength of  $16.2 \pm 5.4$  kg, greater in males ( $20 \pm 5.2$  kg vs.  $13.2 \pm 3.4$  kg in females;  $p < 0.001$ ). Mean total muscle thickness was  $31.6 \pm 7.8$  mm, with the following tertiles: low ( $< 28.3$  mm), intermediate ( $28.3$ – $34.5$  mm), and high ( $> 34.5$  mm). Within the group of individuals with normal muscle strength (25 patients [16.7%]), total muscle thickness was seen to be diminished in 8 cases (32%). Sarcopenia was detected in 42 patients (28.0%) [Fig. 1].

## Univariate analysis

The patient characteristics according to the diagnosis of sarcopenia are shown in Table 1. The patients with sarcopenia were comparatively older ( $85.1 \pm 4.5$  vs.  $82.2 \pm 4.2$  years;  $p < 0.01$ ) and had a lower BMI ( $28.2 \pm 4.4$  vs.  $30.3 \pm 4.3$  kg/m<sup>2</sup>;  $p < 0.01$ ), though no significant sex differences were observed (females 61.9% vs. 52.9%;  $p = 0.29$ ). The patients with sarcopenia moreover presented a higher cardiac risk (EuroSCORE-II  $4.7 \pm 3.6$  vs.  $2.6 \pm 1.6$ ;  $p = 0.001$ ) and global comorbidity (short-form Charlson index  $1.3 \pm 1.3$  vs.  $2.0 \pm 1.4$ ;  $p < 0.01$ ). Furthermore, sarcopenia was associated with a greater prevalence of heart failure (47.6% vs. 21.3%;  $p < 0.01$ ) and higher NT-proBNP levels ( $3954.8 \pm 5304.2$  vs.  $1813.5 \pm 2819.9$  pg/ml;  $p = 0.02$ ).

The patients with sarcopenia presented poorer nutritional status (Mini-Nutritional Assessment—Short Form  $10.6 \pm 2.6$  vs.  $11.8 \pm 2.0$ ;  $p < 0.01$ ) and functional assessment scores (Short Physical Performance Battery  $6.6 \pm 2.8$  vs.  $7.9 \pm 2.5$ ;  $p < 0.01$ ; Lawton index  $4.5 \pm 2.3$  vs.  $5.3 \pm 2.3$ ;  $p = 0.048$ ; and Barthel index  $84.9 \pm 18.3$  vs.  $91.9 \pm 11.7$ ;  $p = 0.03$ ).

## Outcomes and multivariate analysis

The overall survival rate after 6 months was 92%, with 12 deaths out of 150 patients. Eleven deaths (91.7%) were attributed to cardiological causes. The composite endpoint hospital admission and mortality-free survival rate (considering all causes of mortality) was 72% (108 patients). The hospital admission rate due to all causes was 26.7% (40 patients) in this period versus 22% (33 patients) due to cardiological causes.

In the univariate analysis and considering cardiological causes, the patients diagnosed with sarcopenia had higher admission (33.3% vs. 17.6%;  $p = 0.04$ ) and mortality rates (16.7 vs. 3.7%;  $p = 0.01$ ) after 6 months than the patients without sarcopenia. In this regard, the composite endpoint mortality and urgent hospital admission due to cardiac causes occurred more often in the sarcopenia group (35.7% vs. 18.5%;  $p = 0.03$ ) after 6 months [Fig. 2, Supplementary Table S2].

In the multivariate analysis, on examining the composite endpoint mortality and hospital admission due to all causes after 6 months [Supplementary Table S3], the following parameters were retained in the final regression model: male sex (adjusted hazard ratio [HR]: 2.05; 95% confidence interval [CI] 1.11–3.80;  $p = 0.02$ ), EFT score (HR: 2.52; 95% CI 1.30–4.88;  $p < 0.01$ ), and sarcopenia (HR: 1.80; 95% CI 0.96–3.39;  $p = 0.07$ )—the latter proving nonsignificant. In contrast, the adjusted multivariate analysis of the primary composite endpoint mortality and hospital admission due to cardiac causes after 6 months [Table 2] did retain

sarcopenia with statistical significance (HR: 2.25; 95% CI 1.14–4.45;  $p = 0.02$ ), in the same way as male sex (HR: 2.35; 95% CI 1.19–4.66;  $p = 0.01$ ) and EFT score (HR: 2.36; 95% CI 1.15–4.84;  $p = 0.02$ ). This is reflected by the adjusted cumulative risk curves versus the primary endpoint [Fig. 3].

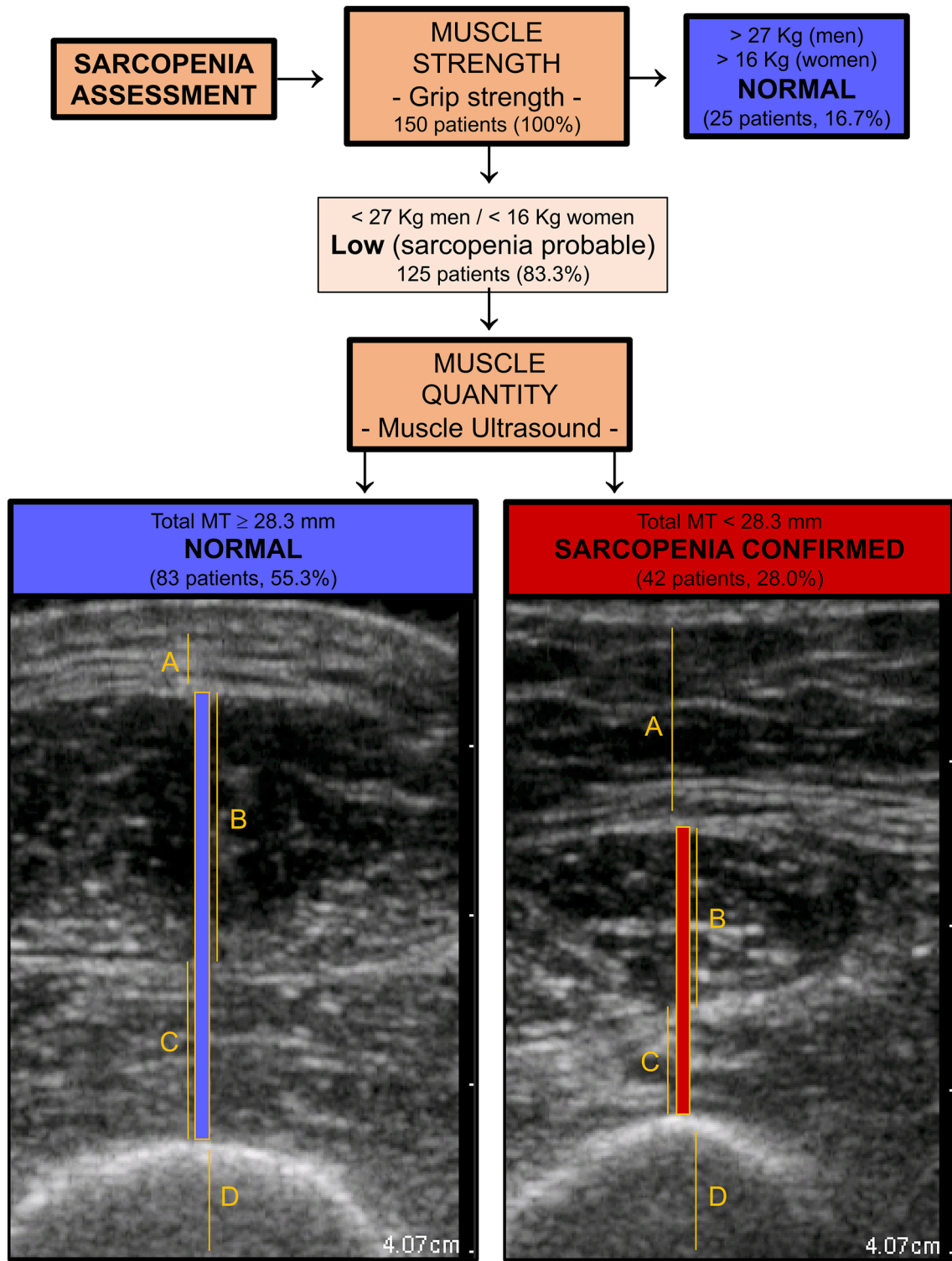
A supplementary analysis of the primary endpoint was conducted, using an alternative definition of sarcopenia that also differentiated muscle thickness by sex. The lower tertile of muscle thickness was identified as 26.2 mm for females and 29.8 mm for males. Employing these sex-specific cutoff points for the confirmation of sarcopenia, among the 125 patients with reduced grip strength, 43 patients (34.4%) had decreased muscle thickness. The supplementary regression analysis also retained sarcopenia (HR: 2.11; 95% CI 1.08–4.14;  $p = 0.03$ ), male sex (HR: 2.17; 95% CI 1.10–4.28;  $p = 0.03$ ) and EFT (HR: 2.47; 95% CI 1.20–5.06;  $p = 0.01$ ) [Supplementary Table S4].

## Discussion

To our knowledge, no study to date has employed muscle ultrasound to assess sarcopenia in people with AS eligible to AVR. Based on our results, the confirmation of sarcopenia using muscle ultrasound in older patients with severe AS and diminished grip strength is associated with a more than twofold increase in the risk of severe cardiac decompensation, hospital admission, or death 6 months after diagnosis.

Muscle ultrasound is helpful for quantifying muscle mass and identifying sarcopenia [24], as shown by several population-based studies of older patients [25]. The measurement of muscle thickness is easily applicable in clinical settings and has been widely investigated. However, the existing studies differ in decisive factors such as the positioning of the ultrasound probe, the analyzed muscle or muscle group, and the type and positioning of patient involved. This situation dramatically complicates quantitative comparisons between series and the definition of cutoff points for classifying low muscle mass. Consequently, initiatives such as those of the SARCUS group [23] or the ECOSARC project [26] have sought to establish the bases for standardized ultrasound evaluation of sarcopenia in routine clinical practice. For example, Kawai et al. measured muscle thickness in over 1000 older subjects using a protocol resembling our study and recorded a similar prevalence of sarcopenia (31.5%) [27]. However, Minetto et al., also using a protocol similar to ours (though involving a smaller sample size), recorded a very different prevalence of sarcopenia, reaching 81% [28].

In addition to the discrepancies in the prevalence of sarcopenia between series inherent to the ultrasound-guided diagnosis of the disorder, other relevant factors also contribute to the heterogeneity of the results. We know that aging is accompanied by a progressive loss of strength and muscle



**Fig. 1** Diagnosis of sarcopenia using ultrasound. Image at left: ultrasound view of an individual with normal muscle mass in our sample; image at right: ultrasound view of an individual with diminished muscle mass in our sample. Obtained and shared with patient permis-

sion. Abbreviations: *MT* muscle thickness. **A** represents thickness of the subcutaneous adipose tissue; **B** represents thickness of the rectus femoris muscle; **C** represents thickness of the vastus intermedius muscle; **D** represents the femur. Total *MT* is the sum of **B** and **C**

**Table 1** Differences according to the diagnosis of sarcopenia

	All	No sarcopenia	Sarcopenia	<i>p</i> -value
Variables	150 (100)	108 (72)	42 (28)	
General				
Age (years)	83.4±4.4	82.8±4.2	85.1±4.5	<0.01*
Sex (female)	83 (53.3)	57 (52.8)	26 (61.9)	0.31
BMI (kg/m <sup>2</sup> )	29.8±4.4	30.3±4.3	28.2±4.4	<0.01*
LVEF<50%	15 (10.0)	9 (8.3)	6 (14.3)	0.36
NYHA≥3	32 (21.3)	20 (18.5)	12 (28.6)	0.18
EuroSCORE-II	3.2±2.5	2.6±1.6	4.7±3.6	<0.01*
Diseases				
Arterial hypertension	111 (74.0)	77 (71.3)	34 (81.0)	0.23
Anemia	56 (37.3)	40 (37)	16 (38.1)	0.90
Atrial fibrillation	48 (32)	30 (27.8)	18 (42.9)	0.08
Heart failure	43 (28.7)	23 (21.3)	20 (47.6)	<0.01*
Diabetes mellitus	43 (28.7)	27 (25.7)	16 (36.6)	0.11
Chronic kidney disease	38 (25.3)	23 (21.3)	15 (35.7)	0.07
Charlson SF	1.5±1.3	1.3±1.3	2.0±1.4	<0.01*
High comorbidity (>3)	30 (20)	17 (15.7)	13 (31.0)	0.04*
Biomarkers				
Hemoglobin (g/dl)	12.9±1.8	13.0±1.9	12.7±1.5	0.28
Creatinine (mg/dl)	1.1±0.4	1.1±0.4	1.1±0.4	0.57
Albumin (g/l)	44.3±3.2	44.4±3.4	44.0±2.8	0.51
NT-proBNP (pg/ml)	2413.1±3792.4	1813.5±2819.9	3954.8±5304.2	0.02*
Nutritional assessment				
MNA SF	11.5±2.2	11.8±2.0	10.6±2.6	<0.01*
Mental assessment				
MMSE	26.4±4.5	26.7±3.2	24.9±6.6	0.06*
Frailty and function				
EFT	1.4±1.0	1.3±1.0	1.6±1.1	0.16
SPPB	7.6±2.7	7.9±2.5	6.6±2.8	<0.01*
Lawton index	5.1±2.3	5.3±2.3	4.5±2.3	0.05*
Barthel index	89.9±14.1	91.9±11.7	84.9±18.3	0.03*

Results: mean and standard deviation [mean ± SD] or cases and percentage [*n* (%)]

*BMI* body mass index, *LVEF* left ventricular ejection fraction, *NYHA* New York heart association functional class, *SF* short form, *MNA* mini-nutritional assessment, *MMSE* mini-mental state examination, *EFT* essential frailty toolset, *SPPB* short physical performance battery

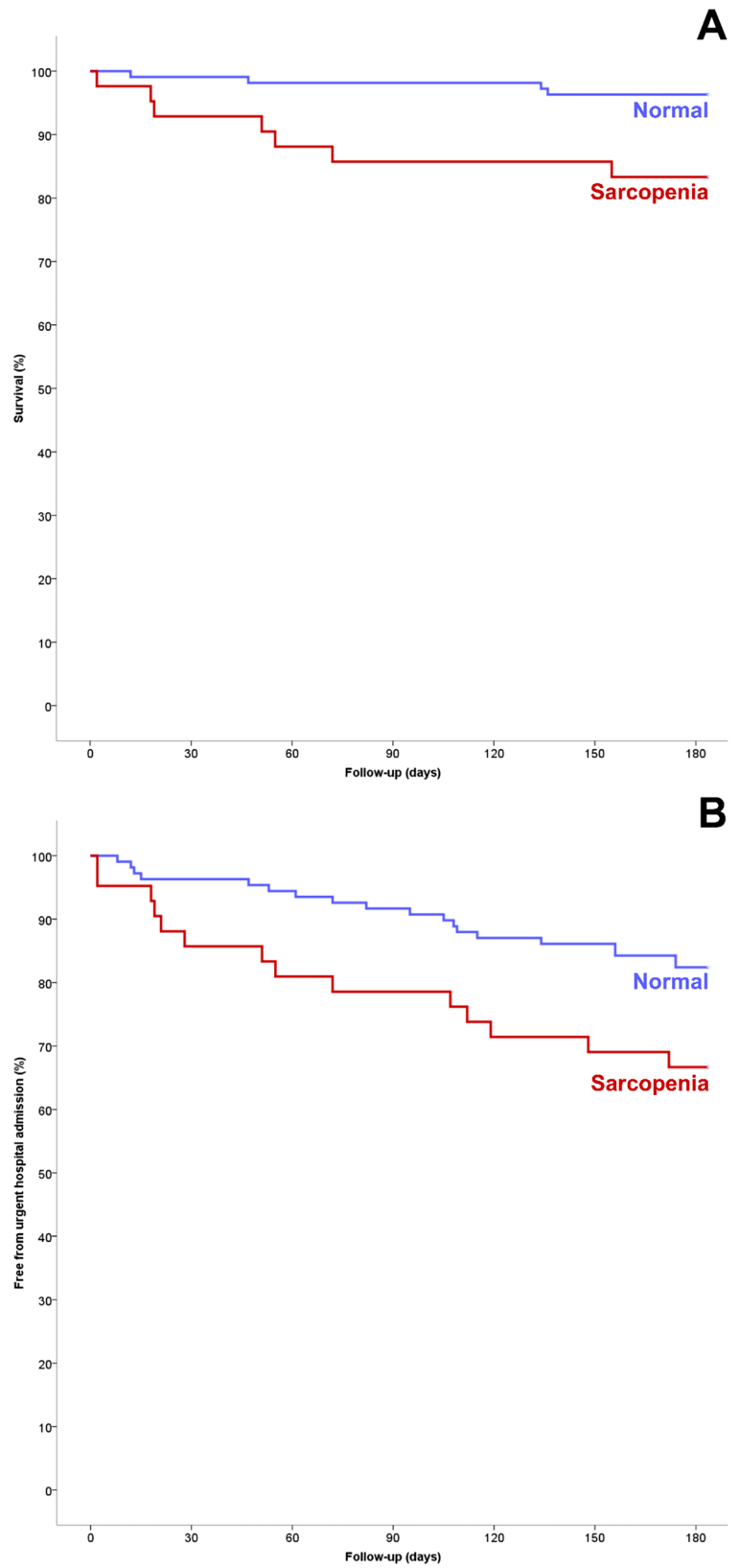
\*Statistical significance (*p*<0.05)

mass. Hence, the prevalence of sarcopenia increases markedly with age [29], in addition to being influenced by different classifications, diagnostic methods, and study populations involved [30]. Specifically in patients with AS, most studies on the role of sarcopenia analyze the results after transcatheter AVR, with opportunistic assessment of muscle mass using the computed tomography (CT) images needed to plan the procedure. A systematic review has reported the prevalence of sarcopenia across different series of patients subjected to transcatheter AVR to vary between 21.0 and 70.2% [31]. Only 1 of the 18 studies analyzed in the review mentioned included muscle performance in the assessment of sarcopenia, which was identified in 21% of the patients

and was predictive of mortality, disability, and institutionalization after AVR [15].

By systematically evaluating all older patients undergoing AVR with CGA, we found that the individual's functional capacity is one of the main determining factors of patient evolution after the intervention. This is in line with the observations of other investigators [32]. In addition to performing a detailed risk assessment [7], CGA seeks to establish a specific intervention plan targeting defects susceptible to management before AVR is performed [10]. This period constitutes a critical step for these patients since the seriousness of their heart condition confers significant vulnerability on its own. Close monitoring is, therefore, required,

**Fig. 2** Impact of the diagnosis of sarcopenia upon mortality and urgent hospital admissions due to cardiological causes after 6 months. **A** Cumulative mortality curve due to cardiological causes after 6 months (*log-rank*  $p=0.005$ ). **B** Cumulative urgent admissions curve due to cardiological causes after 6 months (*log-rank*  $p=0.026$ )



**Table 2** Independent predictors of mortality and/or admission due to cardiological causes after 6 months. Results of the Cox regression analysis

Variable	HR	Lower CI	Upper CI	<i>p</i> value
Sex (male)	2.35	1.19	4.66	0.01*
EFT (frail)	2.36	1.15	4.84	0.02*
Sarcopenia	2.25	1.14	4.45	0.02*

Model adjusted for patient age, sex, body mass index (BMI), the EuroSCORE-II, the *New York Heart Association* functional class, the short-form Charlson index, the degree of functional dependency (based on the Barthel index), and frailty (according to the Essential Frailty Toolset) (EFT)

HR hazard ratio, CI confidence interval, EFT essential frailty toolset

\*Statistical significance ( $p < 0.05$ )

considering mainly the clinical manifestations and the echocardiographic parameters to adequately guide treatment, since the evolution of the disease is sometimes unpredictable, and the rate of severe cardiological complications is high [33]. In older adults with AS being evaluated for aortic valve replacement, high rates of urgent hospitalization, up to 40%, have already been described in the period immediately preceding the procedure [34]. This highlights the need to identify parameters that allow the detection of patients at higher risk of decompensation. In our study, approximately one out of every four patients evaluated in our center required urgent hospital admission in the 6 months following the assessment. Likewise, the primary composite endpoint of admission and mortality after 6 months due to cardiac causes occurred in about one out of every five patients, and the frequency was even higher in those individuals with sarcopenia (one out of every three patients).

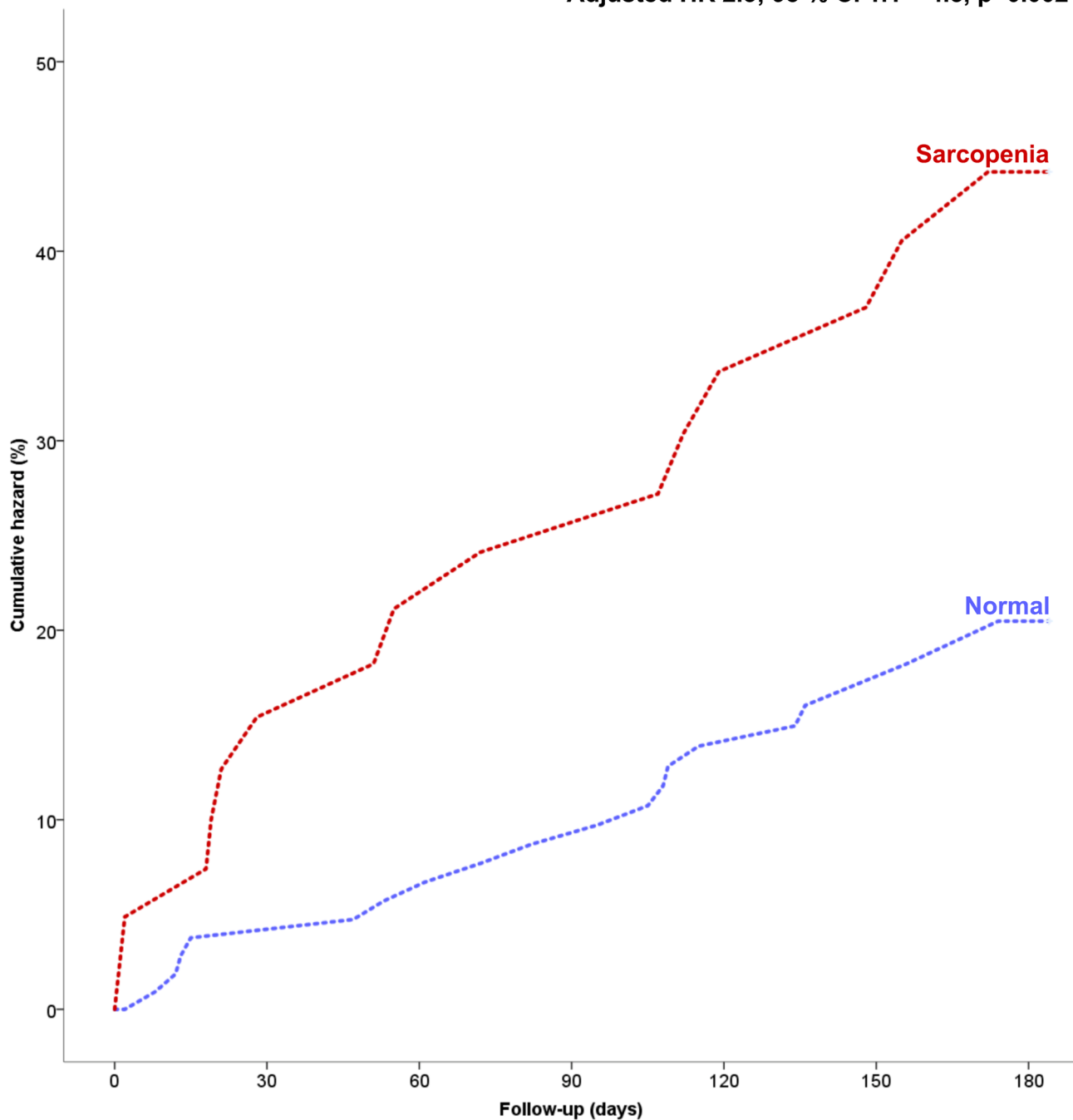
The adjusted analysis confirmed the potential of sarcopenia as a predictor of adverse health outcomes during the period immediately before AVR in our sample, independently of relevant confounders. Our study findings not only support the recommendation of other authors to assess sarcopenia for risk evaluation and guide intervention in these patients [35], but also highlight the significant role of point-of-care ultrasound in its detection, reinforcing its high value in daily clinical practice [36]. A recent systematic review has described how identifying skeletal muscle status using ultrasound can predict major adverse clinical events such as mortality, readmissions, hospital stay, and functional decline. However, most of the mentioned studies investigating the impact of ultrasound-guided sarcopenia diagnosis have been conducted in acute patients, primarily in intensive care units [37]. Specifically, in patients with heart disease, other studies have found associations between muscle ultrasound variables at the quadriceps level and exercise capacity, although these studies were conducted in younger patients than our sample [38, 39].

We also found substantial correlations between the prior muscle status and cardiological condition of our patients: the prevalence of heart failure was more than twice as high among the patients with sarcopenia compared with those without sarcopenia, as were the mean brain natriuretic peptide levels. This could be explained by the intimate relationship between the muscular and cardiac systems; when these fail to function correctly, a systemic energy imbalance is ultimately generated that tends to perpetuate over time [40]. Thus, in older individuals, it is common for a vicious circle to develop in which sarcopenia and heart disease, overlapping through their common pathophysiology, merge and enhance their harmful effects, producing a gradual loss of intrinsic capacity [41]. Muscle ultrasound can be used as a complementary tool in the assessment of other classic prognostic factors in older adults with heart disease, such as NT-proBNP, presenting several advantages. First, it is a noninvasive test that provides immediate results. In contrast to blood tests, muscle ultrasound does not consume additional resources or time of other healthcare professionals, potentially streamlining the process and reducing costs. In addition, muscle ultrasound can be performed using equipment that is typically available in a cardiogeriatrics clinic. It is a repeatable and reliable method that provides information for a direct estimation of muscle mass, which is particularly relevant in the context of sarcopenia, and it can be used to monitor morphofunctional changes over time.

Interestingly, the EFT score was also an independent predictor of urgent hospital admission and mortality due to all causes or cardiac causes within 6 months in our patients. The EFT score is already highly recommended due to its superior capacity to predict unfavorable outcomes after AVR, compared to other frailty scales [12]. Our study further underscores its usefulness and may serve to extend its utility to the period immediately before the intervention. Lastly, it should be mentioned that the male sex was also identified as a prognostic factor in relation to the aforementioned unfavorable composite endpoints in our patients. This finding contrasts with most of the available evidence [42], although the latter is still insufficient because of the great complexity and uncertainty that characterize this clinical scenario [43].

Given the complexity involved, the estimation of the physiological reserves based on CGA should be supported by objective data, allowing us to estimate the stress response capacity of these patients as accurately as possible. This inevitably requires the assessment of sarcopenia, which has already been shown to be predictive of adverse health outcomes in this clinical scenario, though using techniques different from those of our study. Undoubtedly, gaining experience and developing this technique over the coming years will facilitate the translation from sarcopenia assessment research to the clinical setting in geriatric cardiology [44]. It seems necessary to develop new research projects to

Adjusted HR 2.3; 95 % CI 1.1 – 4.5, p=0.002



**Fig. 3** Cumulative mortality and/or urgent hospital admission risk due to cardiological causes after 6 months, according to ultrasound identification of sarcopenia. Curves adjusted for patient age, sex, body mass index (BMI), the EuroSCORE-II, the *New York Heart*

*Association* functional class, the short-form Charlson index, the degree of functional dependency (based on the Barthel index), and frailty (according to the Essential Frailty Toolset)(EFT). Abbreviations: *HR* hazard ratio, *CI* confidence interval

address these limitations and assess other aspects, such as the role of muscle ultrasound in the evolutive course of these patients after AVR. Given our results, future research should evaluate whether a prioritized intervention for AS and targeted programs to address sarcopenia could improve health

outcomes in patients who are suitable for AVR. Moreover, further studies should investigate the post-AVR evolution of patients diagnosed with sarcopenia using ultrasound and evaluate the potential prognostic impact of this method.

Our study provides highly relevant information by showing results in older patients with severe aortic stenosis in a critical outpatient scenario, the period closest to aortic valve replacement. In addition to addressing a significant gap in the current literature, being the first study to our knowledge to evaluate sarcopenia using ultrasound in older adults with severe aortic stenosis, several other strengths of our work should be highlighted. All images were taken by the same observer who was previously trained in muscle ultrasound, ensuring consistency, and reducing the possibility of measurement errors. The study utilized a standardized protocol for sarcopenia assessment, adhering firmly to the diagnostic algorithm established by the EWGSOP2, with no data or follow-up losses. The main limitation of our study is its single-center nature, which implies a relatively low number of patient deaths. This must be considered when extrapolating our results to the clinical setting. In addition, although we did not find statistically significant differences in muscle thickness between sexes, and the association between sarcopenia and the primary endpoint remains unaltered in the population studied when considering this aspect, it seems that further studies with a larger number of patients are necessary to explore potential sex differences in the diagnosis of sarcopenia more comprehensively. Another limitation is that we did not evaluate other more complex muscle ultrasound parameters that should be included in advanced morphofunctional assessments, such as muscle quality [45]. It would also be valuable to obtain additional information by assessing alternative subject positioning and different muscle groups in this same patient population. In addition, muscle ultrasound measurements were not compared with results from other reference techniques used to estimate muscle mass, such as CT or magnetic resonance imaging.

## Conclusions

The method we proposed to diagnose sarcopenia involves the noninvasive determination of two relatively simple parameters—grip strength (using a dynamometer) and muscle mass (using ultrasound)—and shows that sarcopenic individuals have an over twofold greater risk of admission or death due to cardiovascular causes after 6 months.

These results underscore the important clinical implications of our findings and reinforce the usefulness of ultrasonography in daily clinical practice for the evaluation of sarcopenia in older patients with severe AS. Therefore, we recommend the systematic assessment of sarcopenia, ideally supported by ultrasound, in all older patients scheduled to undergo AVR to enhance treatment planning and clinical follow-up.

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**Data availability** The datasets analyzed during the current study are not publicly accessible. However, the data that support the findings of this study are available from the corresponding author upon reasonable request.

## Declarations

**Conflict of interest** The authors declare no conflicts of interest.

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