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RESEARCH ARTICLE

Prevalence and Impact of Sarcopenia in Heart Failure: A Cross-Sectional Study

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Abstract:

Background:

Abnormal structure and function of cardiac muscles in heart failure (HF) may lead to decreased muscle mass and muscle strength, including low physical performance. This may play an important role in the development of sarcopenia.

Objective:

The objectives of this study were to determine the prevalence of sarcopenia among patients with HF and to explore the association between sarcopenia and HF.

Methods:

A cross-sectional study of 152 patients with HF was conducted in Thammasat University Hospital and Central Chest Institute of Thailand. Sarcopenia was defined according to the Asian Working Group for Sarcopenia. Participants were requested to perform handgrip strength, gait speed, and muscle mass. Logistic regression analysis was used to examine the association between sarcopenia occurrence and HF.

Results:

The prevalence of sarcopenia in patients with HF was 19.8% (14.0% in men and 31.1% in women). Participants with sarcopenia had a significantly lower body mass index (BMI) than those without sarcopenia ($p<0.001$). In addition, patients with sarcopenia had significantly lower respiratory muscle strength than those without sarcopenia ($p<0.01$). Sarcopenia was found to be significantly associated with age, sex, BMI, and left ventricular ejection fraction (LVEF) ($p<0.05$). In addition, age, sex, BMI, and LVEF predicted skeletal muscle mass index (SMI) accounted for 76.8% of the variance.

Conclusion:

The prevalence of sarcopenia among patients with HF was similar to that reported in previous studies. Regarding risk factors, age, sex, BMI, and LVEF were related to sarcopenia in the female sex, advanced age, low BMI, and low LVEF.

Keywords: Heart failure, Sarcopenia, Left ventricular ejection fraction, Skeletal muscle dysfunction, Malnutrition, Risk factors.

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1. INTRODUCTION

Sarcopenia is characterized by decreased muscle mass, muscle strength, and low physical performance. Age-related sarcopenia and chronic illness lead to adverse health outcomes (*e.g.*, skeletal muscle dysfunction, risk of falls, physical disability, poor quality of life, and increased mortality) [1 - 3]. In approximately 25% of the cases, sarcopenia leads to hospitalization of a patient, and malnutrition, long-term hospitalization, hormonal changes, and physical inactivity contribute to the reduction in muscle mass and muscle strength [1, 3, 4]. Two types of sarcopenia have been proposed: 'primary sarcopenia' related to advanced age and low muscle mass and 'secondary sarcopenia' associated with organ failure

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or chronic disease-related low muscle mass such as cancer, chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, and cardiovascular disease (*i.e*., heart failure: HF) [5, 6].

HF is prevalent in 37.7 million people globally [7], and sarcopenia is prevalent in 10.1% of patients with HF [2]. In cases of sarcopenia with HF, the destruction of cardiomyocytes, the vascular system, apoptosis, autophagy, and protein synthesis, resulting in changes in myofibril and mitochondrial activities, have been reported [2]. Curcio *et al*. stated that HF is caused by abnormal cardiac structure and/or function, which results in decreased cardiac output and/or increased intracardiac pressure at rest or during stress [2]. These factors damage cardiomyocytes in HF and contribute to exercise intolerance, decreased physical performance, reduced oxygen consumption, and changes in daily activity. Patients with HF experience dyspnoea or breathlessness during rest or during activities. Loss of peripheral muscle and respiratory muscle weakness in the early stage of HF was reported in both HF with reduced ejection fraction (HfrEF) and HF with preserved ejection fraction (HfpEF) [8 - 11]. These symptoms might result in decreased physical activity, decreased exercise tolerance, and reduced daily activity, leading to decreased muscle strength and physical performance.

Several factors contribute to the development of sarcopenia, which leads to a reduction in muscle mass, decreased muscle strength, and low physical performance, as well as a decrease in the quality of life in patients with HF. Therefore, the present study determined the prevalence and association of sarcopenia among patients with HF.

2. MATERIALS AND METHODS

According to Canteri *et al*. [2], the prevalence of HF patients with sarcopenia was 10.1%; therefore, the estimated sample size of the present study was 154 participants. In this cross-sectional study, we explored the prevalence of sarcopenia in patients with HF and its association with the risk of sarcopenia. In total, there were 154 participants (men and women aged ≥18 years). These participants were diagnosed with HF by a cardiologist or medical professional in the outpatient and inpatient departments. Participants who had unstable angina, acute myocardial infarction, or uncontrolled arrhythmias within 3 months prior to the test were excluded. In addition, patients with a high blood pressure >180/100 mmHg at rest or a heart rate >120 beats/min at rest were excluded.

All participants provided their written informed consent, and the study protocol was approved by the institute's committee on human research. In addition, this study protocol was reviewed and approved by the Ethics Human Committee of Thammasat University based on the Declaration of Helsinki, the Belmont Report, the Council for International Organizations of Medical Sciences (CIOMS) Guidelines, and the International Practice (ICH-GCP), approval number COA no. 071/2563.

Based on the Asian Working Group for Sarcopenia (AWGS) 2019 criteria, muscle mass, muscle strength, and physical performance were measured to screen for sarcopenia [12]. All participants were required to perform muscle strength using a handgrip dynamometer (T.K.K.5401 Grip D; Tokyo, Japan). Participants were asked to stand with feet equal to shoulder-width apart and then hold the handgrip on the dominant arm. Low handgrip strength was defined as <28 kg for men and <18 kg for women [12, 13].

In order to perform the gait speed, participants were asked to walk at normal speed in a corridor for 10 m; the time taken to walk from 2 to 8 m was recorded using a stopwatch. Participants who walked <1.0 m/s were defined as having low physical performance [12]. Finally, all individuals were required to measure muscle mass *via* bioelectrical impedance analysis (BIA, Model HBF-375, Osaka, Japan), and the skeletal muscle mass index is calculated using SM mass/ht^2. Low muscle mass was defined as <7.0 kg/m^2 in men and <5.7 kg/m^2 in women [12, 13]. To categorize sarcopenia, all participants underwent physical performance (*i.e*., gait speed, handgrip strength, and muscle mass) evaluation.

2.1. Statistical Analysis

Descriptive statistics were used to present sample characteristics in terms of frequency, percentage, and prevalence of sarcopenia. To explore the difference between the sarcopenia group and the non-sarcopenia group, a t-test or chi-square analysis was used when appropriate. Logistic regression analysis was used to examine the association between the occurrence of sarcopenia and HF. Finally, a series of hierarchical regression analyses were used to determine whether risk factors predicted low muscle mass in HF.

3. RESULTS

Of the 270 participants in outpatient clinics in the hospital, 154 participants met the inclusion criteria. However, two participants were unable to perform gait speed or handgrip strength; therefore, they were excluded. Finally, a total of 152 participants were enrolled, and they completed the sarcopenia screening test (Fig. **1**).

According to the AWGS criteria, the prevalence of sarcopenia in patients with HF was 19.8%. The mean age of the participants was 58.5±11.8 years, and participants in the sarcopenia group were significantly older than those in the non-sarcopenia group. In addition, individuals with sarcopenia were predominantly female (p=0.021), had reduced left ventricular ejection fraction, and had low BMI compared with those without sarcopenia. The skeletal mass index, gait speed, and handgrip strength were also significantly lower in the sarcopenia group than in the non-sarcopenia group ($p<0.001$). In addition, patients with sarcopenia had significantly lower respiratory muscle strength than those without sarcopenia ($p<0.01$). However, there was no association with functional class (defined as the New York Heart Association (NYHA) classification; p>0.05). Table **1** displays the characteristics of Thai patients with HF in the sarcopenia and non-sarcopenia groups.

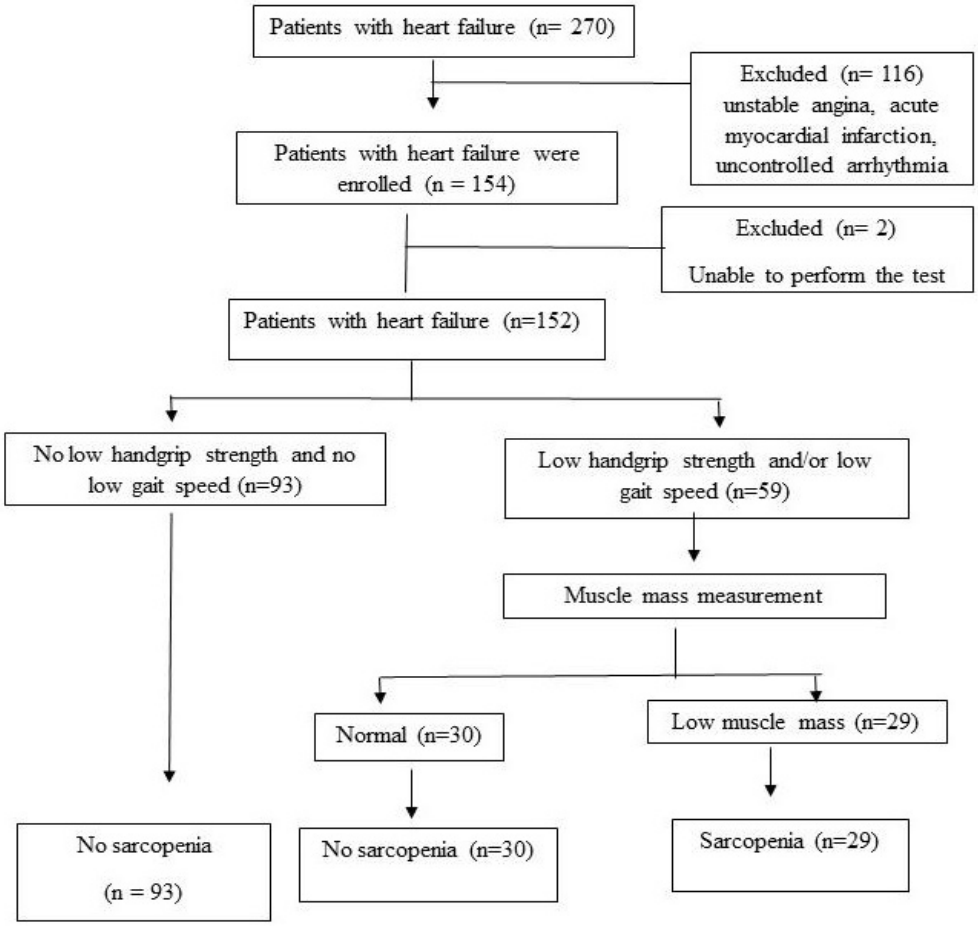

Fig. (1). Sarcopenia category by diagnostic algorithms of Asian Working Group for Sarcopenia.

Table 1. Baseline characteristics of Thai patients with heart failure among sarcopenia and non-sarcopenia (n=152).

Variable	Total (n=152)	Sarcopenia (n=29)	Non-Sarcopenia (n=123)	χ^2	p[a]
Sex (%) Male Female	107(70.39) 45 (29.61)	15 (14.02) 14 (31.11)	92 (85.98) 31 (68.89)	5.994	0.015
LVEF (%) HFrEF (<40%) HFpEF (≥40%)	90 (59.21) 62(40.79)	22 (24.44) 7 (11.29)	68 (75.56) 55 (88.71)	4.114	0.032
NYHA class (%) I II III	73 (48.03) 63 (41.45) 16 (10.53)	12 (16.44) 13 (20.31) 4 (25.53)	61 (83.56) 50 (79.37) 12 (76.47)	0.792	0.673
	Mean±SD	**Mean±SD**	**Mean±SD**	**t**	**p[b]**
Age (years)	58.50±11.83	65.66±9.28	56.81±11.77	3.777	<.001
BMI (kg/m^2)	26.51±4.95	22.97±3.47	27.34±4.89	-4.553	<.001
EF (%)	37.28±13.22	32.07±9.00	38.51±13.78	-2.395	.018
SMI (kg/m^2)	7.18±1.55	5.56±0.79	7.56±1.43	-7.267	<.001
Gait speed (m/s)	1.12±0.27	0.93±0.21	1.17±0.26	-4.661	<.001
Handgrip strength (kg)	29.53±10.79	20.40±5.74	31. 68±10.58	-5.541	<.001

LVEF; left ventricular ejection fraction, HFrEF; heart failure reduced ejection fraction, HFpEF; heart failure preserved ejection fraction, NYHA class; New York heart association class, SMI; skeletal muscle mass index; BMI; body mass index, MIP; maximal inspiratory pressure, MEP; maximal expiratory pressure

[a] analysed by chi-square test.

[b] analysed by t-test.

Table 2. Logistic regression analysis for risk factors of sarcopenia in patients with heart failure.

Risk of Sarcopenia	Odds Ratio (95%CI)	p	Adjusted Odds Ratio (95%CI)	p
Sex Female	Reference group –male 2.770 (1.203-6.380)	0.017	-	-
Age ≥60 years	Reference age group <60 years 4.898 (1.863-12.876)	0.001	-	-
BMI <23 kg/m^2	Reference BMI ≥23 kg/m^2 5.204 (2.188-12.380)	<0.001	0.170 (0.064-0.448)	<0.001
LVEF <40%	Reference LVEF group ≥40% 2.542 (1.011-6.390)	0.047	0.288 (1.103-0.804)	0.018

*Adjusted sex and age

LVEF; left ventricular ejection fraction, BMI; body mass index, MIP; maximal inspiratory pressure, OR; odds ratio, CI; confidence interval.

Table 3. Result of hierarchical logistic regression analysis predicting skeletal muscle index from baseline characteristics and ejection fraction.

Regression Model	B	ß	T	R^2	*F*-value	Δ R^2	Δ *F*
SMI	-	-	-	-	-	-	-
Step 1	-	-	-	0.750	151.628***	0.755	151.628***
Age	-0.030	-0.228	-5.511	-	-	-	-
Sex	-1.4134	-0.425	-10.419	-	-	-	-
BMI	0.212	0.678	16.376	-	-	-	-
Step 2	-	-	-	0.768	121.927***	0.014	8.813**
LVEF	0.014	0.122	2.969	-	-	-	-

SMI; skeletal muscle mass index, LVEF; left ventricular ejection fraction, BMI; body mass index.

*** p < 0.001, ** p <0.01

Risk factors associated with sarcopenia were female sex (odds ratio [OR] = 2.770), 95% confidence interval (CI) = 1.203-6.380, p=0.017), advanced age (*i.e.*, aged ≥60 years) with OR 4.898, (95% CI: 1.863-12.876, p=0.001), low BMI (*i.e.*, <23 kg/m^2) with OR 5.204 (95% CI: 2.188-12.380, p≤0.001), and participants with HFrEF (defined as LVEF <40%) with OR 2.542 (95% CI: 1.011-6.390, p=0.047). The association of sarcopenia with HF persisted after adjusting for age and sex, while BMI and LVEF remained (Table **2**).

A hierarchical regression model was used to predict the skeletal muscle mass index (SMI) (Table **3**). Age, sex, and BMI were entered at step one and accounted for 75.5% of the variance. LVEF accounted for an additional 1.4% of the variance in the prediction SMI (β=0.122, SE=0.005, p=0.003); all predictors together accounted for 76.8% of the variance in SMI, and male sex, young age, high BMI, and high LVEF were associated with high SMI (p<0.001).

4. DISCUSSION

The present study explored the prevalence of sarcopenia among Thai patients with HF and its association with sarcopenia and HF. A total of 152 participants were evaluated for sarcopenia using the AWGS in 2019, and 32 participants were defined as having sarcopenia. Therefore, the prevalence of sarcopenia was 19.1%, and risk factors such as age, sex, BMI, and LVEF were associated with sarcopenia. In addition, the total regression model explained 76.8% of the variance in predicting SMI.

The prevalence of sarcopenia in patients with HF was 19.1% in the present study, which is similar to previous studies [11, 14, 15]. Bekfani *et al*. found that 19.7% of outpatients with HF, aged ≥18 years, were reported to have sarcopenia based on the definition of the European Working Group on Sarcopenia in Older People (EWGSOP) diagnostic criteria [14]. Fulster *et al*. recruited participants aged ≥18 years and ambulatory patients who were clinically stable [15]. They found that the prevalence of sarcopenia was 19.5% in HF (defined using the AWGS diagnostic criteria), which is similar to the prevalence reported in the present study [15]. The prevalence of sarcopenia in patients with HF was 19-21%, whether using the AWGS or EWGSOP diagnostic criteria or recruited from the European or Asian populations. However, Kamiya *et al*. showed that the prevalence of sarcopenia in patients with HF was 35.2% (defined as AWGS criteria) [11], which is consistent with the findings of Izawa *et al*., who found that the prevalence of sarcopenia in patients with HF was 9 out of 20 individuals (according to EWGOSP criteria) [16]. These studies showed a higher prevalence of sarcopenia than in the present study, probably because they recruited participants aged ≥65 years, whereas other studies, including the present study, recruited clinically stable participants or those from outpatient departments [14, 15]. Furthermore, Bianchi *et al*. found that hospitalized patients had limited physical activity, which resulted in decreased muscle strength, leading to decreased daily activities and a trend of sarcopenia [17]. Yuenyongchaiwat *et al*. found that patients who underwent open-heart surgery and had longer stays in the hospital showed a significantly higher risk of developing sarcopenia [18]. Therefore, hospitalized patients may show a high prevalence of sarcopenia.

Regarding age, the present study found that the older

patients with HF (aged ≥60 years) were at high risk for sarcopenia than the younger patients (aged <60 years). In addition, young patients showed high handgrip strength, SMI, and gait speed. Siparsky *et al*. showed that individuals aged ≥40 years associated with a decrease (30-50%) in skeletal muscle mass (SMM) [19]. Lauretani *et al*. showed that muscle strength and muscle power declined considerably with advanced age and therefore affected poor mobility [20]. Springer *et al*. showed that the prevalence of sarcopenia was 5-13% among the elderly (aged 60-70 years) [21]. In addition, an increase in the prevalence of sarcopenia was reported from 13.5-24% in older adults aged under 70 years to 60% in those aged over 80 years [22]. Further, a decline in muscle strength was prevalent in 1.5% per year in those aged 50-60 years old and 3% in those aged over 60 years [23]. It might be a significant loss of muscle fiber type II and lower satellite fiber in old age with sarcopenia, resulting in decreased blood flow to the muscle [24]. Izawa *et al*. showed that advanced age was associated with an increased risk of sarcopenia in patients with cardiovascular disease due to increased catabolic stress in the skeletal muscle (*i.e*., increased breakdown of muscle proteins, particularly myofibrillar proteins) that results in poor physical performance [16]. A systematic review of six studies examined the prevalence and relationships with sarcopenia in HF, and it was reported that increasing age was associated with increased sarcopenia [25]. In addition, other age-related factors, such as malnutrition and decreased physical activity, contribute to the development of sarcopenia *via* protein depletion and decreased neuromuscular function [26]. Therefore, older age is related to a loss of muscle mass, a decrease in muscle strength, and low physical performance, which leads to sarcopenia in patients with HF.

Females show a higher rate of sarcopenia compared with male patients with HF, which is also associated with an increased risk of sarcopenia [11]. This might be because the study collected data from HF patients with sarcopenia aged >55 years [11]. Women post menopause showed a decrease in estrogen hormone levels, resulting in decreased muscle mass and muscle strength [11, 27]. This leads to a decrease in muscle mass and muscle weakness and, therefore, low physical performance. However, some studies reported that men with HF had a higher prevalence of sarcopenia than their female counterparts [14, 15, 28]. Older males showed a decrease in total testosterone, free testosterone, and an increase in sex hormone-binding globulin [18]; therefore, sex differences in sarcopenia may be due to hormonal differences between sexes or other factors. Further studies are needed to explore the differences in sex.

With regard to BMI, HF patients with a low BMI were at risk for developing sarcopenia compared with those without sarcopenia, which is consistent with previous studies [14, 15, 29]. This may be due to a decrease in cardiac output and malnutrition from anorexia, which leads to low physical activity [8]. As a result, weight loss was related to decreased muscle mass. Thus, a low BMI was associated with the loss of muscle mass, muscle strength, and physical performance.

Sarcopenia in HF patients was significantly related to HFrEF (defined as LVEF <40%), which is consistent with the study carried out in Berlin [15]. The following conditions might affect heart function: impairment in the left ventricle leading to an inability to properly pump the blood into the body; thus, a decrease in cardiac output is observed, which leads to increased physical exertion in daily activities. In addition, a lack of physical activity results in a reduction in muscle strength, decreased muscle mass, and low physical performance. Therefore, sarcopenia was noted to be more prevalent in patients with HFrEF than in those with HfpEF.

This study has some limitations. First, the number of male and female participants was different, which might have resulted in sex as a risk factor for the development of sarcopenia. Second, there was a difference in the number of participants in the NYHA class. In this study, the participants completed the sarcopenia screening test with a clinically stable NYHA class I-III. Third, all participants enrolled in the outpatient clinic were clinically stable in the present study. Finally, some information, such as length of stay in the hospital, medication usage, and blood chemistry, which might be associated with sarcopenia, were missing. Due to these limitations, the findings may not be generalizable to all sarcopenia patients with HF. Further studies are needed to explore the association of sarcopenia in HF with a large number of male and female participants with a difference in the classification of NYHA.

CONCLUSION

The prevalence of sarcopenia among patients with HF was 19.1%, which is similar to the findings of previous studies. Age, gender, BMI, and LVEF were associated with sarcopenia. In addition, LVEF predicted SMI after controlling for age, sex, and BMI.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval concerning humans was obtained from Thammasat University, Thailand (COA No. 071/2563).

HUMAN AND ANIMAL RIGHTS

All human procedures were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

All participants provided their written informed consent.

STANDARDS OF REPORTING

STROBE guidelines and methodologies were followed in this study.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author, [K.Y.], on special request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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