ORIGINAL RESEARCH

Axial Muscle Size as a Strong Predictor of Death in Subjects With and Without Heart Failure

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***Background*—**The impact of skeletal muscle size, quantified using simple noninvasive images routinely obtained during cardiac magnetic resonance imaging studies on mortality in the heart failure (HF) population is currently unknown.

***Methods and Results*—**We prospectively enrolled 567 subjects without HF (n=364), with HF with reduced ejection fraction (n=111), or with HF with preserved ejection fraction (n=92), who underwent a cardiac magnetic resonance imaging. Skeletal muscle cross-sectional area was assessed with manual tracing of major thoracic muscle groups on axial chest magnetic resonance images. Factor analysis was used to identify a latent factor underlying the shared variability in thoracic muscle cross-sectional area. Cox regression was used to assess the relationship between these measurements and all-cause mortality (median follow up, 36.4 months). A higher overall thoracic muscle area factor assessed with principal component analysis was independently associated with lower mortality (standardized hazard ratio, 0.51; $P<0.0001$). The thoracic muscle area factor was predictive of death in subjects with HF with preserved ejection fraction, HF with reduced ejection fraction, and those without HF. Among all muscle groups, the pectoralis major cross-sectional area was the most representative of overall muscle area and was also the most robust predictor of death. A higher pectoralis major cross-sectional area predicted a lower mortality (standardized hazard ratio, 0.49; $P<0.0001$), which persisted after adjustment for various confounders (standardized hazard ratio, 0.55; $P=0.0017$).

***Conclusions*—**Axial muscle size, and in particular smaller size of the pectoralis major, is independently associated with higher risk of mortality in patients with and without HF. Further work should clarify the role of muscle wasting as a therapeutic target in patients with HF. **(*J Am Heart Assoc*. 2019;8:e010554. DOI: 10.1161/JAHA.118.010554.)**

Key Words: heart failure with preserved ejection fraction • heart failure with reduced ejection fraction • mortality • muscle mass

There are currently an estimated 6.5 million Americans living with heart failure (HF); this prevalence is expected to increase 46% to >8 million by 2030.[1] As HF progresses, patients experience gradually worsening fatigue and exercise intolerance. The progression of HF is also characterized by a progressive decline in skeletal muscle mass and accumulation of structural and functional abnormalities in the remaining muscle.[2] Loss of muscle mass is a frequent occurrence in patients with chronic HF and leads to worsened exercise capacity and muscle strength in these patients.[3]

Even in the absence of HF, loss of muscle mass occurs as a normal consequence of aging and is independently associated with functional impairment and disability.[4] This loss is accelerated by comorbidities like HF.[5] Additionally, low muscle mass has been shown to be predictive of mortality in a number of different populations: healthy older adults, the frail elderly, end-stage renal disease and after liver transplantation.[6–9] Muscle strength, conversely, has been shown to have a protective effect against mortality.[10] This relationship has also been demonstrated in the HF population. Lean muscle mass, as assessed by mid–upper arm circumference, has been shown to be predictive of prognosis in Japanese patients with HF independent of body mass index.[11] It was also recently shown that pectoralis muscle size and attenuation quantified on routine preoperative computed tomography scan was predictive of all-cause mortality after

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Clinical Perspective

What Is New?

- Manual tracing of skeletal muscle cross-sectional areas from standard axial images from cardiac or chest magnetic resonance imaging was performed.
- This study demonstrates a relationship between axial muscle size and mortality in subjects with and without heart failure.
- The pectoralis major area was the most representative of overall muscle areas, and was the best muscle area indicator at predicting death.

What Are the Clinical Implications?

- Quantification of pectoralis major muscle size from axial chest magnetic resonance images may help identify patients who are at higher risk for death.

left ventricular (LV) assist device implantation,[12] adding to previous reports demonstrating the prognostic value of psoas muscle cross-sectional area.[13] However, the impact of muscle mass on mortality in a broader population of patients with HF without an LV assist device, including HF with preserved (HFpEF) and reduced (HFrEF) ejection fraction, remains unclear.

In this study, we tested the hypothesis that axial thoracic muscle cross-sectional areas are predictive of all-cause mortality among subjects with and without HF.

Methods

The data, analytic methods, and study materials are not publicly available for purposes of reproducing the results or replicating the procedures. Such data may be made available to other researchers for collaborative research through the establishment of appropriate data sharing agreements and regulatory approvals.

We prospectively enrolled 567 subjects without HF (n=364), HFrEF (n=111), or HFpEF (n=92) referred for a cardiac magnetic resonance imaging (MRI) exam at the Corporal Michael J. Crescenz VA Medical Center. The protocol was approved by the Philadelphia VA Medical Center Institutional Review Board, and written informed consent was obtained from all participants.

HFrEF was defined by the presence of symptoms in addition to an LV ejection fraction <50%. HFpEF was defined as: (1) New York Heart Association Class II–IV symptoms consistent with HF; (2) LV ejection fraction ≥50%; (3) a mitral E wave to annular e′ ratio >14[14]; or at least 2 of the following: (1) a mitral E wave to annular e′ ratio >8; (2) treatment with a loop diuretic for control of HF symptoms; (3) left atrial volume index >34 mL/m^2 of body surface area; (4) N-terminal pro B-type natriuretic peptide level >200 pg/mL; (5) LV mass index >149 g/m^2 in men and 122 g/m^2 in women (measured by cardiac MRI). Subjects without HF had an LV ejection fraction >50% and no symptoms and signs consistent with HF.

Key exclusion criteria were as follows: (1) claustrophobia; (2) presence of metallic objects or implanted medical devices in the body; (3) atrial fibrillation, flutter, or significant arrhythmia at the time of enrollment, which may compromise the study measurements; (4) other conditions that would make the study measurements less accurate or unreliable (ie, inability to perform an adequate breath hold for cardiac MRI acquisitions); (5) diagnosed or suspected infiltrative myocardial disease (cardiac or extracardiac amyloidosis or sarcoidosis).

At baseline, a cardiac MRI study was performed, which was used for assessments of axial muscle cross-sectional areas. All-cause mortality was ascertained over a median follow-up period of 36.4 months.

Axial Skeletal Muscle Cross-Sectional Areas

A cardiac MRI was performed using a 1.5 Tesla whole-body MRI scanner (Avanto or Espree, Siemens, Malvern, PA) equipped with a phase-array cardiac coil. An axial stack of steady-state free precession images was obtained, as per our routine cardiac MRI protocol, spanning the entire thorax. Typical acquisition parameters were as follows: repetition time=30.6 ms; echo time=1.2 ms; flip angle=80; slice thickness=5 mm; space between slices=5 mm; matrix size=256×208; parallel image (integrated parallel acquisition technique) factor=2.

Images were analyzed using Horos software version 1.2.1 based on a modification of the method described by Teigen et al in which a cross-sectional area of the pectoralis major was acquired using manual shading of preoperative computed tomography scans in patients with a left ventricular assist device.[12] We expanded this procedure to include a number of additional thoracic muscles. The level of the carina was established as a reference point for measurements of skeletal muscle cross-sectional area on all axial chest MRI images. Thoracic skeletal muscle was then manually traced bilaterally for pectoralis major, pectoralis minor, serratus anterior, latissimus dorsi, paraspinal, and trapezius muscles (Figure 1). The area of each muscle measured in square centimeters was exported from Horos to an electronic database. We found that the serratus anterior muscle was particularly difficult to trace and was visualized inconsistently. As a result, we only analyzed the other muscle groups.

We performed factor analysis to identify a latent factor that underlies the shared variability in the cross-sectional area of the studied muscles. PCA identified a single factor, which we utilized as an indicator of underlying skeletal muscle mass.

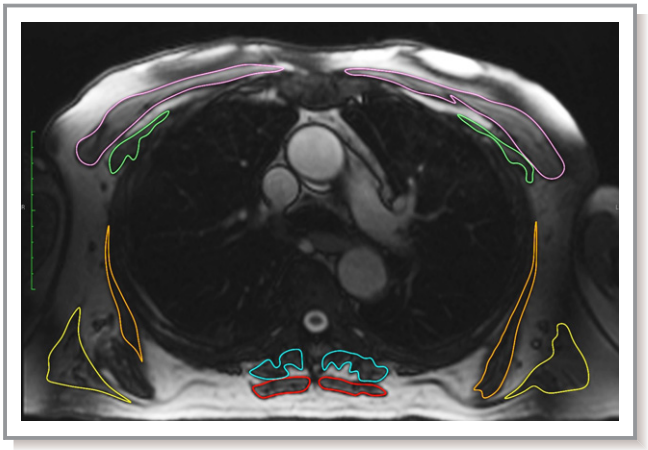

Figure 1. Example of muscle group cross-sectional area measurements. Major thoracic muscle groups are manually traced to determine cross-sectional area. Muscle groups outlined in this image: pectoralis major (pink), pectoralis minor (green), latissimus dorsi (yellow), serratus anterior (orange), paraspinal (blue), trapezius (red).

Statistical Analysis

Data for continuous variables are presented as mean ± SD for normally distributed variables and median (interquartile range) for non-normally distributed variables. Categorical variables are presented as counts and percentages. Comparisons of general characteristics between subjects with HFpEF, HFrEF and no HF were performed using analysis of variance (ANOVA) or the Kruskal–Wallis test as appropriate for continuous variables, and the χ^2 or the Fisher's exact test as appropriate for categorical variables.

Given that skeletal muscle groups are likely to be correlated and their shared variability defined by the degree of overall muscle mass, we used factor analysis to reduce the information provided by all muscle group variables into common factor (s). Factor analysis is a statistical method used to group similar variables into dimensions, in order to identify underlying latent variables or constructs. The purpose of factor analysis is to reduce several individual items into a fewer number of constructs. We performed factor analysis using maximum likelihood estimation and determined the number of factors to extract based on the eigenvalue of individual components, with a cutoff value of >1. Given that factors are difficult to interpret and apply clinically in individual patients, we assessed the factor loading value for each of the individual muscle groups, in order to identify the muscle group with the highest factor loading, which thus best represents the latent factor.

We used proportional hazards (Cox) regression to assess the relationship between various muscle area indicators and latent factors and time to death. For each parameter, we performed both unadjusted analyses and analyses that adjusted for key covariates chosen a priori based on their association with body composition and/or the risk of incident events (age, sex, body mass index, systolic blood pressure, diabetes mellitus and presence of HFpEF or HFrEF at baseline).

We assessed log-log plots, Schoenfeld and Martingale residuals to test the proportionality and linearity assumptions in Cox models. All hazard ratios are standardized (ie, represent the relative risk per SD change in the predictor), to facilitate an intuitive comparison of the association between different indices and the risk of death. A 2-sided *P* value of 0.05 was used to define statistical significance. Analyses were performed using the Matlab statistics and machine learning toolbox (Mathworks, Natick, MA) and SPSS for Windows v22 (SPSS Inc, Chicago, IL).

Results

Table 1 demonstrates the baseline characteristics of the study sample, stratified by absence of HF (n=364) or presence of HF with reduced ejection fraction (n=111) or preserved ejection fraction (n=92). There were small but significant differences in age, and a greater proportion of women in the HFpEF group. Compared to subjects without HF, those with both HFpEF and HFrEF were older, more likely to be black, had higher N-terminal pro B-type natriuretic peptide levels, had greater comorbidity burden with use or relevant medications, and had several echocardiographic indices indicating myocardial remodeling (larger LV mass and left atrial volume index) or elevated filling pressures (greater E/e′) ($P<0.05$ for all comparisons). Body mass index was significantly higher in HFpEF subjects with (35.8 kg/m^2) compared with the other groups. There were 77 deaths among all subgroups (38 in the non-HF group, 26 in the HFrEF group, and 13 in the HFpEF group).

Correlations Between Various Muscle Groups and Underlying Latent Factor

Figure 2A shows a scatterplot matrix demonstrating the relationship between various indicators of skeletal muscle areas in subjects without HF, subjects with HFpEF, and subjects with HFrEF. Figure 2B shows a color map demonstrating the correlation among these indices in the entire cohort.

In general, the cross-sectional areas of various skeletal muscle groups demonstrated modest to moderate correlations. The strongest associations were seen between the pectoralis major, pectoralis minor, and trapezius muscles. The latissimus dorsi area was also moderately correlated with the trapezius and the pectoralis major muscle areas, whereas the paraspinal muscle area was moderately correlated only with the pectoralis major muscle area, demonstrating weak relationships with other muscle groups (Figure 2B).

Table 1. Baseline Characteristics of Study Population

	No HF	HFrEF	HFpEF	*P* value
Age, years	63 (56.5,69)	65 (60,70)	64 (59,71)	0.0162*
Male Sex	338 (92.86%)	110 (99.10%)	78 (84.78%)	0.0005*,#,$
Race				0.009*,#,$
White	189 (51.92%)	48 (43.24%)	36 (39.13%)	
African-American	155 (42.58%)	62 (55.86%)	53 (57.61%)	
Other	20 (5.49%)	1 (0.90%)	3 (3.26%)	
BMI, kg/m^2	29.4 (25.4,33.6)	29 (24.1,32.9)	35.8 (30,41.5)	<0.0001#,$
BSA, m^2	2.13 (1.94,2.32)	2.11 (1.92,2.27)	2.36 (2.07,2.56)	<0.0001#,$
Systolic blood pressure, mmHg	141 (128,156)	140 (127,161)	149 (136,161)	0.0331#
Diastolic blood pressure, mmHg	82.8±12.2	82.4±13.7	85.3±11.2	0.1823
Hypertension	276 (75.82%)	94 (84.68%)	85 (92.39%)	0.0007*,#
Coronary Artery Disease	113 (31.04%)	65 (58.56%)	33 (35.87%)	<0.0001*,$
Obstructive Sleep Apnea	86 (23.62%)	24 (21.62%)	38 (41.30%)	0.0015#,$
Current Smoking	96 (26.37%)	41 (36.94%)	18 (19.57%)	0.0147*,$
Medication Use				
Beta Blockers	172 (47.38%)	99 (89.19%)	62 (67.39%)	<0.0001*,$
Aspirin	213 (58.68%)	93 (83.78%)	64 (69.57%)	<0.0001*,$
Clopidogrel	29 (7.97%)	27 (24.32%)	11 (11.96%)	<0.0001*,$
ACE Inhibitors	168 (46.15%)	69 (62.16%)	52 (56.52%)	0.0071*
ARBs	37 (10.16%)	17 (15.32%)	18 (19.57%)	0.0361#
Furosemide	7 (1.92%)	71 (63.96%)	64 (69.57%)	<0.0001*,#
Spironolactone	10 (2.75%)	16 (14.41%)	8 (8.70%)	<0.0001*,#
Statins	233 (64.01%)	93 (83.78%)	61 (66.30%)	0.0005*,$
Long-acting nitrates	28 (7.69%)	19 (17.12%)	20 (21.74%)	0.0001*,#
Hydralazine	6 (1.65%)	14 (12.61%)	10 (10.87%)	<0.0001#,$
Warfarin	27 (7.42%)	16 (14.41%)	4 (4.35%)	0.0214*,$
Calcium-channel blockers	92 (25.27%)	24 (21.62%)	38 (41.30%)	0.0030#,$
Thiazides	85 (23.35%)	18 (16.22%)	21 (22.83%)	0.2685
eGFR (ml/min/1.73 m^2)	82 (66,101)	76 (58.3,95.8)	70 (57,95.5)	0.0033#
NT-pro-BNP, ng/dL	167 (54,458)	1859 (338,4540)	319 (93,664)	<0.0001*,$
Diabetes Mellitus	153 (42.15%)	69 (62.73%)	62 (68.13%)	<0.0001*,#
Triglycerides, mg/dL	115 (75,197)	114 (78,168)	118 (87,185)	0.6036
HDL-Cholesterol, mg/dL	42 (34.8,50.3)	41 (32,50)	41 (36,50)	0.4289
LDL-Cholesterol, mg/dL	90 (68,115)	85 (64,109.3)	85 (68,107.3)	0.4868
Mitral E wave velocity, cm/s	67.2 (56.7,83)	61.7 (50.3,87.2)	78.4 (63.7,91.6)	0.0014#,$
Mitral deceleration time, s	0.202 (0.17,0.25)	0.2 (0.153,0.26)	0.217 (0.18,0.251)	0.3062
E/e′, septal	9 (7,11.3)	11.4 (8.8,16.1)	12.1 (9.6,14.4)	<0.0001*,#
E/e′, lateral	6.94 (5.5,9.38)	9.1 (6.63,12.53)	8.91 (7.2,12.24)	<0.0001*,#
Mean E/e′	8 (6.5,10.2)	10.3 (8.3,14.5)	10.3 (8.4,13.3)	<0.0001*,#
LA Volume Index (ml/m$_2$ of BSA)	63.1 (46.2,78.9)	86.7 (63.6,119.7)	89.6 (61.2,109)	<0.0001*,#
LV Mass, g	143 (121,170)	181 (160,223)	167 (134,196)	<0.0001*,#,$

Continued

Table 1. Continued

	No HF	HFrEF	HFpEF	*P* value
LV Mass Index (g/m^2 of BSA)	67.3 (57.7,76.4)	86.7 (77.9,101.7)	67.4 (60.6,84.3)	<0.0001*,$
LV Mass Index (g/m$^{1.7}$ of height)	53.9 (46.9,64.3)	70.9 (60,82.7)	63.8 (54.2,75.5)	<0.0001*,#,$

HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LV, left ventricular; LA, left atrial.
Data for continuous variables are presented as mean ± standard deviations for normally distributed variables and median (interquartile range) for normally distributed variables. Numbers for categorical variables represent counts (%).
P values correspond to comparisons between the 3 groups.
*,#,$ indicate *post-hoc* pairwise comparisons <0.05: *No HF vs. HFrEF; #No HF vs. HFpEF; $HFrEF vs. HFpEF.
§Fisher exact test. Other *P* values shown for categorical variables correspond to chi-square tests.

Factor analysis demonstrated a single latent construct underlying all muscle groups for which the most representative indicator was the pectoralis major muscle area (loading=0.842), followed by the latissimus dorsi muscle (loading=0.751), trapezius muscle (loading=0.724) and the pectoralis minor (loading=0.639). The paraspinal muscle demonstrated the weakest factor loading (0.497).

Muscle Areas as Predictors of Death in the Overall Cohort

Table 2 and Figure 3A show unadjusted standardized hazard ratios (HRs) for death in the cohort for individual muscle groups, as well as the overall muscle area factor generated from factor analysis.

The overall thoracic muscle area factor was independently associated with lower mortality (standardized HR, 0.51; 95% CI, 0.39–0.65; *P*<0.0001). This relationship was independent of age, sex, and race (standardized HR, 0.51; 95% CI, 0.39–0.67; *P*<0.0001). No significant interactions were found between HF status and the thoracic muscle area factor as predictors of death. Accordingly, when analyzed separately in models adjusted for age, sex, and race, the overall thoracic muscle area factor was predictive of death among subjects without HF (standardized HR, 0.47; 95% CI, 0.32–0.70; *P*=0.0002), subjects with HFpEF (standardized HR, 0.37; 95% CI, 0.17–0.83; *P*=0.0515) and subjects with HFrEF (standardized HR, 0.67; 95% CI, 0.45–0.98; *P*=0.0373). Subsequent analyses were performed in the entire cohort.

Figure 3B and Table 2 show standardized HRs for death in the cohort in models adjusted for age, sex, body mass index, systolic blood pressure, diabetes mellitus, and heart failure status (HFpEF versus HFrEF versus no HF). In these analyses, the overall thoracic muscle area factor was independently associated with lower mortality (standardized HR, 0.57; 95% CI, 0.42–0.76; *P*=0.0001).

Specific Muscle Groups as Predictors of Death

As shown in Figure 3A and Table 2, in unadjusted analyses, a larger cross-sectional area of all muscle groups was associated with lower mortality. The pectoralis major muscle area demonstrated the strongest association with mortality (standardized HR, 0.49; 95% CI, 0.36–0.66; *P*<0.0001).

After adjustment for age, sex, body mass index, systolic blood pressure, diabetes mellitus, and heart failure status (HFpEF versus HFrEF versus no HF) (Figure 3B), the individual muscle area most strongly associated with mortality was the pectoralis major muscle area (standardized HR, 0.55; 95% CI, 0.38–0.80; *P*=0.0017). Similarly, after further adjustment for LV ejection fraction and LV mass, the pectoralis major area remained independently associated with all-cause mortality (standardized HR, 0.58; 95% CI, 0.37–0.91; *P*=0.02).

Discussion

In this study, we demonstrate that axial thoracic skeletal muscle areas measured by steady-state free precession MRI independently predict all-cause mortality in a multiethnic cohort of subjects with and without HF. We demonstrate this association in subjects with HFpEF or HFrEF and subjects without HF. We also demonstrate that the muscle group that best represents the underlying variability in the thoracic axial musculature is the pectoralis major; the cross-sectional area of this particular muscle was found to be an independent predictor of death, with associations at least as strong as those observed for the underlying latent factor derived from all measured muscle groups.

The clinical detection of muscle wasting is challenging, as early muscle loss often occurs concomitantly with increased obesity, leading to no change in body weight.[15] After weight loss becomes detectable, the patient has developed cardiac cachexia, which carries an 18-month mortality of up to 50%.[16] This suggests a need for better detection as well as an important window of opportunity during which interventions can be made to improve muscle mass and strength and impact mortality. Our findings indicate that a simple and practical assessment of the thoracic musculature can be obtained via measurements of the pectoralis major muscle CSA in <1 minute during routine cardiac MRI examinations. We have additionally found that this simple measure is a robust and strong predictor of future mortality in subjects

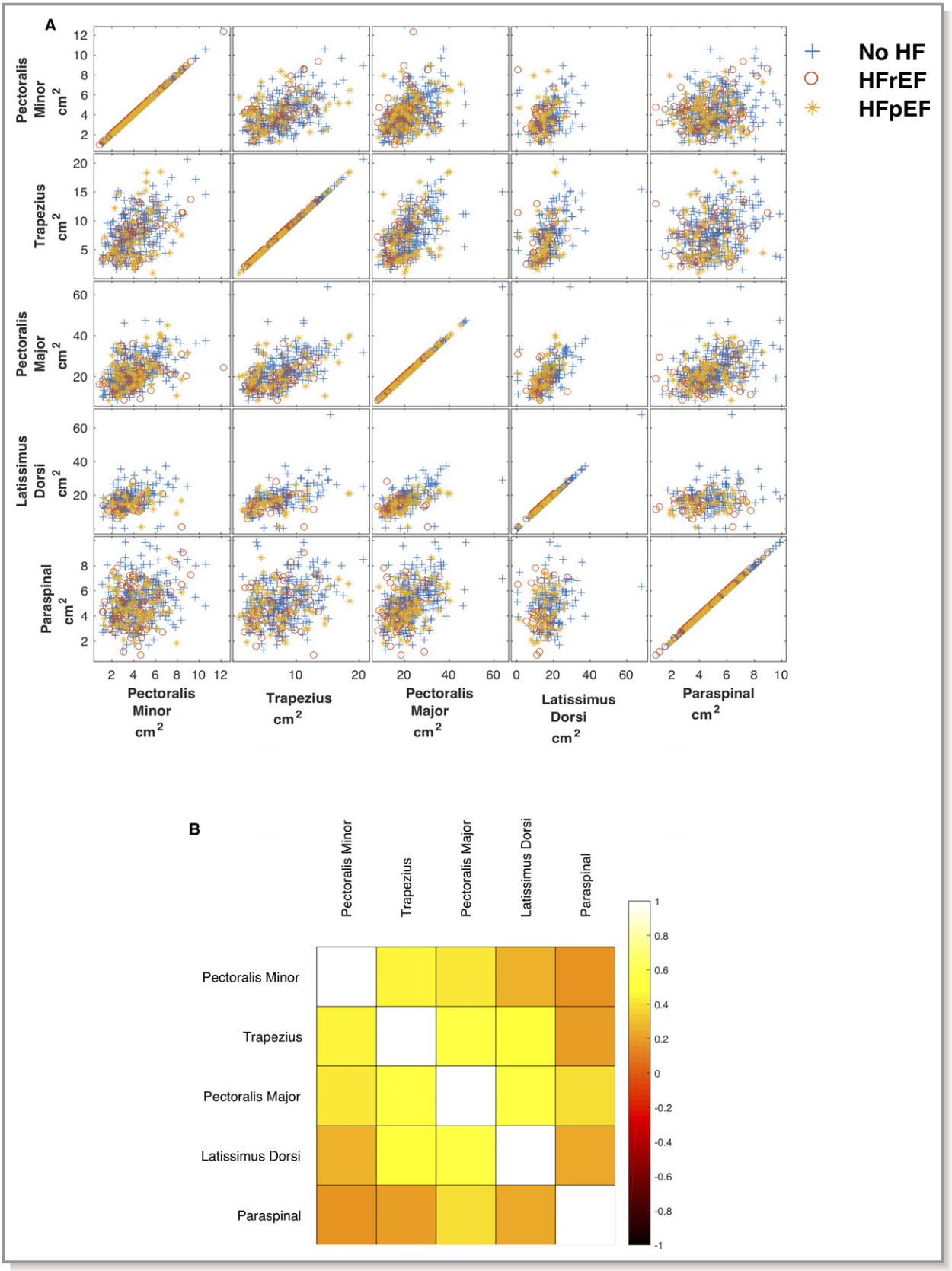

Figure 2. Correlation matrix between cross-sectional areas in various muscle groups. The top panel (**A**) shows correlation scatterplots with groups represented in different colors and symbols. The bottom panel (**B**) shows a color-coded correlation map in the entire cohort.

Table 2. Unadjusted and Adjusted Standardized Hazard Ratios for Death in the Cohort for Individual Muscle Groups, as Well as the Overall Muscle Area Factor

Muscle Group	Unadjusted		Adjusted*	
	Standardized Hazard Ratio (95% CI)	*P* Value	Standardized Hazard Ratio (95% CI)	*P* Value
Pectoralis minor	0.70 (0.53–0.92)	0.01	0.75 (0.57–1.00)	0.0501
Trapezius	0.57 (0.43–0.75)	<0.0001	0.71 (0.52–0.98)	0.0356
Pectoralis major	0.49 (0.36–0.66)	<0.0001	0.55 (0.38–0.80)	0.0017
Latissimus dorsi	0.59 (0.42–0.84)	0.003	0.74 (0.53–1.03)	0.0782
Paraspinal	0.73 (0.58–0.92)	0.007	0.81 (0.63–1.04)	0.1018
Overall muscle area factor	0.51 (0.39–0.65)	<0.0001	0.57 (0.42–0.76)	0.0001

Each hazard ratio shown was obtained from a separate unadjusted or adjusted Cox model.
*Models are adjusted for age, sex, body mass index, systolic blood pressure, diabetes mellitus, and heart failure status (HFpEF vs HFrEF vs no HF).

with and without HF. This suggests that improving muscle mass and strength may be an effective strategy toward improving both functional capacity and mortality in the HF population.[17]

Unfortunately, there are a limited number of interventions that can improve muscle mass. Adequate protein supplementation has been shown to be critical in maintaining muscle mass in older adults.[18] Nutritional protein supplementation

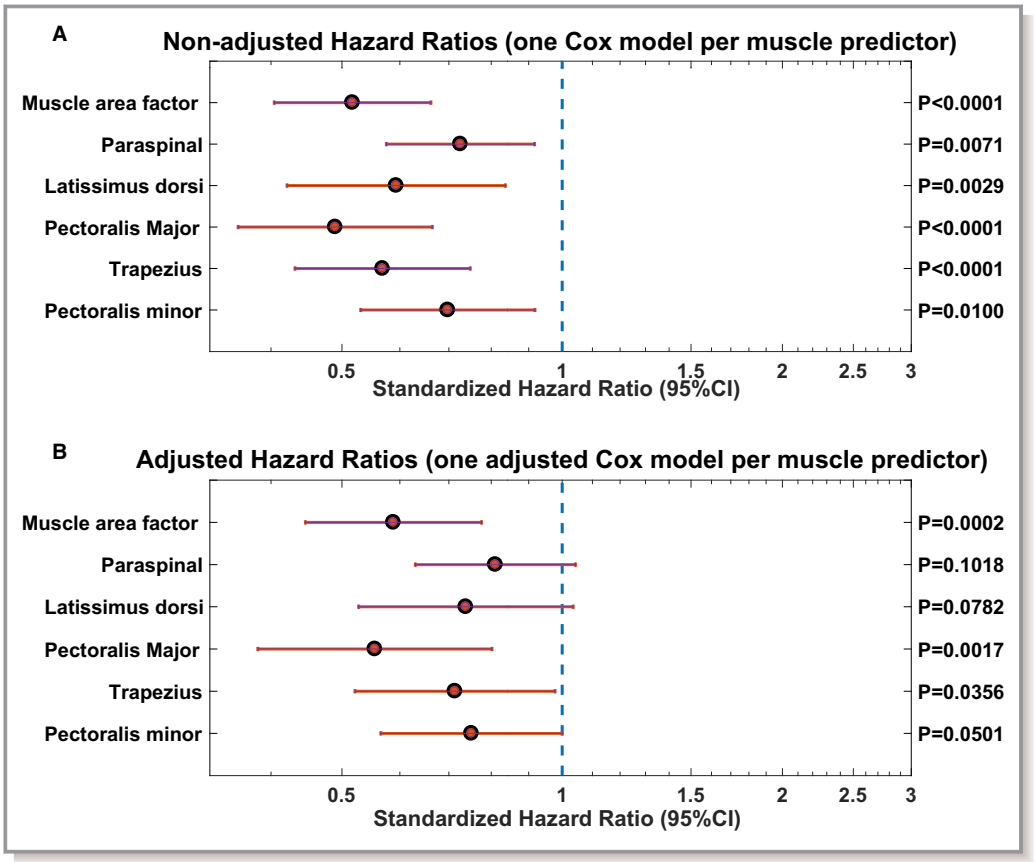

Figure 3. Unadjusted (**A**) and adjusted (**B**) standardized hazard ratios and 95% CIs for individual muscle groups and the overall muscle area factor as predictors of all-cause death in the entire cohort. Models in the (**B**) are adjusted for age, sex, body mass index, systolic blood pressure, diabetes mellitus, and heart failure status (HFpEF vs HFrEF vs no HF). Each hazard ratio shown was obtained from a separate unadjusted (**A**) or adjusted (**B**) Cox model. HF indicates heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

improved exercise capacity in a 2-month randomized, placebo-controlled study of 38 patients with HF.[19] Similarly, another study of patients with HF showed that 6-week protein supplementation improved quality of life and reduced levels of serum tumor necrosis factor-α.[20] Physical activity has also been shown to improve muscle mass in older adults.[21] Previous studies have demonstrated that exercise training in the HF population is protective against HF-related myopathy and improves muscle strength.[22,23] In the HFpEF population specifically, endurance and interval training has been shown to improve exercise capacity.[24,25]

To date, few pharmacologic therapies that improve muscle mass have shown promise in this population. Testosterone therapy has been shown to improve muscle mass, strength, and exercise capacity in both men and women; however, its use and further studies have been hampered by concern for cardiovascular adverse events.[26–28] Selective androgen receptor modulators and myostatin antagonists are emerging drug classes that have shown initial promise in preclinical and small clinical studies on improving muscle mass; however, larger studies of efficacy and safety are pending.[29]

Although the prevalence of muscle wasting and its effect on exercise in HF has been well described,[3] our study shows that loss of muscle mass is predictive of all-cause mortality in HFpEF. This creates an impetus to improve our ability to detect muscle mass and to find therapies that meaningfully improve muscle mass in patients with HFpEF. Additional preclinical and clinical studies are needed to identify pharmacologic therapies that can improve muscle mass safely and could be used as an adjunct to proven nutritional and exercise interventions in HFpEF.

It is important to consider some strengths and limitations to our study. We prospectively enrolled a relatively large clinical cohort and assessed several thoracic muscle groups to systematically assess the best predictors of death. We enrolled a multiethnic sample that included subjects with HFpEF and HFrEF as well as subjects without HF, allowing us to assess the prognostic value of muscle size across the spectrum of HF. Our study also has several limitations. Consistent with the patient population at VA Medical Centers, our sample was composed predominantly of men, and further studies including larger proportions of women would be valuable. Our participants were selected by convenience sampling (subjects referred for a clinically indicated cardiac MRI), which may limit the generalizability of our findings. The overall number of patients and events is also a limitation; this allowed for limited adjustments in multivariable Cox models to avoid overfitting. Similarly, a larger study will be needed to define specific cut points of muscle areas that identify high-risk subgroups for clinical application. Additionally, we lack data on subject muscle strength, physical activity, or general physical fitness; thus, we are unable to establish if there is a correlation between muscle size and strength or activity level. However, the robustness of the prediction achieved by muscle area measurements even in subjects without HF adds confidence to the concept that muscle size assessed in this practical manner is predictive of death across a wide spectrum of older patients with or at risk for HF.

In conclusion, we report a comprehensive analysis of the prognostic value of axial thoracic skeletal muscle cross-sectional area and report that muscle areas assessed in this manner strongly predict death in subjects with HFpEF or HFrEF and without HF. The pectoralis major cross-sectional area is the most representative and prognostic measurement and provides a practical means of assessing skeletal muscle mass in patients with and without HF, which can be readily implemented in the setting of clinical cardiac MRI studies.

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Disclosures

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