Thigh Intramuscular Fat on Prognosis of Patients With Nonischemic Cardiomyopathy

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Yoshida, T., Shibata, A., Tanihata, A., Hayashi, H., Yamaguchi, Y., Kitada, R., Ehara, S., Izumiya, Y., & Yoshiyama, M. (2022). Thigh Intramuscular Fat on Prognosis of Patients With Nonischemic Cardiomyopathy. The American Journal of Cardiology. 169, 113–119. https://doi.org/10.1016/j.amjcard.2021.12.059

Description	〈概要〉 　研究グループは、大腿部の筋肉内脂肪が非虚血性心筋症による心不全の予後に影響を与えることを初めて明らかにしました。本研究成果により、大腿部の筋肉内脂肪を測定することで心不全の予後を推測できる可能性が示されました。 　皮下脂肪や内臓脂肪以外の脂肪組織のことを異所性脂肪と呼び、主なものとしては心臓周囲脂肪や筋肉内脂肪があります。異所性脂肪の一つである心臓周囲脂肪が狭心症や心筋梗塞といった冠動脈疾患や心房細動を引き起こすとの報告はありましたが、身体の他の部位の異所性脂肪が心不全に与える影響についての報告は今までほとんどありませんでした。大腿部の筋肉内脂肪が糖尿病など生活習慣病の発症に影響を与えているという報告は既にあったため、今回、大腿部の筋肉内脂肪が心不全患者の予後に関係するかを調査しました。 　本研究グループは、2017 年 9 月から 2020 年 1 月に大阪公立大学医学部附属病院で、心機能が低下した心不全の精査目的に入院し冠動脈疾患が否定された連続 93 例を対象とし、CT で大腿部のスキャンを行い、筋肉量と筋肉内脂肪を測定して筋肉内脂肪比を算出しました。筋肉内脂肪比を中央値で 2 群に分類し、それぞれの群で心血管死もしくは心血管系の病気による予期しない入院の発生率に差があるか検討を行いました。その結果、筋肉内脂肪比が高い群の方が発生率が高く、筋肉内脂肪比が独立した予後規定因子であることが明らかになりました。 '筋肉内脂肪が多いと心不全予後が悪くなることを明らかに―筋肉量や筋力以外に筋肉の質も心不全に影響―' 大阪公立大学. https://www.omu.ac.jp/info/research_news/entry-00438.html (参照 2022-04-08)

Thigh Intramuscular Fat on Prognosis of Patients with Nonischemic Cardiomyopathy

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Abstract

Skeletal muscle atrophy is an independent prognostic predictor for patients with chronic heart failure, and the concept of sarcopenia is drawing attention. Furthermore, the importance of not only muscle mass but also ectopic fat has been pointed out. However, there is a lack of consensus on the implications of ectopic fat for the prognosis in patients with non-ischemic cardiomyopathy. We investigated whether ectopic fat in the thigh affects the prognosis with non-ischemic cardiomyopathy. This prospective study recruited 145 patients diagnosed with nonischemic cardiomyopathy between September 2017 and January 2020. Finally, 93 patients with a reduced ejection fraction (EF) were enrolled. The clinical endpoints were cardiovascular death or unexpected rehospitalization because of a cardiac event. Using computed tomography, the percentage of intramuscular fat (%IMF) in the thigh was measured in all patients. Patients were divided into two groups based on the median %IMF. The results of Spearman correlation coefficient analysis revealed a correlation among %IMF and peak oxygen uptake (Spearman r=−0.221, p = 0.036). Kaplan–Meier analysis results showed significantly higher risk of adverse events in the high %IMF group (log-rank p = 0.013). Multivariate Cox regression analysis results revealed the %IMF as an independent factor for adverse events (hazard ratio, 1.361; 95% confidence interval, 1.043–1.745; p = 0.018). In conclusion, %IMF may have adverse consequences such as increased cardiac events in patients with nonischemic cardiomyopathy with a reduced EF.

Sarcopenia, which is characterized by the loss of muscle mass, is a prognostic factor for

heart failure (HF).[1] Recent studies have reported that not only the muscle mass but also its quality is

important, and ectopic fat such as intramuscular fat (IMF) has garnered scientific attention.[2, 3]

Ectopic fat secretes hormones and adipocytokines as internal secretion and has a role in

accumulating fat.[4, 5] Ectopic fat has been reported to cause various diseases, and pericardial fat, a

type of ectopic fats, causes coronary artery disease and atrial fibrillation.[6, 7] However, no consensus

has been achieved regarding the correlation of HF with ectopic fat in other parts of the body. To our

knowledge, no studies have demonstrated a correlation between HF prognosis and thigh IMF. This

study, therefore, explored the correlation between thigh IMF and the prognosis of nonischemic

cardiomyopathy with a reduced ejection fraction (EF).

Methods

This single-center, prospective, observational study evaluated 145 patients admitted to

Osaka City University Graduate School of Medicine between September 2017 and January 2020

because of nonischemic cardiomyopathy. The patients were consecutively enrolled after obtaining

informed consent. Eligible patients had to be aged >18 years. All patients were diagnosed with HF

based on the Framingham Diagnostic Criteria for HF, considering two major criteria or one major

criterion and two minor criteria. All patients underwent cardiac catheterization, including coronary

angiography, for the initial diagnosis of nonischemic cardiomyopathy. Exclusion criteria for this

study were 1) patients with a left ventricular EF (LVEF) $\geq$40 %, 2) open heart surgery within the

preceding 3 months, 3) the presence of severe valvular heart disease, 4) inherited myopathy that

appeared to have a strong impact on muscle quality, and 5) unwillingness to provide informed

consent. The final study sample included 93 patients with HF with a diagnosis of nonischemic

cardiomyopathy. The patients were followed until April 2021. The study protocol was approved by

the institutional ethics committee of Osaka City University (approval number: 3785) and was

conducted in accordance with the recommendations of the 1975 Declaration of Helsinki. Written

informed consent was obtained from all patients.

Computed tomography (CT) was performed at baseline using a 64-slice CT scanner

(LightSpeed VCT VISION, GE Healthcare Japan Co., Tokyo, Japan). Afterward, axial images were

transferred to an offline workstation (Synapse Vincent, Fujifilm Medical Co., Tokyo, Japan) for

postprocessing and image analysis. The measurement position of the thigh was set between the

middle part of the femoral head and the midline of the patella. The edges of the muscle groups were

carefully traced using Synapse Vincent to calculate the cross-sectional area of the muscle groups and

the subcutaneous adipose tissue (SAT) of the thigh. The fat volume or area was defined as tissue with

an attenuation of −200 to −30 HU. The thigh IMF area was defined as the fat interior to the thigh

muscle. Thigh SAT was defined as the cross-sectional area of fat exterior to the muscle in the

subcutaneous space. Muscle mass was defined based on the following formula:

Muscle mass = Overall area of the thigh − (IMF + SAT + bone marrow areas)

In the thigh muscle, the percentage of the IMF (%IMF) was evaluated based on the following

formula:

%IMF = (IMF area) / (IMF + muscle areas)

We measured the area of both the left and right thighs, and recorded the average value. CT image analysis was performed in a blinded manner.

Baseline clinical parameters and laboratory data were collected from the patients' medical records. Data on medication were collected at discharge. Routine laboratory analyses were performed for all patients at discharge. The estimated glomerular filtration rate (eGFR) was calculated using the modified IDMS–MDRD Study equation: eGFR (ml/min/1.73 m^2) = 194 × (serum creatinine) − 1.094 × (age) − 0.287 × (0.739 for women).[8] Smoking was assessed as current tobacco smoking.

A symptom-limited cardiopulmonary exercise test (CPX) was conducted for all patients in clinically stable condition before discharge. The exercise stress tests were performed with an upright cycle ergometer (Strength Ergo 8; Fukuda Denshi, Tokyo, Japan) using a ramp protocol. After a 4-min rest on the cycle ergometer, the exercise began with a 4-min warm-up at 0 or 10 W, followed by an incrementally increasing work rate of 10 W every minute. The protocol was selected by the supervising physician depending on the presumed fitness level of the patient. Expired gas analysis was performed following the breath-by-breath method using an expired gas analyzer (Cpex-1; Inter Reha, Tokyo, Japan). Oxygen consumption (VO$_2$), carbon dioxide production (VCO$_2$), and minute ventilation (VE) were measured before, during, and after the exercise. The anaerobic threshold (AT)

was determined using the V-slope method.[9] Peak oxygen uptake (peak VO_2) was defined as the peak

values during incremental exercise. Linear regression analysis revealed the slope of the relationship

between VE and VCO_2 (VE/VCO_2 slope) as a marker of ventilator efficiency.

Grip strength and isometric knee extension muscle strength were measured as reference

values for muscle strength on the same day as CPX. Grip strength was measured using a handgrip

dynamometer (TAKEI GRIP-D [Digital Grip Dynamometer]; Takei Scientific Instruments Co. Ltd.,

Japan). Isometric knee extension muscle strength was measured with a hand-held dynamometer

(JTech Commander PowerTrack II; JTech Medical, Salt Lake City, UT, USA). In each case, two

measurements were taken on each left and right leg or arm, and the highest value obtained during

measurement was recorded.[10]

Patients were followed up during their visit to the clinic, by reviewing their medical records,

and through telephonic conversation with the patients or their physicians. The endpoint was

cardiovascular (CV) death or unexpected rehospitalization because of cardiac events. The cardiac

events were defined as worsening HF, cardiac resynchronization defibrillator implantation, and fatal

arrhythmia. The patients were followed up for a mean period of 17.3 ± 12.7 months.

Continuous variables were described as mean $\pm$ standard deviation for normally distributed

data and median with interquartile range for nonnormally distributed data. The normality of the data

was evaluated using the Shapiro–Wilk normality test. Categorical variables were described as

frequency (percentage). Baseline characteristics of those with the presence and absence of events

were compared using Student's *t*-test for normally distributed data, Mann–Whitney U test for

nonnormally distributed data, and Pearson's chi-square test for categorical variables. The Spearman

correlation coefficient between %IMF and each continuous variable was calculated. The Kaplan–

Meier curves were constructed for time to death or hospitalization for worsening HF; the log-rank

test was used for initial comparison. Univariate and multivariate Cox proportional hazards regression

analyses were performed to identify the predictors of prespecified endpoints. Univariate Cox

proportional hazard analysis was performed with 25 clinical variables that are generally recognized

parameters influencing HF, CPX, and muscle strength. We found a candidate variable with a p <0.10

in univariate analysis and selected variables were considered clinically significant. These variables

were entered into a multivariate model to identify independent predictors of death or hospitalization

due to worsening HF. The results of the Cox proportional hazard models were presented as hazard

ratios (HRs) and 95% confidence intervals (CIs). Statistical analyses were performed using the

software package JMP version 13 (SAS Institute Inc., Cary, NC, USA). All p value <0.05 was

considered significant.

Results

We analyzed the data of 93 patients who met the inclusion criteria. The baseline

demographic and clinical characteristics are shown in **Table 1**. The flow chart of patients leading to

the final cohort is shown in **Figure 1**.

Notably, the use of β-blockers and angiotensin-converting enzyme inhibitors or angiotensin

receptor blockers was very high at discharge. During the follow-up period, 23 patients had a CV

death or unexpected rehospitalization due to cardiac events. In this population, the median %IMF

was 2.8%. On the basis of the median value of %IMF, we divided patients into two groups: low or

high %IMF. The baseline characteristics of these two groups were compared (**Table 1**). Patient

demographics revealed that the percentage of HT was higher in the high %IMF group. The use of

medications at discharge did not vary significantly between the two groups. No significant

differences in laboratory, echocardiogram, and CT data (excluding %IMF) were observed between

the two groups.

The exercise parameters in the CPX and the parameters of physical function are shown in

Table 2. Cardiopulmonary function tended to decline in the high %IMF group; however, we noted

no significant difference in any parameter between the two groups. Despite comparing ectopic fat in

the thigh, leg extension strength did not differ between the two groups. However, the low %IMF

group tended to have a weak grip strength.

Because of a large sex-based difference in muscle strength, additional analyses were

performed for each sex-based group. When categorized by male and female, no significant difference

in grip strength (male: $p = 0.303$; female: $p = 0.156$) and leg strength (male: $p = 0.934$; female:

$P=0.062$) were noted between the two groups.

We evaluated the correlation between %IMF and each continuous variable (**Table 3**). The

Spearman correlation coefficient analysis revealed no correlation between %IMF and the

demographic and clinical characteristics. The analysis of correlation between %IMF and exercise

parameters showed a modest correlation between %IMF and peak VO$_2$. The Spearman correlation

coefficient analysis revealed no significant correlation between %IMF and leg strength but revealed a

significant correlation between %IMF and grip strength. CT data showed a slightly positive

correlation between %IMF and the subcutaneous fat mass/body surface area.

The clinical endpoints were observed in 7 patients in the low %IMF group and 16 patients in

the high %IMF group. There was a significant difference between the two groups (p = 0.032).

Kaplan–Meier analysis results revealed that patients in the high %IMF group had a higher risk of CV

death or unexpected rehospitalization due to cardiac events than those in the low %IMF group

(**Figure 2**). When the endpoint was set to CV death only, four events were noted. Because of the

small number of events, but no difference was observed between the two groups.

Univariate Cox regression analysis results revealed that AT, peak VO$_2$, peak working ratio,

VE/VCO$_2$ slope, albumin, BNP, troponin T, grip strength, leg strength, and %IMF were significant

predictors for CV death or unexpected rehospitalization for cardiac events, with a p value <0.05

(**Table 4**). Four statistically acceptable variables, including %IMF, were calculated based on the

number of events. Therefore, we performed an analysis using a model that combined the predictors

significant in the univariate analysis, and body mass index (BMI) to eliminate the influence of body

size. The results of multivariate Cox regression analysis adjusted for BMI, peak VO$_2$, and leg

strength revealed %IMF as an independent factor of adverse events. This result was similar when

compared with other components (**Table 4**).

Discussion

The key finding of our study was that muscle quality assessed by the %IMF in the thigh may be used to predict long-term outcomes of patients with nonischemic cardiomyopathy with a reduced EF. Recently, skeletal muscle atrophy has been reported to be an independent prognostic factor for chronic HF,[11] and the concept of sarcopenia has been gaining scientific attention. Furthermore, evidence shows that not only muscle mass but also muscle quality is important.[12] However, to our knowledge, no previous studies have quantitatively assessed IMF or evaluated its correlation with the prognosis of patients with nonischemic cardiomyopathy. To the best of our knowledge, this study is the first to explore this correlation.

A correlation was identified between the loss of muscle mass (a core factor in the diagnosis of sarcopenia) and the prognosis of patients with chronic HF. The loss of muscle mass has been reported to result in a poor prognosis.[13] Recently, the IMF of the quadriceps in older people has been shown to be strongly associated with decreased muscle strength, sit-up and sit-down abilities, and gait ability.[14, 15] Akazawa et al. reported that increased intramuscular adipose tissue mass of the quadriceps is more strongly associated with declines in activities of daily living (ADL) than muscle mass loss in older inpatients.[14] And a study reported that the prognosis is not associated with the loss of skeletal muscle mass itself in patients with HF with a reduced EF (HFrEF).[16] Therefore, not only muscle mass but muscle quality is important for the prognosis of patients in HFrEF. In this

study, %IMF and peak VO$_2$, which is an established marker of exercise tolerance, showed a negative

correlation, suggesting that the decrease in IMF contributes to the improvement of ADL and exercise

tolerance.

Several methods have been reported to reduce %IMF. Englund et al. have reported that

physical activity and nutritional supplementation (whey protein and vitamin D) improve thigh

intramuscular adipose tissue in community-dwelling, mobility-limited older people.[17] Regarding the

effect of exercise on IMF, a previous study stated that the effect of reducing IMF is poor.[18]

Conversely, another study reports that it is effective,[19] but the effect has not been determined. Several

studies have demonstrated that aerobic and resistance training improves HF prognosis[20] and exercise

may reduce %IMF. We speculate that an intervention aimed at improving nutritional status and

physical activity is required to improve the thigh IMF.

The target patients in this study were limited to HFrEF. Comorbidities such as being

overweight, abdominal obesity, and DM are common among patients with HF with a preserved EF

(HFpEF) and those with HFrEF; however, these are more severe and occur more frequently in

HFpEF than HFrEF.[21] Perhaps because of these differences, there is a clear difference in body

composition between patients with HFpEF and those with HFrEF.[22] Among obese patients with

HFpEF, a negative correlation was found between thigh IMF and exercise tolerance,[23] but owing to

the difference in body composition between patients with these two pathologies, this study analysis

was limited to HFrEF.

This study had a small sample size and was conducted at a single center. To further improve objectivity, multicenter prospective trials should be conducted. Furthermore, we analyzed patients with nonischemic cardiomyopathy with a reduced EF, which might have included several different HF etiologies. In fact, 25% of these patients had DM, and approximately 50% had a history of HT. Owing to the small number of patients in this study, it was not possible to adjust for all etiologies.

In conclusion, %IMF is an independent factor for predicting adverse cardiac events in patients with nonischemic cardiomyopathy with a reduced EF.

Disclosures

None.

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Figure legend

Figure 1. Patients flow diagram.

Figure 2. Kaplan–Meier estimates of risk of cardiac events.

The patients with high % intramuscular fat in the thigh had a higher risk of cardiovascular death or unexpected rehospitalization for cardiac events than those with low % intramuscular fat in the thigh (log-rank test p = 0.0128).

Table 1

Table 1

Comparison of Baseline Characteristics of Study Patients Based on %IMF

	Total	Percent IMF Group		p value
		Low (≤2.891 %)	High (>2.891 %)	
	(n=93)	(n=47)	(n=46)	
Men	69 (74.2 %)	38 (80.9 %)	31 (67.4 %)	0.237
Age (years)	59.2±14.6	59.1±13.3	59.0±15.9	0.845
NYHA class I	27 (29.0 %)	14 (29.8 %)	13 (28.2 %)	0.822
NYHA class II	66 (71.0 %)	33 (70.2 %)	33 (71.8 %)	0.822
Current smoker	21 (22.6 %)	13 (27.7 %)	8 (17.4 %)	0.349
Hypertension	50 (53.8 %)	19 (40.4 %)	31 (67.4 %)	0.013
Dyslipidemia	28 (30.1 %)	13 (27.7 %)	15 (32.6 %)	0.656
Diabetes mellitus	23 (24.7 %)	9 (19.1 %)	14 (30.4 %)	0.237
BMI (kg/m²)	23.8±5.2	22.9±4.8	24.6±5.5	0.110
Heart rate (bpm)	72.8±14.3	73.1±13.3	72.3±14.3	0.825
Resting systolic BP (mmHg)	113.6±18.9	114.4±21.7	113.0±15.7	0.719
Resting diastolic BP (mmHg)	70.0±15.0	69.3±15.7	70.5±14.4	0.705
Hemoglobin (g/dl)	14.1±2.3	14.2±2.1	14.1±2.4	0.747
Serum sodium (mEq/L)	140.0±2.4	139.9±2.6	139.6±2.3	0.556
eGFR (mg/dl)	62.0±26.2	58.0±17.4	66.2±32.6	0.361
Albumin (g/dl)	3.92±0.51	4.00±0.47	3.83±0.55	0.125
High sensitive troponin T (ng/ml)	0.028±0.030	0.024±0.022	0.031±0.037	0.396
Log BNP (pg/ml)	2.20±0.48	2.18±0.49	2.17±0.46	0.948
Medication at discharge				
ACE inhibitor or ARB	80 (86.0 %)	40 (85.1 %)	40 (87.0 %)	0.773
β-blocker	88 (94.6 %)	46 (97.9 %)	42 (91.3 %)	0.361
MRA	67 (72.0 %)	38 (80.9 %)	29 (63.0%)	0.064
Loop diuretic	66 (71.0 %)	33 (70.2 %)	33 (71.7 %)	0.871
LVEDD (mm)	61.3±7.3	61.3±7.1	61.0±7.7	0.855
LVESD (mm)	53.0±8.6	52.8±8.6	52.9±9.0	0.953
LVEF (%)	25.0±6.6	24.7±6.9	25.4±6.5	0.644
e' (cm/s)	4.3±1.3	4.2±1.3	4.3±1.6	0.787
TRPG (mmHg)	26.4±11.2	24.8±10.9	28.2±11.4	0.171
Thigh muscle/BSA (cm²/m²)	68.9±11.4	70.8±10.4	67.0±12.3	0.112
Thigh SAT/BSA (cm²/m²)	29.4±16.9	26.4±16.4	32.4±17.2	0.093
%IMF in the thigh (%)	3.07±1.52	1.90±0.66	4.20±1.25	<0.001

Values are mean ± standard deviation, median (inter-quartile range), or n (%)

ACE = angiotensin converting enzyme; ARB = angiotensin type 1 receptor blocker; BMI = body mass index; BNP = B-type natriuretic peptide; BP = blood pressure; BSA = body surface area; e' = early diastolic velocity of the medial mitral annulus; eGFR = estimated glomerular filtration rate; IMF = intramuscular fat; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; MRA = Mineralocorticoid receptor antagonists; SAT = subcutaneous adipose tissue; TRPG = tricuspid regurgitation pressure gradient.

Table2

Table 2

Cardiopulmonary Exercise Test Data and Muscle Strength at Discharge

	Total	Percent IMF Group		p value
		Low	High	
		($\leq$2.891 %)	(>2.891 %)	
	(n=93)	(n=47)	(n=46)	
Peak WR (watt)	79.0±29.3	80.8±27.7	77.0±30.7	0.527
Anaerobic threshold (ml/min/kg)	13.1±2.6	13.3±2.4	12.8±2.9	0.342
Anaerobic threshold (%predicted)	84.7±16.1	86.3±14.8	83.2±17.6	0.313
Peak oxygen uptake (ml/min/kg)	18.9±4.9	19.6±4.6	18.3±5.3	0.207
Peak oxygen uptake (%predicted)	75.5±17.5	77.8±16.1	73.3±18.9	0.159
VE/VCO$_2$ slope	29.5±6.9	28.7±7.4	30.3±6.4	0.158
Muscle strength				
Grip strength (kg)	29.1±9.4	31.3±8.9	26.7±9.6	0.024
Leg strength (N)	287.4±108.1	300.8±102.4	273.3±114.6	0.242

Values are mean ± standard deviation

VE/VCO$_2$ slope = ventilatory equivalent versus carbon dioxide output slope; WR = work rate.

Table3

Table 4

Spearman Correlation Coefficient Analysis between %IMF in the Thigh and Each Continuous Variable

	Spearman r	p value
Age	0.082	0.435
BMI (kg/m²)	0.220	0.034
Heart rate (bpm)	0.039	0.712
Resting systolic BP (mmHg)	-0.002	0.985
Resting diastolic BP (mmHg)	0.004	0.967
Hemoglobin (g/dl)	-0.040	0.705
Creatinine (g/dl)	-0.086	0.421
High sensitive troponin T (ng/l)	0.200	0.083
Log BNP (pg/ml)	-0.045	0.667
LVEDD (mm)	0.038	0.719
LVESD (mm)	-0.008	0.939
LVEF (%)	0.089	0.399
e' (cm/s)	-0.064	0.549
TRPG (mmHg)	0.204	0.065
Peak working rate (watt)	-0.183	0.082
Anaerobic threshold (ml/kg/min)	-0.169	0.109
Peak oxygen uptake (ml/kg/min)	-0.221	0.036
Thigh muscle/BSA (cm^2/m^2)	-0.189	0.069
Thigh SAT/BSA (cm^2/m^2)	0.258	0.013
Grip strength (kg)	-0.298	0.005
Leg strength (N)	-0.208	0.054

BMI = body mass index; BNP = B-type natriuretic peptide; BP = blood pressure; BSA = body surface area; e' = early diastolic velocity of the medial mitral annulus; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; SAT = subcutaneous adipose tissue; TRPG = tricuspid regurgitation pressure gradient.

Table 4

Table 4

Univariate and Multivariate Analyses for all-cause Death or Rehospitalization for Heart Failure

| | Univariate Analysis | | | Multivariate Analysis | | | | | | | | |
| | | | | Model 1 | | | Model 2 | | | Model 3 | | |
	HR	(95% CI)	p value	HR	(95% CI)	p value	HR	(95% CI)	p value	HR	(95% CI)	p value
Age	1.026	0.995-1.061	0.112									
Male gender	0.785	0.334-2.047	0.595									
BMI (kg/m^2)	0.958	0.867-1.045	0.360	0.915	0.806-1.023	0.144				0.952	0.856-1.045	0.328
Heart rate (bpm)	0.969	0.943-0.998	0.033									
Resting systolic BP (mmHg)	0.989	0.971-1.006	0.293							0.995	0.969-1.019	0.690
Resting diastolic BP (mmHg)	0.972	0.939-1.003	0.085									
Diabetes mellitus	1.206	0.434-2.917	0.695									
LVEDD (mm)	1.034	0.973-1.093	0.258									
LVESD (mm)	1.027	0.975-1.080	0.303									
LVEF (%)	0.989	0.925-1.053	0.728				0.944	0.872-1.016	0.142			
e' (cm/s)	1.070	0.793-1.428	0.649									
TRPG (mmHg)	1.027	0.991-1.062	0.131									
Anaerobic threshold (ml/kg/min)	0.789	0.646-0.943	0.014				0.952	0.768-1.164	0.637			
Peak oxygen uptake (ml/kg/min)	0.851	0.753-0.949	0.006	0.856	0.752-0.961	0.013						
Peak WR (watt)	0.980	0.961-0.998	0.042									
VE/VCO$_2$ slope	1.116	1.064-1.168	<0.001									
Hemoglobin (g/dl)	0.854	0.707-1.026	0.095									
Serum sodium (mEq/l)	0.924	0.786-1.094	0.350									
Albumin (g/dl)	0.331	0.152-0.746	0.006							0.352	0.150-0.842	0.017
eGFR (ml/min/1.73m²)	0.997	0.978-1.011	0.705									
Log BNP (pg/ml)	4.928	1.926-13.962	0.002				5.614	1.827-19.256	0.004			
High sensitive troponin T (ng/l)	1.013	1.001-1.021	0.011									

Grip strength (kg)	0.947	0.916-0.981	0.002								
Leg strength (N)	0.996	0.992-0.999	0.019	1.004	0.998-1.010	0.204					
Thigh muscle/BSA (cm^2/m^2)	0.982	0.946-1.020	0.348								
Thigh SAT/BSA (cm^2/m^2)	0.999	0.971-1.023	0.916								
%IMF in the thigh (%)	1.379	1.089-1.724	0.006	1.361	1.043-1.745	0.018	1.47	1.108-1.967	0.008	1.33	1.054-1.657	0.013

Abbreviations as in Table 1 and 2. CI, confidence interval; HR, hazard ratio.

BMI = body mass index; BNP = B-type natriuretic peptide; BP = blood pressure; BSA = body surface area; e' = early diastolic velocity of the medial mitral annulus; eGFR = estimated glomerular filtration rate; IMF = intramuscular fat; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; SAT = subcutaneous adipose tissue; TRPG = tricuspid regurgitation pressure gradient; VE/VCO$_2$ slope = ventilatory equivalent versus carbon dioxide output slope; WR = work rate.
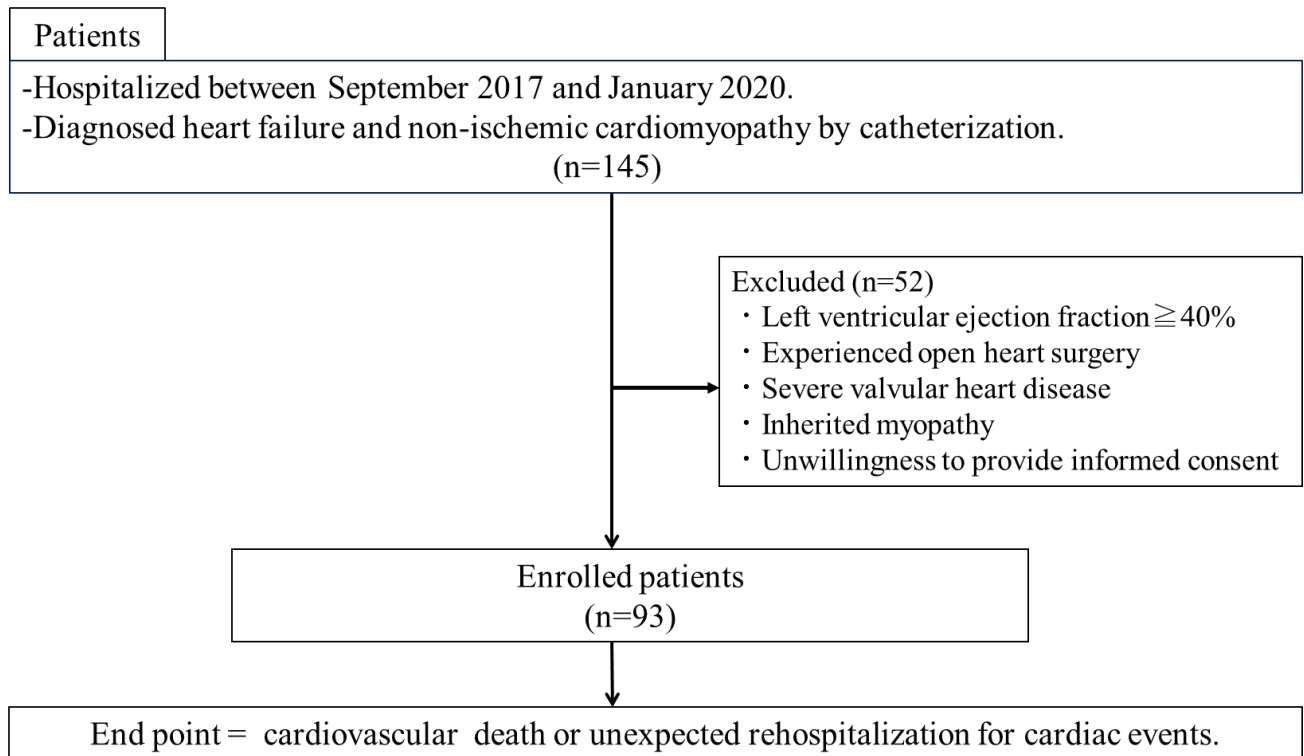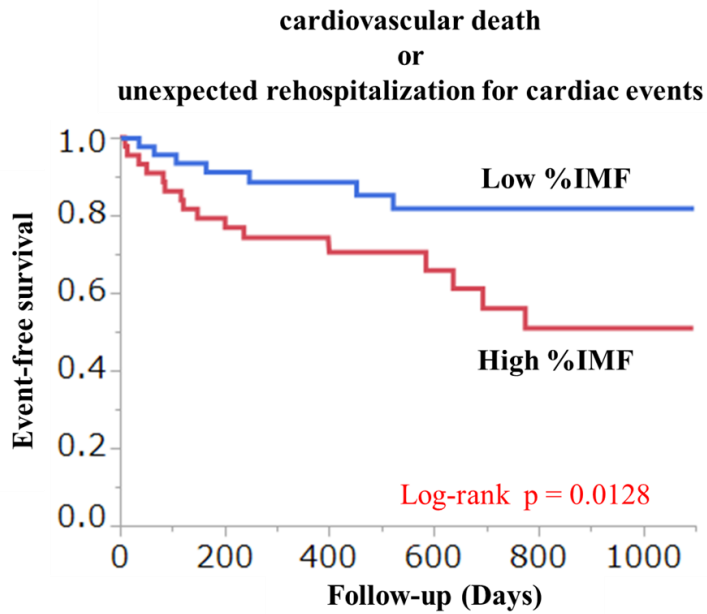
Figure

Patients

-Hospitalized between September 2017 and January 2020.
-Diagnosed heart failure and non-ischemic cardiomyopathy by catheterization.
(n=145)

Excluded (n=52)
・Left ventricular ejection fraction≧40%
・Experienced open heart surgery
・Severe valvular heart disease
・Inherited myopathy
・Unwillingness to provide informed consent

Enrolled patients
(n=93)

End point＝ cardiovascular death or unexpected rehospitalization for cardiac events.

Figure 1. Patients flow diagram.

cardiovascular death
or
unexpected rehospitalization for cardiac events

Figure 2. Kaplan-Meier estimates of risk of cardiac events. The patients with high % intramuscular fat in the thigh had a higher risk of cardiovascular death or unexpected rehospitalization for cardiac events than those with low % intramuscular fat in the thigh (log-rank test p = 0.0128).