Table 1
Summary of the main studies evaluating lipomatous metaplasia (LM) in ischemic cardiomyopathy using multi-slice computed tomography (MSCT) or cardiac magnetic resonance (CMR).

	Ichikawa et al. [7]	Ahn et al. [8]	Goldfarb et al. [9]
Imaging modality	MSCT	MSCT	CMR
Number of patients	53	161	25
Age (years)	66 ± 10	61 ± 10	64 ± 11
Male gender	38 (72%)	129 (80%)	22 (88%)
LM	32 (60%)	36 (22%)	17 (68%)
Previous anterior MI (LM+ vs. LM−)	11 (34%) vs. 10 (48%)	27 (75%) vs. 62 (40%)	–
Infarcted myocardium (% of LV) (LM+ vs. LM−)	–	–	23.5 ± 11.3 vs. 10.6 ± 3.2
Infarct age (years) (LM+ vs. LM−)	8.2 ± 4.4 vs. 2.2 ± 2.6	5.6 ± 4.8 vs. 2.4 ± 3.6	14.0 ± 9.3 vs. 10.0 ± 6.6
Distribution of LM			
Subendocardium	30 (94%)	36 (100%)	1 (6%)
Middle-layer	1 (3%)	–	12 (71%)
Subepicardium	1 (3%)	–	4 (24%)

Data are expressed as mean ± standard deviation, and n (%).
LV: left ventricle; MI: myocardial infarction.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [13].

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Effects of exercise training on neurovascular responses during handgrip exercise in heart failure patients

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Exaggerated central sympathetic outflow typifies chronic heart failure (HF) [1]. Augmented plasma catecholamine levels, norepinephrine spillover and muscle sympathetic nerve activity (MSNA) have been demonstrated in HF patients [2,3]. In addition, HF patients have reduced skeletal muscle blood flow (FBF) [4,5], which may explain, at least in part, the skeletal myopathy and exercise intolerance in HF patients [1].

Exercise training markedly reduces MSNA and muscle vasoconstriction in HF patients [6,7]. However, previous studies were limited to the effects of exercise training on resting neurovascular control. It remains unknown whether exercise training improves sympathetic outflow and muscle vascular resistance during physiological manoeuvres, such as exercise. This is an important question, since previous observations strongly suggest that altered muscle afferent reflex control contributes to the increased sympathetic nerve activity and exercise intolerance in HF [8,9].

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We tested the hypothesis that exercise training would reduce MSNA and increase FBF during handgrip exercise in HF patients.

The study included thirty-five clinically stable HF patients aged 40 to 75 years old, ejection fraction ≤40% from our data base (1998–2004) of previous randomized studies [7,8] in a 1:1 ratio of the Unit of Cardiovascular Rehabilitation and Exercise Physiology, Heart Institute, Medical School, University of São Paulo. Seventeen age-matched healthy individuals in our data base were used as controls. MSNA had been recorded from the peroneal nerve and FBF had been measured by venous occlusion plethysmography [6,7]. Exercise was elicited by isometric handgrip exercise (30% of MVC) for three minutes [3].

Exclusion criteria were: unstable angina, a recent myocardial infarction, severe chronic obstructive pulmonary disease, uncontrolled systemic arterial hypertension, and/or neurological or orthopaedic disabilities. The exercise group underwent 4 months of supervised exercise training. The study was approved by The Human Subject Protection Committee of the Heart Institute (InCor) and Clinical Hospital, University of São Paulo, Medical School.

Initial differences were tested by one-away ANOVA with repeated measures. Two-away ANOVA with repeated measures was used for between-group comparison. When significance was found, Scheffé's post hoc comparison test was performed. The level of significance was set at $p<0.05$.

Baseline characteristics of the exercise-trained and untrained HF patients and normal controls are shown in Table 1. There were no significant differences between HF patients and normal controls in gender, heart rate, systolic and mean arterial pressure. Exercise-trained HF patients were older than normal controls. Body weight and BMI were greater in normal controls than in both HF groups. HF patients had lower peak VO_2 ($p<0.001$), left ventricular ejection fraction ($p<0.001$) and higher MSNA ($p=0.001$), and forearm vascular resistance ($p<0.001$) than normal controls. FBF was lower in exercise-trained HF patients than in normal controls ($p=0.002$). No significant differences were found in FBF between untrained HF patients and normal controls.

Table 1
Baseline physiological characteristics in exercise-trained and untrained heart failure patients.

	Exercise-trained HF patients ($n=19$)	Untrained HF patients ($n=16$)	Normal controls ($n=17$)
Age (years)	56 ± 2.01	51 ± 1.9	48 ± 1.09*
Sex (M/F)	13/6	11/5	10/7
Weight (kg)	56 ± 2.30	62 ± 3.24	78 ± 2.70**
BMI (kg/m^2)	24 ± 0.70	23 ± 0.76	25 ± 0.58**
HR (beat/min)	71 ± 2.76	75 ± 3.74	65 ± 1
SBP (mmHg)	122 ± 4	119 ± 5	132 ± 2
DBP (mmHg)	79 ± 1	79 ± 2	69 ± 13*,**
MAP (mmHg)	93 ± 3.55	96 ± 3.13	99 ± 2
LVEF (%)	30 ± 1	31 ± 2	68 ± 4*,**
Peak VO_2 (mL/kg/min)	14 ± 1	15 ± 1	26 ± 1*,**
HF aetiology			
Chagasic	5	5	
Idiopathic	7	8	
Ischaemic	4		
Hypertensive	3	3	
Medications			
ACEI/ARB	18	16	
Digoxin	18	13	
Diuretics	16	12	
Beta-adrenergic blocker	11	7	
Spironolactone	15	9	
MSNA (bursts/min)	44 ± 3	45 ± 4	27 ± 2*,**
MSNA (bursts/100HB)	73 ± 5	74 ± 6	46 ± 3*,**
FBF (mL/min/100 mL)	1.67 ± 0.11	2.04 ± 0.13	2.40 ± 0.17*
FVR (units)	58 ± 3	50 ± 4	45 ± 3*,**

Values are mean ± SE. HF = heart failure; BMI = body mass index; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure; EF = ejection fraction; VO_2 = oxygen uptake; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blockers; MSNA = muscle sympathetic nerve activity; HB = heart beats; FBF = forearm blood flow; and FVR = forearm vascular resistance.
* $p<0.05$ vs. exercised-trained patients.
** $p<0.05$ vs. untrained patients.

Table 2
Absolute values of PAM, HR and FBF at baseline and during isometric exercise at 30% of maximal voluntary contraction (MVC) post/pre-exercise or sedentary period.

		Baseline	Exercise (30% MVC)		
			HG 1	HG 2	HG 3
MAP (mmHg)					
Untrained HF	Pre	96 ± 3.13	99 ± 3.60*	102 ± 3.98*	106 ± 4.83*
	Post	94 ± 2.81	97 ± 2.91*	100 ± 3.67*	104 ± 3.39*
Exercise-trained HF	Pre	99 ± 3.55	99 ± 3.85*	100 ± 3.45*	103 ± 3.65*
	Post	91 ± 2.84	94 ± 3.15*	100 ± 3.54*	104 ± 3.77*
Normal control	Pre	99 ± 2	106 ± 3*	112 ± 3*	116 ± 4*
HR (beats/min)					
Untrained HF	Pre	75 ± 3.74	78 ± 3.28*	81 ± 3.11*	83 ± 3.30*
	Post	73 ± 3.33	76 ± 3.50*	79 ± 3.57*	80 ± 3.60*
Exercise-trained HF	Pre	71 ± 2.76	74 ± 2.86*	78 ± 3.09*	79 ± 3.35*
	Post	66 ± 2.94	72 ± 3.16*	73 ± 3.10*	75 ± 3.12*
Normal control	Pre	65 ± 1	69 ± 2*	73 ± 2*	74 ± 3*
FBF (mL/min/100 mL)					
Untrained HF	Pre	2.04 ± 0.13	2.13 ± 0.12*	2.27 ± 0.13*	2.38 ± 0.15*
	Post	1.73 ± 0.14	2.00 ± 0.16*	2.20 ± 0.20*	2.22 ± 0.17*
Exercise-trained HF	Pre	1.67 ± 0.11**	2.13 ± 0.13*,**	2.26 ± 0.16*,**	2.41 ± 0.21*,**
	Post	2.44 ± 0.20	2.86 ± 0.22*	3.16 ± 0.26*	3.24 ± 0.25*
Normal control	Pre	2.40 ± 0.17	2.67 ± 0.22*	2.89 ± 0.23*	3.05 ± 0.25*

Values are mean ± SE. HG = handgrip; MAP = mean arterial pressure; HF = heart failure; and FBF = forearm blood flow.
* $p<0.05$ vs. baseline.
** $p<0.05$ vs. normal control.

During exercise, heart rate and mean arterial pressure increased significantly and similarly in all groups (Table 2). FBF during exercise increased progressively in all groups, but this parameter was significantly lower in HF patients (group effect $p=0.01$, Table 2). Sympathetic burst frequency during exercise increased significantly in all groups (Fig. 1A). However, MSNA values were higher at baseline and remained significantly higher during exercise in HF patients compared to normal controls (group effect $p=0.003$, Fig. 1A). There were no significant differences in forearm vascular resistance during exercise between HF patients and normal controls (Fig. 1C).

Exercise training significantly increased peak VO_2 in HF patients ($p<0.001$). No significant changes were observed in untrained HF patients. Exercise training significantly reduced resting and exercise MSNA in HF patients. Sympathetic burst frequency values throughout experimental protocol were significantly lower in exercise-trained HF patients compared to untrained HF patients, and now similar to normal controls (Fig. 1B).

Exercise training significantly increased FBF at rest and during handgrip exercise in HF patients. Thus, FBF was no longer different in exercise-trained HF patients and normal controls and significantly greater than in untrained HF (Table 2). Exercise training significantly reduced forearm vascular resistance throughout the experimental protocol in HF patients. Thus, forearm vascular resistance was no longer different in exercise-trained HF patients and normal controls and significantly lower than untrained HF (Fig. 1D). Exercise training provoked no changes in heart rate and mean blood pressure in HF patients (Table 2).

Previous studies have demonstrated that increasing levels of sympathetic nerve activity, which is observed at rest and during