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Respiratory muscle endurance is limited by lower ventilatory efficiency in post-myocardial infarction patients

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ABSTRACT | Background: Reduced respiratory muscle endurance (RME) contributes to increased dyspnea upon exertion in patients with cardiovascular disease. **Objective:** The objective was to characterize ventilatory and metabolic responses during RME tests in post-myocardial infarction patients without respiratory muscle weakness. **Method:** Twenty-nine subjects were allocated into three groups: recent myocardial infarction group (RG, n=9), less-recent myocardial infarction group (LRG, n=10), and control group (CG, n=10). They underwent two RME tests (incremental and constant pressure) with ventilatory and metabolic analyses. One-way ANOVA and repeated measures one-way ANOVA, both with Tukey post-hoc, were used between groups and within subjects, respectively. **Results:** Patients from the RG and LRG presented lower metabolic equivalent and ventilatory efficiency than the CG on the second (50 ± 06 , 50 ± 5 vs. 42 ± 4) and third part (50 ± 11 , 51 ± 10 vs. 43 ± 3) of the constant pressure RME test and lower metabolic equivalent during the incremental pressure RME test. Additionally, at the peak of the incremental RME test, RG patients had lower oxygen uptake than the CG. **Conclusions:** Post-myocardial infarction patients present lower ventilatory efficiency during respiratory muscle endurance tests, which appears to explain their inferior performance in these tests even in the presence of lower pressure overload and lower metabolic equivalent.

Keywords: cardiac disease; physical therapy; exercise tolerance; respiratory muscles; muscle fatigue.

HOW TO CITE THIS ARTICLE

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● Introduction

In most myocardial infarction patients, exercise limitation is manifested as dyspnea or lower limb fatigue¹⁻⁶. The dyspnea is related, among other possibilities, to respiratory muscle strength and endurance⁷, which are expressed as maximal inspiratory pressure (MIP) and respiratory muscle endurance (time [Tlim] or pressure [PTH_{MAX}]), respectively. Respiratory muscle weakness (MIP <60% of predicted values)^{2,8-10} and reduced respiratory muscle endurance (RME) contribute to greater dyspnea upon exertion in patients with chronic diseases, including cardiovascular disease^{1,2,8-10}, affecting their exercise tolerance^{2,11-14}.

In any muscle work, ventilatory and metabolic responses are representative of the body's ability to capture, transport, and use oxygen for energy production and eliminate carbon dioxide in order to maintain a relatively normal pH¹². Several methodologies are used to evaluate RME. When

assessing RME in healthy subjects, the ventilatory and metabolic responses are similar in low-intensity long-duration exercise¹⁵. We believe that reduced RME performance, proportional to the pressure used, might be a consequence of higher metabolic demand, which indicates greater effort during RME testing.

However, to our knowledge, the magnitude of ventilatory and metabolic responses during RME tests has not been well established in patients with acute or chronic myocardial infarction (MI) without respiratory muscle weakness. We hypothesize that the ventilatory efficiency of post-MI patients without respiratory muscle weakness during RME tests is less than that of healthy subjects.

The aim of the present study was to evaluate ventilatory and metabolic responses during respiratory muscle endurance tests in post-myocardial infarction patients and healthy subjects, all with preserved respiratory muscle strength.

● **Method**

This cross-sectional study was approved by the Human Research Ethics Committee of Universidade Federal de São Carlos (UFSCar), São Carlos, SP, Brazil (protocol 353/2009) and conducted in compliance with Declaration of Helsinki guidelines at the Cardiovascular Physical Therapy Laboratory of the Exercise Research Center in the UFSCar Physical Therapy Department. All participants signed an informed consent form.

Post-myocardial infarction patients (35-65 years of age) diagnosed with a single episode of myocardial infarction (Killip I) were recruited and allocated into two groups according to the time since occurrence: recent infarction group (RG, n=09; up to 45 days post-MI) and less-recent infarction group (LRG, n=10; at least 6 months post-MI). A control group (CG,

n=10) was formed from sedentary healthy subjects matched with the other groups for age, body mass, and height. The post-myocardial infarction patients were identified and recruited from the Coronary Unit of the Santa Casa de Misericórdia de São Carlos either directly during admittance (RG) or from the hospital's database (LRG). CG subjects were identified and recruited from the UFSCar School Health Unit (Figure 1). For all subjects, an adequate cognitive level and absence of musculoskeletal, joint, respiratory, neurological or vascular disorders was required for inclusion.

Subjects were excluded if they presented at least one of the following conditions: body mass index ≥ 35 kg/m², systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg (at rest), functional capacity ≤ 4 metabolic equivalents;

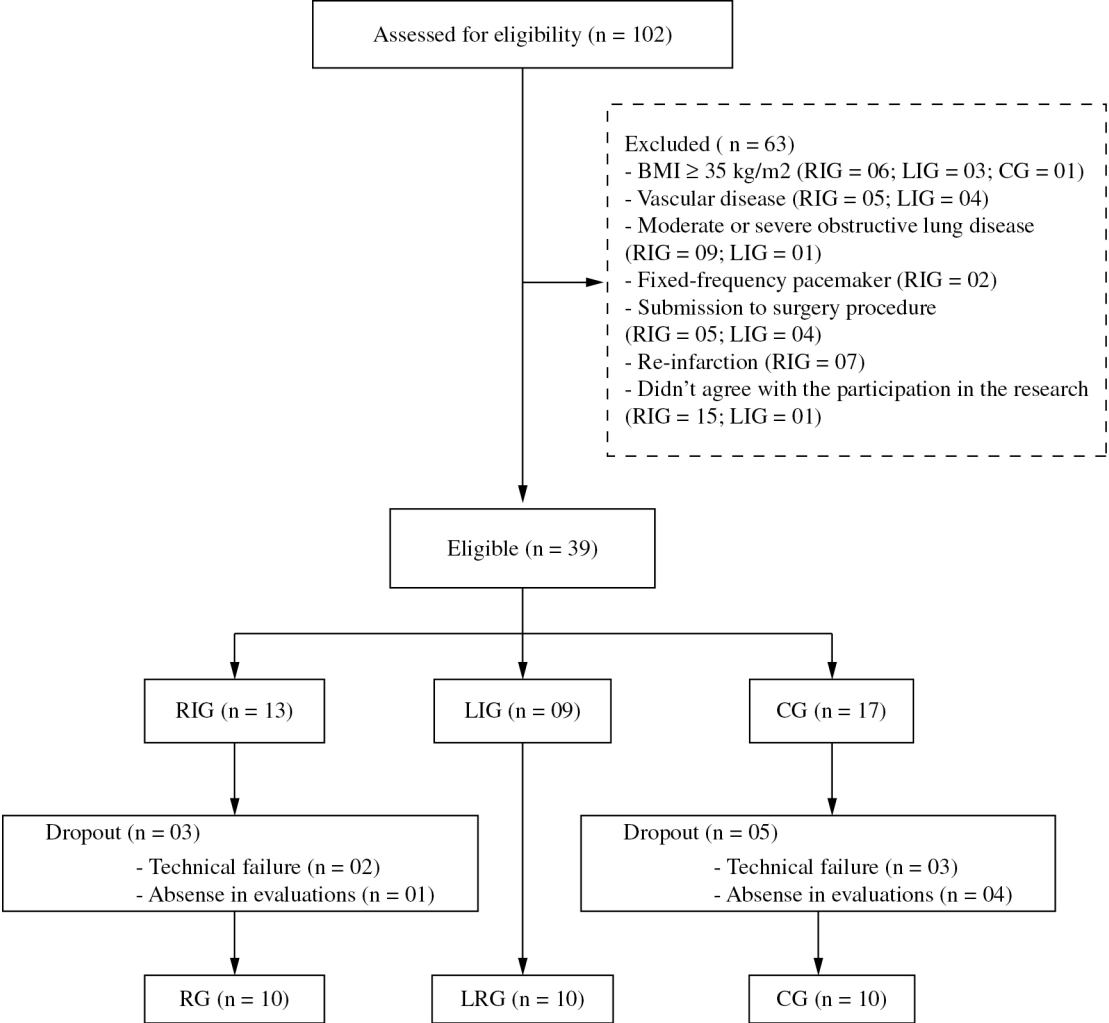


Figure 1. Diagram of sample distribution for the recent post-myocardial infarction group (RG), the less-recent post-myocardial infarction group (LRG), and the control group (CG).

ST-segment depression >2 mm, angina pectoris during exercise; exercise-induced decrease in systolic blood pressure ≥ 15 mmHg, sustained ventricular arrhythmia, supraventricular arrhythmia that compromised cardiac function, moderate or severe valve disease, a fixed-frequency pacemaker, uncontrolled diabetes, obstructive lung disease, difficulty performing a self-assessment of effort using the Borg scale or respiratory muscle weakness ($MIP < 60\%$ of the predicted)^{10,16}.

Clinical and functional evaluation

The subjects underwent a) a physical examination of cardiovascular and respiratory parameters at rest, b) a pulmonary function test – slow and forced vital capacity and maximal voluntary ventilation¹⁶ (CPX-D, Medical Graphics, St Paul, MN, USA), c) a 12-derivation electrocardiogram at rest (Schiller, AT1, Altgasse, Baar, Switzerland) in the supine position, and d) a clinical treadmill exercise test conducted by a cardiologist.

Cardiopulmonary exercise test

A symptom-limited cardiopulmonary exercise test (CPX) was performed on a treadmill (Master ATL, Inbramed, Porto Alegre, RS, Brazil) using a ramp protocol. A 4-min warm-up period (1.5 mph, no slope) was followed by an incremental increase in walking velocity (over 3 min to achieve maximal walking velocity) and then by 0.5% increases in elevation every 15 s. Ventilatory and metabolic parameters were monitored and registered breath-by-breath (CPX-D/BreezeSuite 6.4.1, Medical Graphics, St Paul, MN, USA) and were analyzed after smoothing the data by moving averages of eight respiratory cycles¹⁷. The electrocardiogram was continuously monitored (Schiller, AT1, Altgasse, Baar, Switzerland), and the heart rate was recorded with a digital telemetry system (Polar® S810i; Polar Electro Oy, Kempele, Oulo, Finland). Every two minutes, blood pressure was assessed and perceived exertion was rated with the Borg scale. The ventilatory method was used by three independent evaluators to identify the anaerobic threshold (AT)^{17,18}. Oxygen uptake at this point (VO_{2AT}) was identified. The highest oxygen uptake observed in the last 30 seconds of exercise was defined as VO_{2peak} ¹⁸.

Evaluation of respiratory muscle strength and endurance

Respiratory muscle strength (RMS) was assessed using a digital pressure transducer (MVD-300,

Globalmed, Porto Alegre, RS, Brazil)¹⁹. The values observed in the first second after peak pressure were used to define MIP¹⁰. RME, ventilatory, and metabolic parameters were assessed and registered breath-by-breath while the patients breathed continuously through the mouthpiece of a linear inspiratory load resistor (Power Breath®, IMT Technologies Ltd., Birmingham, UK) connected to a ventilatory and metabolic system (CPX-D/BreezeSuite 6.4.1, Medical Graphics, St Paul, MN, USA).

Incremental and constant pressure tests were employed to assess RME, as previously described¹⁴. Briefly, the incremental test was based on 3 min steps and began with a load corresponding to 50% of the MIP, followed by load increments equivalent to 10% MIP until the patient failed to achieve the pressure in three consecutive inspirations. The greatest inspiratory pressure sustained at least for 1 min was taken as the measure for inspiratory muscle endurance ($P_{th_{max}}$)^{11,19}. In the next protocol, a constant load (80% of the $P_{th_{max}}$) was employed. The time elapsed to task failure was defined as respiratory muscle endurance time (Tlim).

Statistical analysis

The data were analyzed using Statistica 7 (StatSoft Inc., Tulsa, OK, USA). Based on the results of a pilot study ($n=4$), we estimated that a sample size of six individuals in each group would be sufficient to detect a 10-point difference in ventilatory efficiency (statistical power of 80%). The level of significance was set at 5%. Normally-distributed data (Shapiro-Wilk test) are presented as mean \pm SD; Non-normally distributed data are expressed as median (minimum and maximum values). One-way ANOVA with Tukey post-hoc and repeated measures one-way ANOVA with Tukey post-hoc were used to analyze data between groups and within subjects, respectively.

Results

Clinical and functional evaluation

The sample consisted of middle-aged men without respiratory muscle weakness and with similar anthropometric characteristics between groups. For all groups, spirometric values were within the range predicted for the Brazilian population, with no difference among groups²⁰. In the post-myocardial infarction groups, the mean time elapsed between infarction and inclusion in the study was 33 (range: 16 to 45) days in the RG and 702 (range: 219 to 923) days in the LRG. Most had an anterior or inferior

infarction (53%) with bi-arterial involvement (48%) and had undergone percutaneous transluminal coronary angioplasty (95%). All RG and LRG subjects had preserved ventricular function with a left ventricular ejection fraction greater than 50%, according to ventriculography.

Cardiopulmonary exercise test

During the cardiopulmonary exercise test, VO_{2AT} and VO_{2peak} (absolute and corrected for body mass) were higher in the CG than in the RG or LRG (Table 1).

Ventilatory and metabolic responses during RME protocols

The majority of the ventilatory variables (tidal volume, respiratory rate, inspiratory time, expiratory time, inspiratory time relative to total respiratory cycle, minute volume, and partial CO_2 pressure at the end of expiration) and metabolic variables (CO_2 output and respiratory exchange ratio) remained constant during the incremental and constant pressure tests and did not differ among groups. At 70 and 80% of MIP during the incremental pressure test and during the second and third parts of the constant pressure test, the RG had lower MET and higher VE/VCO_2 than the CG. At 90% MIP during the

incremental pressure test, the RG had lower VO_2 and MET than the CG (Tables 2 and 3).

Furthermore, at all stages of respiratory endurance tests the RG requires a higher percentage of VO_{2peak} (~5% above compared to CG) to maintain a lower pressure and product pressure-time¹⁴ (Figure 2). This behavior was not presented at the higher stage (90% MIP) of incremental pressure test.

Discussion

The main results of this descriptive, cross-sectional study provide new evidence about the source of reduced RME in recent post-MI patients without inspiratory muscle weakness. The reduction seems to be due to the lower ventilatory efficiency observed from the middle to the final part of the protocols, even when they experienced lower pressure overload than sedentary healthy subjects. The sample consisted of middle-aged men with similar anthropometric characteristics and similar clinical characteristics between post-MI groups. Only subjects with normal respiratory function were included in the present study in order to reduce the influence of obstructive or restrictive diseases on RME performance. Impaired exercise tolerance is a characteristic of cardiac patients who have undergone angioplasty, although

Table 1. Anthropometric characteristics and cardiopulmonary capacity of the recent infarction group (RG), the less-recent infarction group (LRG) and the control group (CG).

Values	RG (n=9)	LRG (n=10)	CG (n=10)	p-value
Anthropometric				
Age (years)	48±8	51±6	49±9	0.45
Body mass (kg)	81±11	83±15	79±10	0.73
Height (m)	1.7±0.1	1.7±0.1	1.8±0.1	0.89
BMI (kg/m²)	28±4	29±4	25±3	0.10
MIP (cmH ₂ O)	87±21	101±12	106±26	0.09
MIP (% predicted)	71±18	87±23	84±20	0.06
CPX				
VO_{2AT} (mL.min ⁻¹)	1203±171	1426±298	1601±262 [‡]	<0.01
VO_{2AT} (mL.kg ⁻¹ .min ⁻¹)	15±3	18±4	21±4 [‡]	<0.01
VO_{2peak} (mL.min ⁻¹)	2030±446	2268±391	2931±341 [#]	<0.01
VO_{2peak} (mL.kg ⁻¹ .min ⁻¹)	26±6	28±6	38±4 [#]	<0.01
Dyspnea (CR10)	6.4±2.8	7.3±2.3	6.3±2.6	0.72
Fatigue (CR10)	5.0±3.2	6.2±2.9	4.9±3.4	0.70

BMI: body mass index; MIP: maximal inspiratory pressure; CPX: cardiopulmonary exercise test; VO_{2AT} : anaerobic threshold oxygen uptake; VO_{2peak} : peak oxygen uptake; VO_{2AT} : anaerobic threshold oxygen uptake; [‡]p<0.05 compared to RG with one-way ANOVA (Tukey post-hoc); [#]p<0.05 compared to RG and LRG with one-way ANOVA (Tukey post-hoc). Part of the data was originally published in Neves et al.¹⁵, used with permission (2951481234155).

Table 2. Ventilatory and metabolic response during respiratory muscle endurance test (incremental pressure protocol) for recent infarction group (RG), less-recent infarction group (LRG), and control group (CG).

Values	RG (n=9)					LRG (n=10)					CG (n=10)				
	50%	60%	70%	80%	90%	50%	60%	70%	80%	90%	50%	60%	70%	80%	90%
T (s)	180±0	180±0	180±0	180±0	150±50	180±0	180±0	168±38	160±40	171±24	180±0	180±0	180±0	176±15	159±40
Vt (L)	1.0±0.4	1.1±0.3	1.0±0.5	1.1±0.7	0.9±0.3	1.1±0.3	1.0±0.2	1.1±0.4	1.0±0.3	1.1±0.5	1.2±0.4	1.2±0.3	1.2±0.3	1.2±0.2	1.2±0.2
f (irpm)	12±1	13±2	13±2	13±3	13±4	12±1	12±1	12±1	13±2	13±2	11±1	12±2	12±1	13±2	13±2
Ti (s)	2±0.5	1±0.2	2±0.3	1±0.5	2±0.5	2±0.5	2±0.4	2±0.5	2±0.5	1±0.6	2±0.3	2±0.2	2±0.2	1±0.3	2±0.2
Te (s)	4±0.9	4±0.8	3±0.8	4±1.5	4±1.1	4±0.7	3±0.6	3±0.6	3±0.6	3±0.8	4±0.6	4±0.5	3±0.5	3±0.7	3±0.7
Ti/Tot	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1
VE (L.min ⁻¹)	12±4	14±2	12±4	13±4	11±3	12±3	12±2	13±4	13±4	14±5	13±3	13±3	14±3	15±3	15±3
VO ₂ (mL.min ⁻¹)	315±62	307±54	295±37	310±45	281±56	336±22	318±51	305±59	315±56	324±66	351±58	341±62	365±52	374±38	403±60*
VCO ₂ (mL.min ⁻¹)	288±87	312±55	263±70	272±76	244±72	304±49	291±47	292±75	281±71	290±82	350±90	351±93	360±74	372±56	366±54
PETCO ₂ (mmHg)	36±5	35±5	35±5	36±5	36±4	35±3	34±4	34±6	33±5	34±5	37±4	36±4	37±5	36±5	37±5
RER	0.9±0.2	0.9±0.1	0.9±0.1	0.9±0.1	0.9±0.1	0.9±0.2	1.0±0.1	0.9±0.1	0.9±0.2	0.9±0.1	1.0±0.2	1.0±0.1	1.0±0.1	1.0±0.1	0.9±0.1
VE/VCO ₂	42±5	46±6	46±6	51±10	50±6	44±7	45±5	46±5	50±6	50±5	38±5	39±4	40±4 ^s	41±3 ^s	41±4 ^s
MET (mL.Kg ⁻¹ .min ⁻¹)	1.2±0.2	1.1±0.2	1.1±0.2	1.1±0.2	1.0±0.2	1.1±0.3	1.1±0.1	1.1±0.2	1.1±0.1	1.1±0.1	1.3±0.3	1.3±0.2	1.3±0.2 ^s	1.4±0.2 ^s	1.4±0.2 ^s

50,60,70,80,90% of MIP; steps of incremental pressure test; T: mean duration of step; Vt: tidal volume; ; f: respiratory rate; VE: minute volume; VCO₂: carbon dioxide output; PETCO₂: partial CO₂ pressure at the end of expiration; RER: respiratory exchange ratio ; VE/VCO₂: ventilatory equivalent ratio for CO₂; MET: metabolic equivalent; *p<0.05 compared to RG with one-way ANOVA (Tukey post-hoc); ^sp≤0.05 compared to RG and LRG with one-way ANOVA (Tukey post-hoc).

Table 3. Ventilatory and metabolic response during respiratory muscle endurance test (constant pressure protocol) for the recent infarction group (RG), the less-recent infarction group (LRG), and the control group (CG).

Values	RIG (n=9)			LRG (n=10)			CG (n=10)		
	I	II	III	I	II	III	I	II	III
Vt (L)	0.9±0.3	0.8±0.2	0.8±0.1	0.9±0.2	0.9±0.3	0.9±0.3	1.1±0.3	1.3±0.6	1.3±0.6
f (irpm)	12±2	13±2	14±2	13±1	14±1	14±2	12±1	12±2	13±2
Ti (s)	2±0.3	2±0.3	2±0.4	2±0.5	1±0.5	1±0.5	2±0.7	2±0.9	2±0.7
Te (s)	3±0.8	3±0.6	3±0.1	3±0.4	3±0.7	3±0.6	3±0.6	3±0.8	3±0.5
Ti/Tot	0.3±0.1	0.4±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1	0.3±0.1
VE (L.min ⁻¹)	10±2	11±2	11±3	11±3	13±5	12±4	13±3	14±6	17±8
VO ₂ (mL.min ⁻¹)	308±50	293±28	279±26	313±40	306±49	296±63	354±67	336±45	350±62
VCO ₂ (mL.min ⁻¹)	258±48	261±30	245±39	253±53	273±64	255±58	326±60	318±51	329±77
PETCO ₂ (mmHg)	38±3	37±3	37±4	36±4	35±6	35±5	35±5	33±7	31±8
RER	0.8±0.1	0.9±0.1	0.9±0.1	0.8±0.1	0.9±0.1	0.9±0.1	0.9±0.2	1.0±0.2	0.9±0.2
VE/VCO ₂	41±7	50±6	50±11	41±7	50±5	51±10	41±5	42±4 [§]	43±3 [§]
MET (mL.kg ⁻¹ .min ⁻¹)	1.1±0.2	1.0±0.1	1.0±0.1	1.1±0.1	1.1±0.1	1.0±0.2	1.3±0.2	1.2±0.2 [§]	1.3±0.2 [§]

I, II and III: constant pressure time (initial, middle and end); Vt: tidal volume; f: respiratory frequency ; Ti: inspiratory time; Te: expiratory time; Ti/Tot: inspiratory time relative to total respiratory cycle; VE: minute volume; VO₂: oxygen uptake; VCO₂: carbon dioxide output; PETCO₂: partial CO₂ pressure at the end of expiration; RER: respiratory exchange ratio; VE/VCO₂: ventilatory equivalent ratio for CO₂; MET: metabolic equivalent; [§] p ≤ 0.05 compared to RG and LRG with one-way ANOVA (Tukey post-hoc).

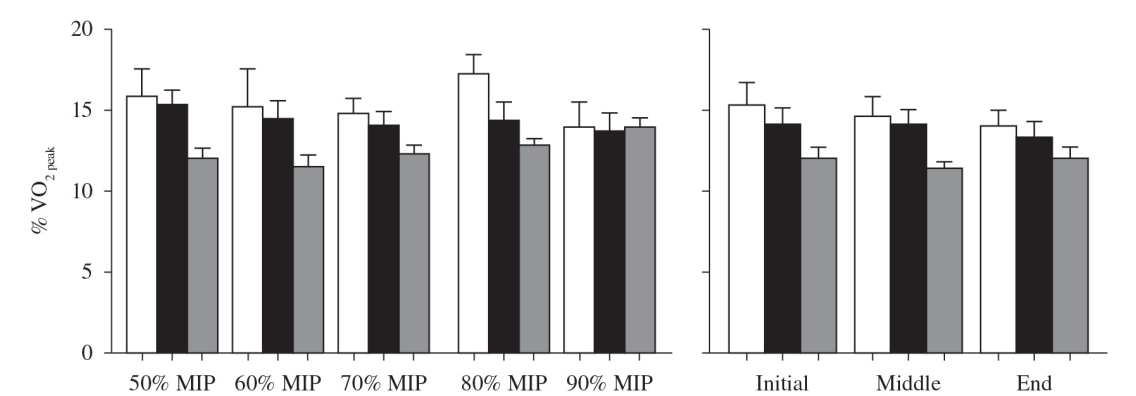


Figure 2. Illustration of the percentage of oxygen uptake at peak exercise (%VO_{2 peak}) during the incremental and constant pressure protocol endurance tests for the recent infarction group (RG-white), the less-recent infarction group (LRG-black), and the control group (CG-gray).

their exercise tolerance tends to increase with exercise programs²¹⁻²³. The exercise tolerance of the post-MI sample was greater than that found in other studies of cardiovascular disease^{11,24}. This difference is likely due to the preserved left ventricular ejection fraction observed in the present study and also to the fact that our sample was younger and had a lower body mass index and fewer comorbidities.

The low variation in ventilatory and metabolic values in both incremental and constant pressure RME tests may reflect a low and almost constant work rate²⁴. Analyzing other similar studies^{22,25-31}, we inferred that the RME assessment methods involved are the most probable contributors to the variation in

results. The differences include the type of applied load (elastic or resistive), the mode of load application (constant or incremental), the degree of motivation and the respiratory pattern (free or controlled)²⁶. The assessment of oxygen uptake percentage at peak exercise in the RME tests was an attempt to classify the intensity level of the achieved work rate, and we observed similar values between groups. However, the fact that the RG performed the RME tests with a 20% lower pressure than the CG could indicate that the RME tests represented a proportionally higher intensity for the RG. The consensus for respiratory tests is that the greater the pressure imposed with higher tidal volume, inspiratory time or inspiratory

flow, the lower the test tolerance is³². Furthermore, the influence of other factors such as gender, age, and height on RME test performance is poorly understood¹³. We observed that in post-MI patients, lower ventilatory efficiency was not compensated with superficial breathing and a consequent increase in respiratory rate²⁸ but, rather, increased recruitment and contraction of respiratory muscles was the means of generating enough inspiratory flow to deal with the imposed pressure¹⁴. Considering that the variables were kept constant, other dynamic factors such as the recruitment of respiratory muscles and changes in airway resistance²⁸ appear to influence respiratory muscle function and interfere with RME test performance in post-MI patients.

Study limitations

In this small descriptive cross-sectional study, we showed that there is lower ventilatory efficiency in the second part of test protocols in recent infarction patients without respiratory muscle weakness, even in the presence of lower pressure overload. Our findings were limited by the absence of a breath-by-breath respiratory muscle strength evaluation and patient follow-up over the recent and less recent myocardial infarction periods. Another limitation is related to the lack of predicted values for respiratory muscle endurance in each population.

Clinical implications

Our findings indicate that the reduced RME with increased respiratory effort observed in recent post-MI patients during RME tests could be influenced by their lower ventilatory efficiency. This is the first time that a possible limiting factor for dynamic exercise capacity in post-myocardial infarction has been associated with ventilatory efficiency due to a respiratory muscle component. Our results also raise the question of whether the addition of inspiratory muscle training in cardiac rehabilitation can improve RME performance and ventilatory efficiency in recent post-MI patients without respiratory muscle weakness.

Conclusion

In this descriptive, cross-sectional study with recent and less-recent post-MI patients without inspiratory muscles weakness, the lower ventilatory efficiency observed during respiratory muscle endurance tests appears to clarify the inferior performance on these tests, even in the presence of lower pressure overload.

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