

Recebido em: 01 mar. 2024 - Aprovado em: 06 set. 2024 Editora Chefe: Daniela Aparecida Biasotto-Gonzalez Editor Científico: Cid André Fidelis de Paula Gomes

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## MUSCLE OXYGENATION, PHYSICAL CAPACITY, AND QUALITY OF LIFE IN MALE HEART FAILURE PATIENTS

#### OXIGENAÇÃO MUSCULAR, CAPACIDADE FÍSICA E QUALIDADE DE VIDA DE HOMENS COM INSUFICIÊNCIA CARDÍACA

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#### Abstract

**Objective:** To verify peripheral muscle oxygenation and quality of life (QoL) in male patients with heart failure (HF) during a submaximal physical capacity test.

**Methods:** Cross-sectional study, in individuals with HF, functional class II or III, left ventricular ejection fraction <45%, divided into sedentary group (SG) and cardiovascular rehabilitation group (CRG). QoL was assessed by the Minnesota Living with Heart Failure Questionnaire, muscle oxygenation by near-infrared spectroscopy before, during and after the six-minute walk test. Inferential statistical tests were used with a significance level of 5%, according to the normality test. The correlation analysis was performed through the Spearman correlation test.

**Results:** There were inversely proportional results between physical aspects of QoL and oxyhemoglobin in the SG group. The distance covered was greater for CRG. We noted a significant increase in oxyhemoglobin post-test for CRG. **Conclusions:** Oxygen measurements correlate with physical aspects related to QoL in individuals with heart failure and the dynamics of peripheral muscle oxygenation in the most appropriate kinetic subjects.

Keywords: Walk test. Near-Infrared spectroscopy. Quality of life.

#### Resumo

**Objetivo:** Verificar a oxigenação muscular periférica e qualidade de vida (QV) em pacientes do sexo masculino, com insuficiência cardíaca (IC) durante teste de capacidade física submáxima.

**Métodos:** Estudo transversal, em indivíduos com IC, classe funcional II ou III, fração de ejeção do ventrículo esquerdo <45%, divididos em grupo sedentário (GS) e grupo reabilitação cardiovascular (GRC). A QV foi avaliada pelo *Minnesota Living with Heart Failure Questionnaire, a* oxigenação muscular por espectroscopia no infravermelho próximo antes, durante e após o teste de caminhada de seis minutos. Foram utilizados testes estatísticos inferenciais com nível de significância foi de 5%, de acordo com teste de normalidade. A análise de correlação foi feita através do teste de Spearman.

**Resultados:** Houve correlação inversamente proporcional entre aspectos físicos da QV e oxihemoglobina no grupo GS. A distância percorrida foi maior para o GRC. Notamos um aumento significativo no pós-teste de oxiemoglobina para o CRG.

**Conclusões:** As medidas de oxigênio correlacionam-se com aspectos físicos relacionados à QV em indivíduos com insuficiência cardíaca e a dinâmica da oxigenação muscular periférica nos sujeitos ativos apresentou cinética mais adequada.

**Descritores:** Teste de caminhada. Espectroscopia de luz próxima ao infravermelho. Qualidade de vida.

## Cite como

Vancouver

Gonzáles, AI, Lima, DP, Fontes, YGS, Sonza, AS, Carvalho, T. Muscle oxygenation, physical capacity, and quality of life in male heart failure patients. *Conscientiae Saúde* 2024;23(1):1-17, e26178. https://doi.org/10.5585/23.2024.26178





#### Introduction

Heart failure (HF) is clinically characterized by the presence of fatigue, dyspnea, and reduced physical exertion tolerance. These manifestations contribute to reduced physical capacity and lower quality of life (QoL)<sup>1,2,3</sup>.

During exercise, there is an increase in energy expenditure with a greater oxygen supply  $(O_2)$  so that the metabolic reactions take place properly to meet the demand. The  $O_2$  availability is partly decreased by a reduction in cardiac output and endothelial dysfunction<sup>4</sup>.

Additionally, the peripheral musculature undergoes morphological and metabolic changes that interfere with the response to exercise, contributing to reducing physical capacity<sup>5,6,7</sup>. In this context, it seems peripheral muscle oxygenation is a relevant measure for understanding the relationship between the supply and use of  $O_2$  during exercise and detecting possible flaws that may be reflected in muscle metabolism<sup>8,9</sup>.

The peripheral muscle oxygenation being measured during a submaximal physical capacity test, of simple applicability, widely used in clinical practice, can help in the evaluation of clinical stability, and the prognosis of patients with functional limitations, such as in HF<sup>10</sup>.

In this context, the six-minute walk test (6MWT) is characterized as a test of submaximal functional capacity, capable of reproducing the activities of daily living, being safe, and well-tolerated by patients with  $HF^{11,12}$ , being an important predictor of mortality and hospitalization in  $HF^{13,14}$ .

The mechanisms related to musculoskeletal changes and their role in exercise intolerance in HF are still unclear in the literature. Thus, the objective of the present study was to verify peripheral muscle oxygenation in male sedentary heart failure participants and others in a cardiovascular rehabilitation program during the performance of a submaximal physical capacity test and the interaction of these measures with the physical aspects that interfere in the quality of life of these subjects.

## Methods

It is a cross-sectional observational study carried out with male subjects diagnosed with HF, clinically stable and optimized concerning pharmacological treatment, recruited from cardiac rehabilitation centers in Brazil. Participants in functional classes II or III of the New York Heart Association (NYHA), previously determined in the cardiological diagnosis, were included, with impaired left ventricular systolic function and left ventricular ejection fraction





(LVEF) <45% by echocardiogram. For this study, patients were divided into two groups, the sedentary group (SG), formed by those who had been sedentary for at least three months before the evaluations, who were referred by a cardiologist to start a cardiac rehabilitation program and without the practice of any regular physical exercise; and the cardiac rehabilitation group (CRG), formed by patients participating in cardiac rehabilitation programs, having performed a minimum of 24 exercise sessions within the program. An intentional non-probabilistic sample was used.

Subjects clinically decompensated, with an inability to understand the applied tests, neurological diseases, and orthopedic changes were excluded.

This study was approved by the Research Ethics Committee on Human Beings at the University of the State of Santa Catarina (UDESC), registered with number 2,073,548 respecting the declaration of the Helsinki Statement of Ethics and Principles. All subjects who voluntarily agreed to participate in the research and signed the free and informed consent form were submitted for data collection.

The patients were assessed for anthropometric measurements, the Minnesota Living with Heart Failure Questionnaire (MLHFQ), and peripheral muscle oxygenation during a submaximal test (6MWT).

The anthropometric assessment was performed using a stadiometer (210Wiso, Brazil) to verify the height (cm) and a digital scale (Balmak, BK-200F, Brazil) to verify body mass (kg) for later calculation of the body mass index (BMI).

The MLHFQ, translated into the Portuguese version<sup>15</sup>, was used to assess the patients' perceptions of the physical and psychological aspects of QoL in HF. The total score can vary from 0 to 105, with the lowest scores reflecting the best QoL. The items are subdivided into three domains (dimensions): physical aspects, emotional and general aspects. For the present study, we chose to use only the physical aspects (PA) domain to show the relationship between these aspects and the peripheral muscle oxygenation variables.

The 6MWT was performed according to the American Thoracic Society's Six-Minute Walk Test Guideline<sup>13,16</sup>. The test was performed on a 30-meter flat track. Two tests were performed on the same day and a minimum interval of 30 min was allowed between them or until the physiological and symptoms variables returned to baseline levels. Information related to the distance covered was recorded. The assessment of peripheral muscle oxygenation was performed continuously, before, during, and after the 6MWT.

The measurement of muscle oxygenation was performed employing near-infrared spectroscopy (NIRS) (Portamon, Artinis®, Netherlands). For this, the equipment was





positioned in the vastus lateralis muscle of the patient's right quadriceps, according to the norms of the SENIAM project (Surface Electro MyoGraphy for the Non-Invasive Assessment of Muscles).

The optode was wrapped in a film roll to avoid direct contact with the skin and sweat. The trichotomy procedure was performed previously in the area of interest if necessary.

Then, the sensor was wrapped in a small black cloth to prevent the penetration of light close to the sensor. A neoprene band was used to keep the equipment in the same position during data collection.

In total, 10 minutes of information related to each subject were collected at 10 Hz, this time divided into a) pre-test - corresponding to the first two minutes before starting the 6MWT (one minute with the subject seated and another minute in the standing position) at rest; b) during the 6MWT (six minutes of testing); c) and in the post-test, with one minute with the patient in the standing position at rest after completing the 6MWT and one minute seated.

#### Statistical analysis

The data were tabulated and analyzed using the Statistical Package for the Social Sciences (IBM, SPSS version 20.0, USA). Data normality was analyzed using Shapiro-Wilk's normality test. Continuous variables were expressed in mean  $\pm$  standard deviation values or median and interquartile ranges according to data distribution and categorical variables were expressed through absolute and relative frequencies.

The values of Tissue Saturation Index (TSI%), Oxyhemoglobin (O<sub>2</sub>Hb), Deoxyhemoglobin (HHb), and Total Hemoglobin (tHb) were treated using the moving average technique with an interval of 5 seconds, resulting in 12 data per minute of the test. The Student's t-test was used for comparison between groups. The correlation analysis was performed through the Spearman correlation test. Friedmann's ANOVA test was used to analyze repeated measures. For comparisons between means of independent samples, the Mann-Whitney U test was used, with a significance level of 5%.

#### Results

The study sample consisted of 27 men with a clinical diagnosis of HF. The characterization of the general sample of the study participants can be seen in Table 1.





# Table 1 - Sample characterization and baseline values of peripheral muscle oxygenation of the vastus lateralis muscle at rest, general (n=27) and divided into sedentary groups (n=16) and cardiac rehabilitation participants (n=11)

Variables	SG (n=16) CRG (n=11)		Overall (n=27)	
	Mean (SD)	Mean (SD)	Mean (SD)	р
Age (years)	64.06 (±5.57)	60(±5.89)	63.29 (±6.81)	0,06
BMI (Kg/m <sup>2</sup> )	28.51 (±4.49)	26.44 (±3.58)	27.64 (±4.18)	0,28
Distance on the 6MWT (m)	421.56 (72.24)	531.35 (±82.25)	421.66 (±74.77)	0,00
They reached the predicted 6MWT <sup>1</sup> (%)	31% (4)	25% (3)	11.1 % (3)	
LVEF (%)	32.87 (±5.47)	38.20 (±3.22)	35.33 (±5.83)	0,53
Minnesota Living with Heart Failure Questionnaire (MHLFQ)				
Physical aspects	10.46 (±8.83)	9.00 (±7.86)	9.81 (±8.29)	0,56
Emotional Aspects	5.80 (±4.95)	3.35 (3.01)	4.88 (±4.26)	0,54
General aspects	8.73 (±7.50)	9.41 (±7.03)	9.03 (±7.17)	0,99
Total score	25.00 (±19.31)	22.16 (±14.16)	23.74 (±16.96)	0,62
	Median (IQR)	Median (IQR)	Median (IQR)	
Peripheral Muscle Oxygenation				
O <sub>2</sub> Hb (µmol/l)	0,27(-1,5/3,9)	1,60(-2,33/5,84)	1,46(-2,19/10,40)	
HHb (µmol/l)	2,47(0,19/5,78)	4,88(1,59/9,75)	4,22(2,25/12,06)	
tHb (µmol/l )	3,52(-1,05/9,46)	6,67(0,64/14,21)	5,69(-2,45/11,12)	
TSI (%)	68,89(65,62/73,91)	69,56(66,92/71,36)	69,48(60,78/73,89)	
-	% (n)	% (n)	% (n)	
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Functional Class (NYHA)				
П	46.2 (6)	77.8 (7)	59.1 (13)	
II III				
II III Associated Diseases	46.2 (6) 53.8 (7)	77.8 (7) 22.2 (2)	59.1 (13) 40.9 (9)	
II III Associated Diseases SAH	46.2 (6) 53.8 (7) 100 (16)	77.8 (7) 22.2 (2) 100 (11)	59.1 (13) 40.9 (9) 100 (27)	
II III Associated Diseases	46.2 (6) 53.8 (7)	77.8 (7) 22.2 (2)	59.1 (13) 40.9 (9)	

**Legend:** SD – standard deviation; IQR – interquartile range; SG – sedentary group; CRG – Cardiac Rehabilitation Group; TSI – tissue saturation index; kg/m<sup>2</sup> - kilograms per square meter; BMI – body mass index; LVEF - left ventricular ejection fraction; 6MWT – six-minute walk test; O<sub>2</sub>Hb: Oxyhemoglobin; HHb: Deoxyhemoglobin, tHb: Total Hemoglobin; SAH: Systemic Arterial Hypertension, DM: Diabetes Mellitus, DAOP: Peripheral Obstructive Arterial Disease; NYHA – New York Heart Association;  $\mu$ mol/l - Micromol per liter; <sup>1</sup> – Britto et al., 2013; \* t Student test.

Sourche: research data

Samples were considered homogeneous with no significant difference between groups for the variables age, BMI, and LVEF.

In Table 1, the results between the groups showed that the means of the different domains regarding MHLFQ and the total score did not present a difference between the groups. However, the PA domain presented the highest mean value in the SG. As for the total score, both groups had a mean value below 26 points, indicating good QoL.





	SG (n=16)	CRG (n=11)
Variables	PA Domain	PA Domain
Distance on the 6MWT (m)	p=0,99/R=0,00	p=0,26/R= -0,36
Baseline	PA Domain	PA Domain
O2Hb (µmol/l)	p=0,12/R=-0,43	_
HHb (µmol/l)	p=0,71/R=0,10	-
tHB (µmol/l)	P=0,27/R=-0,31	p = 0,01, R = 0,70
TSI (%)	p=0,43/R=0,22	-
6MWT (3 <sup>rd</sup> and 6 <sup>th</sup> min)	The 6MWT (m)	The 6MWT (m)
O2Hb 3 <sup>rd</sup> (µmol/l)	p = 0.02, R = -0.58	-
O2Hb 6 <sup>th</sup> (µmol/l)	p = 0.00, R = -0.73	-

#### Table 2 - Correlation Analysis between SG and CRG groups

**Legend**: SG – sedentary group; CRG – Cardiac Rehabilitation Group; TSI – tissue saturation index; 6MWT – six-minute walk test; O<sub>2</sub>Hb: Oxyhemoglobin; HHb: Deoxyhemoglobin, tHb: Total Hemoglobin; PA Domain - Physical aspects;  $\mu$ mol/l - Micromol per liter; m – meters; Spearman correlation test. **Sourche:** research data.

No correlations were found between the PA domain score and the distance covered on the 6MWT in both groups. For peripheral muscle oxygenation variables at baseline, in the SG, there were no correlations between the PA domain and the pre-test (baseline) for the O<sub>2</sub>Hb, HHb, tHB, TSI. In the evaluation during the 6MWT' for the SG, there was a moderate and inversely proportional correlation between the PA domain and O<sub>2</sub>Hb measurements in the third minute and sixth minute of the test. No correlations were identified between the PA domain and O<sub>2</sub>Hb in the CRG in no time.

The HHb measurements showed no correlations with the PA domain for the SG group during the 6MWT'. In the CRG, the pre-test HHt values correlated strongly and directly proportional with the PA domain.

Regarding the TSI% results, both groups presented means above 60%, and no correlations were found between TSI% before, after, and during the 6MWT' with the PA domain.

The performance in the 6-minute walk test (6MWT) showed that only 11.1% of the total number of subjects reached the distance predicted by Britto's formula (2013), all belonging to CRG. The average distance covered for the SG and CRG groups was 421.56 and 531.35,





Gonzáles, AI, Lima, DP, Fontes, YGS, Sonza, AS, Carvalho, T. Peripheral Muscle Oxygenation in Heart Failure/Oxigenação Muscular Periférica na Insuficiência Cardíaca

respectively. In addition, there was a significant difference in the mean value in meters between the groups, which was higher in the CRG (p < 0.05).

Table 3 shows the peripheral muscle oxygenation variables for all subjects, as well as divided into groups. The variables  $\Delta O_2$ Hb,  $\Delta$ HHb,

and  $\Delta tHb$  were used to quantify the variation of the values obtained at each minute and post-test, using the pre-test values as a reference.

 Table 3 - Values of the variables of Tissue Saturation Index, Oxyhemoglobin, Deoxyhemoglobin, Total Hemoglobin in the overall sample and the sample was divided into 3 moments, before, during, and after the 6MWT' represented at one-minute intervals and comparison of these variables during the 6MWT in relation to the resting position

Pre-Test			Six Minute Walk Test				Post-Test	
Variables	Orthostatic Position	M1	M2	M3	M4	M5	M6	<b>Orthostatic Position</b>
				Sedentary Group (n	=14)			
O <sub>2</sub> Hb (μmol/l)	0,27(-1,5/3,9)	-10,92(-16,17/-8,99) <sup>†</sup>	-12,04(-14,13/-9,71) <sup>†</sup>	-11,59(-14,68/-9,37) <sup>†</sup>	-11,63(-14,81/-8,20) <sup>†</sup>	-10,82(-14,36/-7,67) <sup>†</sup>	-10,38(-13,34/-6,76)	0,42(-3,58/6,04) <sup>†</sup>
HHb (µmol/l)	2,47(0,19/5,78)	-2,32(-5,46/-1,45) <sup>†</sup>	-1,65(-4,62/0,73) <sup>†</sup>	-1,53(-4,51/0,79) <sup>†</sup>	-1,90(-4,76/1,74) <sup>†</sup>	-1,93(-4,81/2,08)	-1,09(-4,48/2,74)	3,51(-1,33/6,22)
tHb (µmol/l)	3,52(-1,05/9,46)	-14,81(-17,69/-11,25)†	-14,91(-16,87/-11,52)†	-14,96(-16,94/-10,83)†	-12,12(-13,39/-5,27) <sup>†</sup>	-13,33(-16,14/-8,61)	-11.93(-14,35/-7,49)	1,69(-8,90/4,42)
TSI (%)	68,89(65,62/73,91)	64,82(63,02/69,73)	61,20(59,89/67,42)	61,51(50,14/69,68)	61,68(48,82/69,87)	62,53(60,01/67,85)	61,73(48,32/69,00)	68,53(65,05/71,16)
			C	ardiac Rehabilitation Gro	oup (n=11)			
O <sup>2</sup> Hb(µmol/l)	1,60(-2,33/5,84)	-12.49(-13,93/-10,08)†	-12.85(-14,88/-10,24) <sup>†</sup>	-11,30(-14,59/-8,85) <sup>†</sup>	-10,15(-13,57/-7,98)†	-9,61(-12,62/-6,51)	-9,80(-11,55/-5,65)	5,38(1,99/9,56) <sup>†</sup>
HHb (µmol/l)	4,88(1,59/9,75)	-4,65(-8,14/-0,56)†	-2,95(-7,21/0,61)†	-3,33(-7,18/0,90) <sup>†</sup>	-3,39(-7,70/0,31)†	-3,02(-7,81/0,43)	-3,28(-8,35/-0,89)	2,41(-1,15/6,37)
tHb (µmol/l)	6,67(0,64/14,21)	-16,51(-10,50/-12,22)*	-16,50(-16,87/-11,52) <sup>†</sup>	-14,59(-18,92/-10,75) <sup>†</sup>	-11,30(-9,98/9,89)*	-12,13(-17,62/-8,90)	-14,42(-17,67/-8,09)	-3,16(-9,55/7,49)
TSI (%)	69,56(66,92/71,36)	67,69(65,09/72,32)	65,51(61,65/69,92)	65,87(61,30/69,81)	65,86(61,53/69,96)	66,52(62,08/70,99)	66,78(62,86/71,62)	69,08(66,22/72,33)
				Overall Sample (n=	25)			
O <sup>2</sup> Hb	1,46(-2,19/10,40)	-10,40(-14,41/-13,45)	-10,41(-12,40/-14,50)	-10,41(-13,36/-15,35)	-10,41(-12,79/-14,25)	-9,07(-11,36/-14,35)	-8,18(-13,13/-9,89)	4,73(-7,09/11,20)
(µmol/l)								
HHb (µmol/l)	4,22(2,25/12,06)	-3,05(-8,40/-0,55)	1,47(-7,16/1,71)	1,77(-6,31/1,46)	1,67(-4,83/1,60)	1,75(-4,49/2,34)	1,87(-4,37/2,32)	3,50(-4,49/7,89)
tHb (µmol/l)	5,69(-2,45/11,12)	-9,65(-18,98/-12,10)	-9,27(-7,27/-14,71)	-8,63(-17,32/-10,85)	-8,23(-11,30/-14,36)	-10,32(-15,48/-8,45)	-12,31(-16,32/9,89)	4,27(-1,46/6,49)
TSI (%)	69,48(60,78/73,89)	67,45(54,81/77,84)	64,64(53,93/74,29)	62,42(61,30/74,99)	62,30(61,80/74,95)	65,18(50,94/75,07)	62,62(61,20/75,93)	68,69(59,84/77,65)

Legend: Data in Median/interquartile range; M – moment of the six-minute walk test, being M1: minute 1, M2: minute 2 up to the sixth minute; TSI% - Tissue Saturation Index; O2Hb – Oxyhemoglobin; HHb – Deoxyhemoglobin; tHb - Total Hemoglobin;  $\mu$ mol/1 - Micromol per liter; 6MWT – Six-minute walk test; Delta values were expressed for variables O2Hb, HHb, and tHb for M1, M2, M3, M4, M5, M6, and post-test, and expressed as median and interquartile range. †p <0.05: intra-group comparison between pre-test M1, M2, M3, M4, M5, M6, and post-test – Friedman ANOVA test.. Sourche: Research data.

Conscientiae Saúde, 2024 jan./dez.;23(1):1-17, e26178





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When comparing the means of the peripheral muscle oxygenation variables between the groups, we verified the post-test variable  $\Delta O_2$ Hb was higher for the CRG (p = 0.03).

Regarding the O2Hb values, we found worse pre-test and post-test values in the SG compared to the CRG and when comparing the means of the  $\Delta$ O2Hb post-test between the groups, we verified values higher for the CRG (p = 0.03).

Furthermore, when comparing the values of the  $\Delta$ O2Hb obtained during the 6MWT, a significant reduction was observed for the SG at moments M1, M2, M3, M4, and M5 and moments M1, M2, M3, and M4 for the CRG.

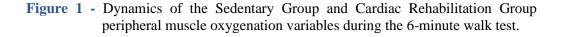
When analyzing the  $\Delta$ HHb values, it can be seen in Table 2 that there was no significant difference in the results obtained during the 6MWT to the pre-test moment in the SG. As for the CRG, there was a significant reduction between the pre-test moment and the sixth minute of the 6MWT (M6).

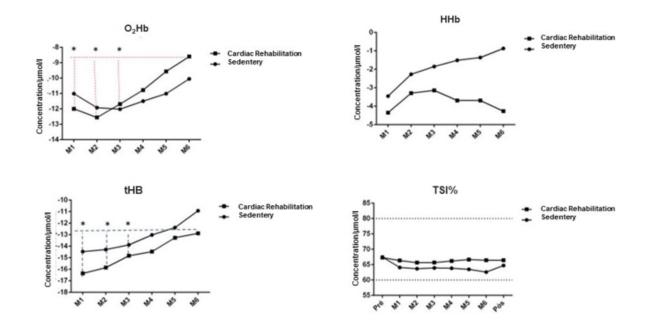
The results of  $\Delta$ tHb showed a significant difference between the pre-test values and minutes one, two, three, and four of the 6MWT (M1, M2, M3, M4) in both groups.

Table 2 shows that the TSI values (%) of the SG and CRG groups in the pre-test showed similar values. When analyzing the post-test values, it was noticed that the SG presented worse values than those obtained by the CRG, although without significant differences. There was no significant difference between pre-test values and minutes during the 6MWT in both groups for this variable.









**Legend:** O<sub>2</sub>Hb: Oxyhemoglobin; HHb: Deoxyhemoglobin, tHb: Total Hemoglobin; TSI - Tissue Saturation Index; M – the moment of the test, where M1: minute 1, M2: minute 2 to the sixth minute; %: percentual -. Delta values were expressed for the variables HbO2, HHb, tHb, and IST. \*p <0.05: Comparison between groups - Mann-Whitney U test.

Figure 1 presents the O<sub>2</sub>Hb, HHb, tHb deltas, and TSI% during the 6MWT and its minute-by-minute analysis.

Regarding the variable  $O_2Hb$ , in both groups, there was a similar behavior with a tendency for its values to decrease from the first (M1) to the second minute (M2) of the 6MWT, with a reduction in the purchase of oxygen. Additionally, it is interesting to note that this trend was maintained until the third minute (M3) of testing in the SG, where the moment of inversion of the curve begins, maintaining a pattern of elevation of O2 extraction, which is maintained until the sixth minute (M6) of the test, but without significant difference between the minutes.

In the CRG, the increase in  $O_2Hb$  started from the second minute (M2) of the test, showing a linear tendency to increase until the sixth minute (M6) of the test, with a significant difference between the first, second, and third minutes versus the sixth minute of the test (M1, M2, and M3 *vs*. M6).

For the variable HHb, we found an increase in both groups from the first (M1) to the second minute (M2) of the test, which remained milder from the second to the third minute.





After the third minute (M3) of the 6MWT, it is observed that in the SG, the upward trend is maintained until the last minute (M6). In the CRG, there is a decrease from the third to the fourth minute (M4), which is repeated from the fifth to the sixth minute (M6). However, no significant differences were found between test minutes in both groups.

For the tHb results, there is a tendency for their values to increase from the first to the sixth minute of testing in both groups. However, only in the CRG, there was a significant increase between minutes 1, 2, and 3 versus the sixth minute (M1, M2, M3 *vs*. M6).

When the TSI% values were verified during the 6MWT, there was a greater decrease in the standing position for the first minute of the test in the SG, which remained stable until the fifth minute, demonstrating another decrease from the fifth to the sixth minute. In the CRG, there is a stabilization of the TSI% from the first to the fourth minute (M4) of the test, with a slight increase from the fourth to the fifth minute (M5) and a new stabilization until the end of the test. In both groups, the TSI% values during the 6MWT remained above 60%, and even though the SG had lower values in the test, there was no significant difference between the groups.

#### Discussion

In individuals with HF, abnormalities in skeletal muscle metabolism are evidenced by reduced mitochondrial components and functions, reduced amount of type I muscle fibers, and impaired ability to increase cardiac output immediately during exercise when compared to healthy individuals<sup>17,18</sup>.

Given these factors, the speed of metabolic processes in these patients occurs more slowly, resulting in an impaired response to physical exercise and contributing to exercise intolerance, limitation of physical activities<sup>9,19,20</sup>, and affecting the QoL of these patients<sup>21</sup>. In this sense, physical training can induce important adaptations in the skeletal muscle, including an increase in the number of mitochondria, in the respiratory capacity of muscle fibers, an increase in capillary supply, and a reduction in sympathetic nervous activity<sup>22,23,24</sup>.

Quality of life refers to a discrepancy between satisfaction or dissatisfaction in certain areas of life, according to the individual's perception<sup>15,25</sup>. The "physical aspects" (PA) domain of the Minnesota Living with Heart Failure Questionnaire quality of life questionnaire refers to how much HF limits physical activities, including activities of daily living<sup>15</sup>. This measure can be used as a clinical parameter in assessing physical limitations perceived by patients due to the impact of the disease on their QoL.





In our findings, the PA domain showed no difference between male HF with a sedentary lifestyle and in cardiac rehabilitation. Likewise, it did not correlate with performance on the 6MWT. These results differ from those found in the study by Nogueira et al  $(2010)^{26}$ , who found a correlation, albeit weak, inversely proportional, between the distance covered and the QoL in individuals with HF assessed by MLHFQ. However, the results cannot be compared, as this study used the total QoL score and did not mention whether or not the patients underwent cardiac rehabilitation at the time of evaluation. In the study by Ulbrich et al.  $(2013)^{25}$ , there was no correlation between the distance covered in the 6MWT and the PA domain in newcomers and participants of a cardiac rehabilitation program with HF. These data corroborate the present study.

In Santos, J.J. et al., (2009) study, they found correlations between functional capacity and the PA domain in patients with HF. However, the functional capacity was assessed using cardiopulmonary tests <sup>27</sup>, not allowing comparison with our findings.

Performance on the 6-minute walk test in patients with HF has been associated with the degree of disease impairment, where values less than or equal to 300 meters indicate a worse prognosis for these individuals compared to patients who walk more than 300 meters<sup>28,29,30</sup>. In both groups, the individuals remained with a mean value of the distance covered above 300 meters. However, there was a difference in the values obtained between the SG and CRG, being significantly greater for the CRG. Studies indicate that cardiac rehabilitation represents an effective strategy in the treatment of patients with HF, with significant improvement in clinical symptoms, including functional capacity and performance results <sup>24,31,32, 33</sup>, which corroborates our findings.

Near-infrared spectroscopy (NIRS) was used to assess the muscle oxygenation and deoxygenation variables in patients with HF, during the performance of a submaximal walk test. Most of the studies that proposed to analyze such results, performed evaluations during exercise tests of the maximum incremental type<sup>34,35,36</sup>.

In our study, the pre-test measurements of peripheral muscle oxygenation in male HF  $(O_2Hb, HHb, tHb, and TSI\%)$  did not differ between the groups at the pretest moment. The TSI% values remained above 60%, being higher than the minimum value considered for healthy individuals<sup>22</sup>. To the best of our knowledge, there are no studies that have established cut-off points for peripheral muscle oxygenation variables in patients with HF, which makes comparisons difficult given our results.

However, we found that in sedentary male individuals with HF, the O<sub>2</sub>Hb values present worse O<sub>2</sub> extraction from the second minute of the submaximal test, with a significant reduction

from the first to the fifth minute of the submaximal test concerning the values presented in the pre-test. In the CRG subjects, this reduction occurred from the first to the fourth minute, also significantly, but with higher  $O_2$  extraction values compared to the SG. Such results may demonstrate that men with HF present alterations in the peripheral muscle oxygenation mechanism, and those who practice cardiac rehabilitation may present better results in  $O_2$  extraction when submitted to submaximal exercises with better stabilization.

In parallel with the HHb values, there was an increase throughout the SG test, but without significant differences to the pre-test moment. On the other hand, in the CRG, the HHb values increased until the third minute, followed by a reduction from the fourth minute of exercise, with a significant difference in the HHb in the sixth minute concerning the baseline values. Although the results for HHb did not show a significant difference between the groups, these findings may demonstrate a smaller drop and variation in blood volume during submaximal exercise in individuals with HF who practice cardiac rehabilitation.

Although there are no studies to date that have verified this variable in male patients with HF undergoing submaximal exercise, in the study of Barroco et al. (2017) during an incremental exercise protocol, the group composed of healthy individuals showed a decline in HHb values near the end of the exercise. In contrast, male patients with HF systematically increased HHb levels correlating it with a lower rate of work. The authors interpret these results as evidence of faster and greater  $O_2$  extraction to compensate for the deficiency of the diffusive and convective  $O^2$  flow to the muscle fibers<sup>34</sup>.

As for the tissue saturation index (TSI%), the results of this study were similar between the groups at the pre-test moment. However, during submaximal exercise, lower values were observed in the SG in relation to the CRG, but no differences were found between baseline values and each minute of the 6MWT. In addition, no differences were found in the TSI% values at rest and minute-by-minute between groups. In patients with HF, studies report that there is a delay in the muscle oxygenation kinetics (TSI%) when compared to healthy subjects in moderate exercise<sup>37</sup>. However, as there are no studies performed with submaximal tests in this population, our findings cannot be compared.

Regarding the peripheral muscle oxygenation values immediately after the test (recovery), we found that the muscle oxygenation variables did not reach baseline values in both groups. However, we found higher O<sub>2</sub>Hb after exercise in the CRG compared to the SG, demonstrating a possible better recovery in the HF male patients in cardiac rehabilitation.



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#### Limitations

Even though this study presents originality, and its findings demonstrated a correlation between measurements of peripheral muscle oxygenation and quality of life in male individuals with HF, as well as a more adequate dynamic of this oxygenation in the submaximal test in patients in the group practicing cardiovascular rehabilitation, some limitations must be recognized. First, we investigated a relatively small sample size, which may still produce inconclusive results. A larger sample size would allow for better generalization.

Although our results are promising and the 6MWT is a widely used submaximal physical capacity test to evaluate individuals with HF, most studies carried out to date to observe peripheral muscle oxygenation in patients with HF are performed on maximal exercise tests, limiting comparisons with other studies.

Also, the sample was composed only of male individuals, which does not permit extrapolation of data to female patients with HF. Finally, a larger number of individuals may allow for a more robust analysis of the results.

Whereas the characteristics of the present study do not grant us to establish generalized relationships, we believe that the available information constitutes an original contribution, taking into account that there are no articles in the literature that have carried out this type of assessment. However, more studies are needed to address the points raised.

## Conclusion

This study showed that peripheral muscle oxygen measurements through a submaximal 6 min walking test are correlated with physical aspects related to the quality of life in male individuals with HF. In addition, they allowed to verify the dynamics of peripheral muscle oxygen during the submaximal test, where the cardiac rehabilitation program participants evaluated presented better kinetic results during the test when compared to the sedentary ones. This indicates a possible interaction between the central and peripheral components involved, being innovative and safe to be used in the evaluation of male patients with HF.





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