

Upper and lower limb muscles in patients with COPD: similarities in muscle efficiency but differences in fatigue resistance

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Abstract

Background: Peripheral muscle dysfunction is a common finding in patients with chronic obstructive pulmonary disease (COPD); however, the structural adaptation and functional impairment of the upper and lower limb muscles do not seem to be homogenous. **Objective:** To compare muscle fatigue and recovery time between two representative muscles of the upper limb (middle deltoid, MD) and lower limb (quadriceps femoris, QF). **Methods:** Twenty-one patients with COPD (with forced expiratory volume in 1 s of $46.1 \pm 10.3\%$ predicted) underwent maximal voluntary isometric contraction (MVIC) and an endurance test (ET, 60% MIVC) to the limit of tolerance. The MVIC was repeated after 10 minutes, 30 minutes, 60 minutes and 24 hours for both the QF and MD. Surface electromyography was recorded throughout the ET. **Results:** A significant fall in MVIC was observed only for the MD between ten and sixty minutes after the ET. A significant increase of the root mean square and a greater decline in median frequency throughout the ET occurred for the MD compared with the QF. When dyspnea and fatigue scores were corrected by endurance time, higher values were observed for MD (0.07 and 0.08, respectively) in relation to QF (0.02 and 0.03, respectively). **Conclusion:** Patients with COPD presented a higher fatigability of a representative upper limb muscle (MD) compared with a lower limb muscle (QF).

Keywords: COPD; muscle fatigue; electromyography; upper limbs; lower limbs

Introduction

It is well established that patients with chronic obstructive pulmonary disease (COPD) present impaired skeletal muscle function, which plays a role in reducing exercise tolerance¹. Although the impairment of lower limb (LL) muscles are largely responsible for limitations in activities such as walking and climbing stairs, it is known that activities of daily living (ADL) performed with upper limbs (UL), especially unsupported, are also poorly tolerated by patients with COPD².

Although reduced skeletal muscle function has been reported in both the lower limbs and the shoulder girdle muscles of patients with COPD, it has been speculated that the metabolic and structural adaptations differ among LL and UL muscles³. For LL, the quadriceps femoris (QF) is the peripheral muscle most commonly tested in COPD⁴. Abnormalities of this muscle include¹ reduced muscle mass, strength, endurance, oxidative enzymes, proportion of type I fibers, augmentation of the proportion of type II fibers, and decreased cross-sectional area of type I, IIa, and IIab fibers. These changes increase the fatigability of the QF, which has been demonstrated in both dynamic^{5,6} and isometric contractions⁷.

For UL, a variety of muscles has been studied, making it difficult to generalize UL performance results^{2,8}. Because of the finding that the isometric handgrip force is conserved in patients with COPD, some studies infer that the upper limb function is preserved⁹⁻¹¹. It appears that oxidative capacity is preserved or even increased in the deltoid muscles of patients with COPD⁹, as opposed to what is observed in lower limb muscles. One possible explanation for this difference is that patients continue to perform, to a certain extent, the ADLs that involve the upper limbs but reduce their performance of the activities that involve the lower limbs, adopting a sedentary lifestyle in order to minimize dyspnea. That finding was prevalent in patients with severe COPD.

However, patients present higher metabolic and ventilatory demand when performing activities involving unsupported arm elevation with important dyspnea¹²⁻¹⁴. In this context, the middle deltoid (MD) is directly involved in all ADLs with upper limbs, especially those that require elevation of shoulders. It is interesting to note that, unlike the QF, it seems that the MD has a multi-mode fibre distribution, i.e., normal, atrophic and hypertrophic sizes¹⁵, which could influence the development of muscle fatigue when performing ADLs with upper limbs.

Few studies have compared LL and UL muscle function^{4,16-19}. Some studies support a greater impairment of LL^{10,17,19} in relation to the UL muscles, as patients reduce physical activities in daily life using the LL²⁰, thus preserving UL activities. On the other hand, studies have shown that the muscle impairment between the upper and lower limbs muscles is similar¹⁸, with comparable mechanical efficiency¹⁷.

Due to ongoing controversy about the muscle impairment distribution between LL and UL, this study was undertaken (1) to contrast the muscle fatigue between two representative muscles of the lower (QF) and upper (middle deltoid, MD) limbs by analyzing electromyographic changes at equivalent workloads and (2) to compare the recovery time of muscle fatigue.

Material and methods

We studied 21 consecutive patients from the outpatient clinic of Nove de Julho University. The inclusion criteria were clinical diagnosis of COPD and clinical stability (no change in medication dosage in the preceding four weeks or during the study). The exclusion criteria were presence of cardiac, orthopedic, and neurological diseases. Informed consent was obtained from all patients prior to their inclusion in the study. This study was approved by the institutional ethics committee.

Study design

This was a prospective, cross-sectional study performed in two visits (24 hours apart). The subjects were assessed at the same time of day (between 2:00 and 3:00 pm), and they were instructed to refrain from any strenuous activities in the 72h before the procedure. After study enrollment, the patients were randomized to determine the order of evaluation of the muscles (QF and MD or MD and QF). On the first visit, the patients underwent the following sequence of tests: (1) maximum voluntary isometric contraction (MVIC), (2) an isometric endurance test (60% of the MVIC) to the limit of tolerance, and (3) repetition of MVIC after 10 minutes, 30 minutes, 60 minutes and 24 hours later. Then, the other muscle was evaluated in the same sequence. At the second visit, the patients underwent MVIC of QF and MD to compare the recovery time of muscle fatigue. All measurements were made with electromyographic recording. There was a rest period of five minutes between sequences 1 and 2.

Spirometry

Spirometric tests were performed using a CPFS/D USB (Medical Graphics Corporation®, St. Paul, MN). The subjects completed at least three acceptable maximal forced expiratory maneuvers, according to acceptability and reproducibility ATS/ERS criteria²¹. The following variables were recorded: FVC, FEV₁, and FEV₁/FVC. The data were expressed in absolute values and in predicted percentage²².

Skeletal muscle function assessment

The strength of the QF was obtained on the dominant leg by MVIC. This measurement was taken with the subject seated on a leg extension chair (Carci®, São Paulo, Brazil) at 60° knee flexion. A non-elastic strap connected the ankle to a load cell

(EMG System model EMG800C, São José dos Campos, Brazil) that was interfaced to a computer for MVIC recording. A strap was also placed across the patient's pelvis to minimize hip movement during the tests. The patients performed three repetitions of MVIC of the knee extensors, each one maintained for 5s, with a minute of rest between them. The highest value from the three reproducible contractions (<5% variability among attempts) was considered for analysis²³.

After a rest period of 5 min, endurance of the QF was evaluated by the isometric endurance test, at 60% of the MVIC, to the limit of tolerance (Tlim)²³. A visual reference mark corresponding to the submaximal workload was shown on a computer screen in front of the subject for visual feedback. In addition, during whole test verbal encouragement was given for the patient maintain contraction as long as possible. The isometric endurance test stopped when a 20% drop of the produced force occurred.

The MVIC of the MD of the dominant arm was measured with the patient seated on a chair. The shoulder was placed at 90° abduction, with the elbow extended and the palm of the hand facing up. This level of shoulder elevation was chosen because it is a common position for several ADLs performed with the UL. A load cell was attached with a strap to the wrist of the patient's dominant arm. Following the same sequence used in the QF assessment, the patients first performed three brief (5s) reproducible MVIC s of the MD, with a minute of rest between them. Again, the highest value was considered for analysis. Then, the patients sustained a submaximal isometric contraction (SIC) against 60% of the MVIC, to the Tlim. Visual feedback was provided on the computer screen during all measurements.

Scores for dyspnea and leg (QF) and arm (MD) fatigue, before and after endurance tests, were assessed by the modified Borg scale²⁴. Dyspnea and fatigue scores

were corrected for endurance time in order to adjust the perception of effort for work performed by each muscle.

Surface electromyography recording

Surface electromyography (sEMG) signals were recorded (EMG System, model EMG800C, Sao José dos Campos, Brazil) during the MVIC, SIC, and endurance tests. The sEMG signals were also recorded with a preamplifier (gain 1,000x), common mode rejection >-85 dB. The participants' skin was prepared before placement of the EMG electrodes by shaving the hair at the site of electrode placement and cleaning the skin with alcohol. Bipolar passive disposable dual Ag/AgCl snap electrodes (1cm diameter) for each circular conductive area, with 2cm center-to-center spacing, were placed over the longitudinal axes of the QF and MD in the direction of the muscle fiber, according to the SENIAM/ISEKI protocol²⁵. A ground electrode was placed on the contralateral elbow. The sampling frequency was 1000 Hz²⁶. The criterion adopted to normalize the sEMG data was the MVIC. Then, the digitized sEMG data were first band-pass filtered at 20–400 Hz, using a fourth order Butterworth filter with zero lag. For the temporal analysis, the amplitude of the sEMG signals was expressed as RMS (1s moving window) and normalized by MVIC. For the time-frequency analysis, sEMG data were analyzed with a short-time Fourier transform applied to 1s epochs. The median frequency (MF) of the spectrum for each epoch was computed, and the linear regression of the median frequencies versus time was determined. The slope of the straight line (indicating the rate of frequency change per second) was adopted as a second index of fatigue²⁷⁻²⁹. All data were analyzed using a customized program written in MATLAB (Math Works Inc., Natick, MA). The MVIC was corrected by muscle mass.

Body composition assessment

Body mass index

Body mass index (BMI) was calculated as weight/height² (kg/m²). Body weight was assessed with a beam scale to the nearest 0.1 kg, with subjects standing barefoot and in light clothing. Body height was determined to the nearest 0.1 cm with subjects standing barefoot.

Estimation of mid-arm muscle area

The mid-arm muscle area (AMA) was estimated using the following equation: $AMA = \text{mid-arm circumference, cm} - (0.314 \times \text{triceps skinfold, cm})^2 / (4 \times 3.14)^{30}$. The mid-arm circumference was measured at the midpoint of the arm, between the tip of the acromion and the olecranon process, with a steel tape with the arm relaxed and parallel to the trunk. A skinfold caliper (Lange®, Cambridge, MD) was used to measure the triceps skinfold, which was taken over the triceps muscle, halfway between the elbow and acromial process of the scapula³¹. The unit was expressed in cm².

Estimation of mid-thigh muscle area

To estimate the mid-thigh muscle area (TMA), mid-thigh circumference (MTC) and anterior thigh skinfold (ATS) were taken midway between the inguinal crease and the top of the patella, with the patient standing with feet shoulder-width apart. The same steel tape and skinfold caliper were used as for the AMA. The TMA was obtained as follows: $TMA = \text{mid-arm thigh, cm} - (0.314 \times \text{anterior thigh skinfold, cm})^2 / (4 \times 3.14)^{32}$. The unit was expressed in cm².

Statistical analysis

Based on the results from the five first patients, we obtained a standard deviation (SD) for MF of 8 Hz and a difference of 7 Hz between the pre- and post-endurance test. Assuming a type I error of 0.05 and a type II error of 0.2, the sample size resulted in 21 patients with COPD. The normal distribution of data was verified by the Kolmogorov–Smirnov test. The variables (age, BMI, muscle area for MD and QF, lung function, and Borg scores for dyspnea and fatigue) were expressed as mean and SD by presenting a parametric distribution. Changes in variables (MVIC, RMS, and MF) over time were analyzed by repeated-measures analysis of variance. Linear regression analysis over time was applied to rate of change of MF to obtain the slope of the regression line. The level of significance was set at $P < 0.05$.

Results

Baseline characteristics of the 21 patients (two women) are shown in Table 1. According to the GOLD criteria, most of the patients ($n = 15$) presented severe obstruction, and the six remaining patients had moderate obstruction.

Insert Table 1

Table 2 shows the variables obtained from the strength and endurance tests. MD showed reduced MVIC compared to QF ($P < 0.05$). However, no significant difference was observed when MVIC was corrected for muscle mass, but we found statistical difference for the limit of tolerance in the endurance test corrected for the maximal voluntary isometric contraction ($P < 0.05$). The submaximal workload performed by MD was lower than that of QF. Although the same MVIC percentage (60%) for the endurance test was used for both muscles, the endurance time for MD was about 40% of that performed by QF (Figure 1).

Insert Table 2

Insert Figure 1

A significant drop in MVIC was observed in MD, at 10 and 60 minutes, but not 30 min and 24h after the endurance test (Figure 2).

Insert Figure 2

Figure 3A shows a significant increase in RMS of MD compared to QF only in 25% of endurance test (% duration). Figure 3B shows a greater decline in MF throughout the endurance test for MD compared to QF.

Insert Figure 3

There was a significant difference in the slope of the MF over time between MD and QF (-3.77 ± 1.4 and -2.68 ± 1.2 , respectively; $p < 0.03$).

In relation to perceived exertion, the majority of the patients stopped the endurance test due to local muscle fatigue (MD: 18 patients and QF: 16 patients), and three patients presented higher scores of dyspnea for MD and five patients for QF. Ratings of perceived exertion for dyspnea and fatigue increased significantly for QF (from 1.3 ± 0.8 to 2.1 ± 1.2 and 1.3 ± 1.0 to 2.8 ± 1.3 , respectively) and MD (from 1.4 ± 0.9 to 2.7 ± 1.9 and 1.6 ± 1.1 to 3.2 ± 1.7 , respectively). When dyspnea and fatigue scores were corrected for endurance time, higher values of this index were observed for MD (0.07 and 0.08, respectively) compared to QF (0.02 and 0.03, respectively) ($P < 0.05$).

Discussion

This study compared fatigue between two representative muscles of the upper and lower limbs in patients with COPD. The main finding is that, despite similar muscle efficiency, muscle fatigue was evident earlier and was more pronounced in the MD.

The lower muscle strength presented by MD compared to QF was expected. Similar results have been showed for the biceps brachii (BB) in relation to QF¹⁸. Although Gosker et al¹⁸ have measured the fat free mass, muscular strength has not been corrected for muscle mass, which reflects the efficiency of muscle. In this context, in our study, the difference observed in muscle strength between MD and QF disappeared after correcting them for the respective muscle mass. Therefore, muscle efficiency was similar between MD and QF, indicating that the contractile apparatus was preserved¹⁹. Then, the difference in endurance time between MD and QF suggests that neither strength nor muscle mass would be a determinant of muscle endurance.

The reduction of muscular endurance, regardless of loss of muscle mass, in patients with COPD has been related to intrinsic muscular alterations, such as reduction of type I fibers and reduced oxidative enzyme activity¹. Consequently, there is a predominance of anaerobic metabolism, resulting in early lactate accumulation and muscle fatigue. In absolute values, the dyspnea and fatigue scores were similar at the peak of both endurance tests. However, the endurance time was lower for MD than for QF (Table 2). When corrected for the endurance time, i.e. work performed, dyspnoea and fatigue, in fact, were superior for MD compared to QF. Local muscle fatigue possibly occurred due to increased lactate production per unit of muscle mass. A possible mechanism related to dyspnea is the change in lung volume during the UL activities, characterized by decreased forced vital capacity, increased functional residual capacity, and inspiratory capacity decrease^{12,33}. In addition to the changes in lung

mechanics, it is speculated that reduction of blood flow during elevation of the UL leads to increased production of lactate, which increases ventilation demand and, consequently, dyspnea^{34,35}.

One of the most common methods used to quantify the development of muscle fatigue is the decline in maximum strength³⁶. In our study, a greater drop in strength was observed for the MD compared to the QF (Figure 1). This result is similar to that found by Gosker et al.¹⁶; however, the magnitude of the reduction in strength was lower in our study in both muscles (MD: 20.6% and QF: 10.6%) when compared to the study of Gosker et al.¹⁶ (BB: 42% and QF: 28%). The larger decline in strength observed in the study of Gosker et al.¹⁶ may be attributed to a more intense fatigue-inducing protocol (i.e., 15 sequential maximal voluntary contractions at an angular velocity of 90° s), as well as to differences in disease severity compared to our patients (FEV₁: 32 ± 11% vs. 46 ± 10%, respectively) and the fat free mass and the strength was also lower in patients than control subjects.

Several studies have evaluated QF fatigability after cycling, walking, repeated maximum voluntary contractions, and local endurance tests³⁷⁻³⁹. However, to the best of our knowledge, only our study has analyzed the recovery time of fatigue for UL after a fatigue-inducing protocol. In addition to the greater decrease in strength compared to the QF, MD presented longer recovery time of the baseline MVIC. Beyond smaller muscle mass, this finding may be explained by the dual function of the accessory respiratory muscles during unsupported arm exercise, ventilation, and postural maintenance, which can contribute to more pronounced fatigue¹⁵. Unlike that observed in the lower limb muscles, alterations in fiber-type distribution and decreased metabolic capacity do not seem to be involved in early fatigue of the upper limb muscles. This assertion is based on previous studies that demonstrated preserved or even increased

oxidative capacity⁷, as well as a concomitant presence of the normal, atrophic, and hypertrophic pattern of fibers within the MD when compare to control group¹⁵.

Although widely used for evaluation of muscle fatigue, submaximal sustained isometric contraction⁴⁰⁻⁴⁴ has the disadvantage of being dependent on motivation. However, we associate the use of electromyography during the tests which resulted in a more objective evaluation of muscle fatigue. In this context, a 4% decrease in MF has been recommended as an indirect marker of contractile fatigue evaluated by sEMG⁴⁵. Therefore, while our patients certainly presented muscle fatigue for both QF and MD, it was more pronounced in the MD, as seen in the higher slope in the MF over time (Figure 2B). This data can not be directly compared with other studies in patients with COPD because we are unable to find any study that has analyzed it. Comparing with healthy subjects⁴⁶, a more pronounced drop in the slope of the MF over time was observed in our patients (-0.67 vs. -3.77, respectively). It is worth noting that even in healthy subjects (61 ± 6 years old) performing ADL with unsupported arm elevation, Panka et al⁴⁷ found changes in breathing pattern and greater activation of the sternocleidomastoid.

This study had some limitations. Muscle fatigue was evaluated by volitional measurements (MVIC and endurance time); however, we used outcomes from sEMG in order to confirm the muscle fatigue. The results found in our study cannot be extrapolated to other body positions such as standing position. The lower and upper limb muscle mass were estimated, but the measures used in our study have traditionally been used in the literature^{30,48}. A huge variability was observed for Tlim for MD. Our patients did not undergo muscle biopsy, but previous study has identified three patterns of muscle composition of deltoid in COPD¹⁵: normal sized fibres, atrophic fibres and hypertrophic fibres. Then, we speculated that the patients who presented with higher

endurance time probably had a predominance of normal sized fibers and/or hypertrophic fibres, while those with less endurance time could have a pattern of atrophic fibers.

Currently resistance training is one of the components of the pulmonary rehabilitation program for patients with COPD. Based on our findings, we suggest that training the upper limbs in patients with COPD should be accomplished with high repetition/low resistance to increase muscular endurance. Further studies measuring pulmonary gas exchange while patients perform a fatigue-inducing protocol should be conducted to verify whether changes in electromyography outcomes reflect higher oxygen consumption, carbon dioxide production, and ventilation. In addition, studies evaluating lung volume, especially inspiratory capacity, could help to explain the increased perception of dyspnea observed in the upper limb endurance tests.

In conclusion, we have found that patients with COPD presented with higher fatigability of upper limb muscle compared to lower limb muscle with longer recovery time.

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Table 1 – Subjects characteristics.

Variables	Mean \pm SD
Age, years	70 \pm 10.2
BMI, kg/m ²	25.5 \pm 5.2
Arm muscle area, cm ²	49.7 \pm 18.9
Thigh muscle area, cm ²	128.8 \pm 32.6
FVC, L (% pred)	2.2 \pm 0.8 (68.2 \pm 16.8)
FEV ₁ , L (% pred)	1.1 \pm 0.3 (46.1 \pm 10.3)
FEV ₁ /FVC ratio, %	58.7 \pm 12.9

BMI: body mass index; FVC: forced vital capacity; FEV₁: forced expiratory volume in one second in liters and in percentage of predicted; L (% predicted): in liters and in percentage of predicted.

Table 2 – Data from tests of muscle strength and endurance.

Variables	MD	QF
MVIC (kg)	6.7 ± 2.5	16.0 ± 5.2 *
MVIC/muscle mass	0.15 ± 0.05	0.13 ± 0.05
Load of endurance test (kg)	4.0 ± 1.6	9.8 ± 3.1 *
Tlim (s)	49.6 ± 39.2	127.1 ± 76.5 *
Tlim/load endurance test (s/kg)	13 ± 9	15 ± 12 *

MVIC: maximal voluntary isometric contraction; kg: kilograms; s: seconds; Tlim: limit of tolerance of the endurance test; Tlim/MVIC: limit of tolerance of the endurance test corrected for the maximal voluntary isometric contraction *P < 0.05.

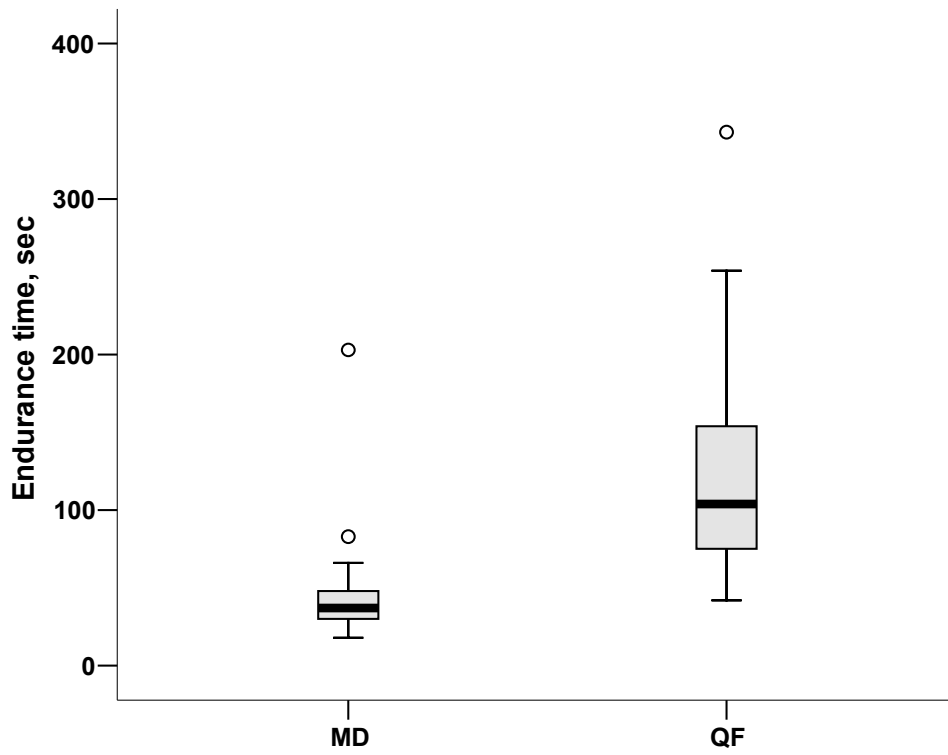


Figure 1- Endurance time for MD and QF. Open circles correspond to outliers.

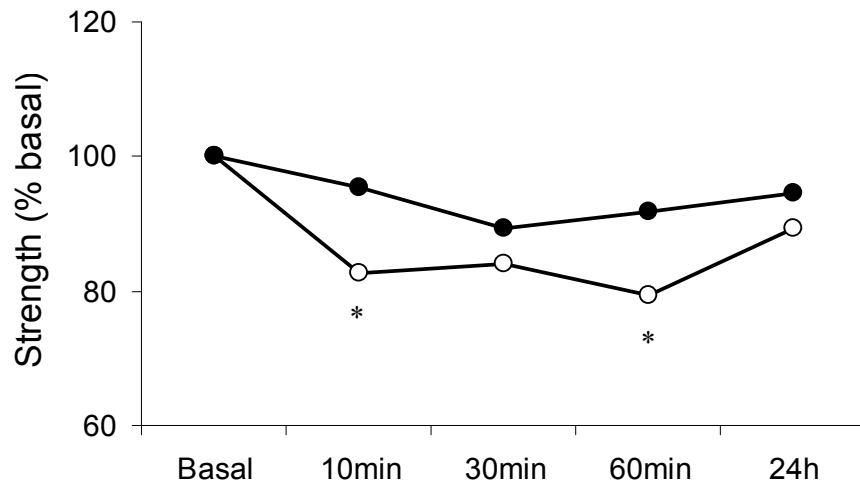


Figure 2 – Changes in MVIC for QF (solid circles) and MD (open circles). * P < 0.05 in relation to basal for MD.

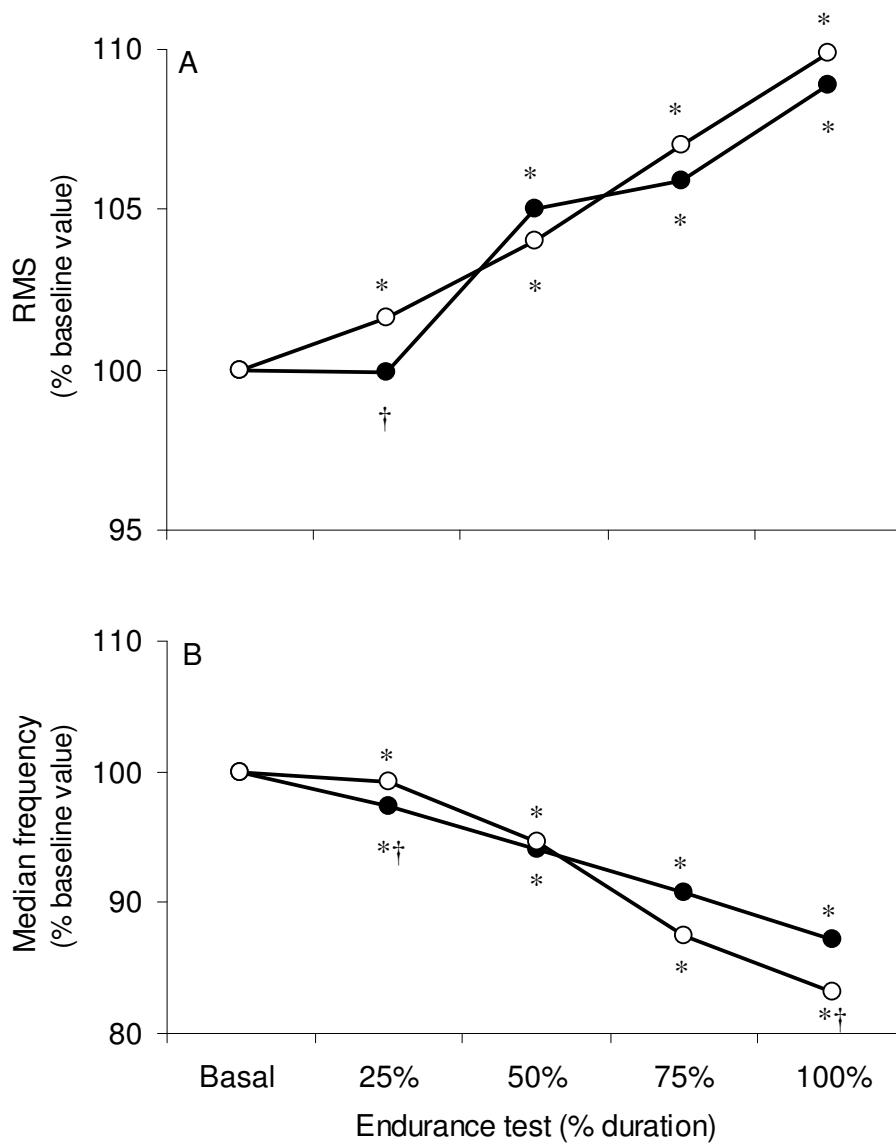


Figure 3 – Changes in RMS (A) and MF (B), expressed in percentage of baseline values, for QF (solid circles) and MD (open circles). * P < 0.05 compared to baseline values and among exercise time (% duration) for both muscles. † P < 0.05 for comparison between QF e MD.