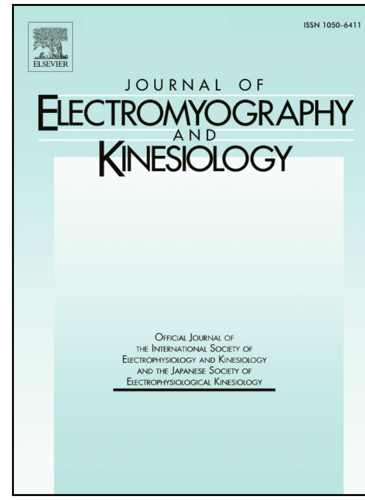


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TITLE

**Effect of exercise training on neuromuscular function of elbow flexors and knee extensors of type 2 diabetic patients**

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KEY WORDS

Type II Diabetes; Electromyography; Isokinetic strength; Muscle fatigue

ABSTRACT

PURPOSE: The effects of exercise training on neuromuscular function of arm and leg muscles in type 2 diabetic patients (T2D) was investigated.

METHODS: Eight T2D sedentary male patients (61.0±2.3 years) and eight sedentary healthy age matched control subjects (H, 63.9±3.8 years) underwent a 16-week supervised combined endurance and resistance exercise program. Before and after training, maximal isometric (MVIC), isokinetic (15, 30, 60, 120, 180, 240°$s^{-1}$) torque and muscle endurance of the elbow flexors (EF) and knee extensors (KE) were assessed. Simultaneously, surface electromyographic signals from biceps brachii (BB) and vastus lateralis (VL) muscles were recorded and muscle fiber conduction velocity (MFCV) estimated.

RESULTS: Following training, maximal torque of the KE increased during MVIC and isokinetic contractions at 15 and 30°·$s^{-1}$ in the T2D (+19.1±2.7% on average; $p<0.05$) but not in the H group (+7±0.9% $p>0.05$). MFCV recorded from the VL during MVIC and during isokinetic contractions at 15 and 30°$s^{-1}$ increased (+11.2±1.6% on average; $p<0.01$), but in the diabetic group only. Muscular endurance was lower in T2D (20.1±0.7 s) compared to H (26.9±1.3 s), with an associated increase in the MFCV slope after training in the KE muscles only.

CONCLUSION: The effect of a combined exercise training on muscle torque appears to be angular velocity-specific in diabetic individuals, with a more pronounced effect on KE muscles and at slow contraction velocities, along with an associated increase in the MFCV. MFCV appears to be a more sensitive marker than torque in detecting the early signs of neuromuscular function reconditioning.

# INTRODUCTION

Deleterious changes in muscle contractile properties (Oberbach et al. 2006) as well as degeneration of the motor nerves (Ijzerman et al., 2011) in type 2 diabetes increase the risk of physical disability (Andersen, 2012; Drouin et al., 2009), with a reduction in muscle strength, power and muscle mass being well documented in this patient population (Leenders et al., 2013; Park et al., 2006, 2009; Shah et al., 2011; Volpato et al., 2012). Recent findings suggest that these muscular deficiencies are greater in the lower than in the upper limbs. Further, the extent of diabetes-related muscle weakness is seen to be dependent on both the muscle contraction type and velocity with the greater deficits seen at the higher contraction velocities (Sacchetti et al., 2013). This trend is similar to what is observed for the decay of muscle function that occurs with aging (Bazzucchi et al. 2004). The combination of diabetes and aging may accelerate the strength decline especially in the lower limbs and compromise the quality of life of these individuals. Indeed, older men with type 2 diabetes have been found to have a two- to three-fold increased risk of developing physical disability, in which the declines in the functional capacity of the neuromuscular system is a contributor (Park et al., 2006).

The benefits of exercise training for counteracting the detrimental effect of diabetes on both glyco-metabolic control and neuromuscular function have been well reported. Resistance training in particular has been seen to improve both muscle strength and mass as well as insulin sensitivity (Brooks et al., 2007; Cauza et al., 2005; Dunstan et al., 2002; Holten et al., 2004; LeBrasseur et al., 2011; Mann et al., 2014). For these reasons, it may be desirable that type 2 diabetes patients would begin an appropriate exercise training program as soon as possible after diagnosis to prevent, or at least limit, the decline in neuromuscular function. More information, however, is needed on the effects of exercise training on the torque-angular velocity relationship, which reflects the fundamental mechanisms of force generation during different contractile tasks (Larsson et al., 1979). Similarly, muscle endurance, another important determinant of performance during functional task/activities of daily living, has been poorly explored in relation with diabetes, with the few investigations performed leading to conflicting results (Almeida et al., 2008; Andersen et al., 2005; Andersen, 1998; Fritschi & Quinn, 2010). The use of surface electromyography (EMG), a non-invasive measure of myoelectric activity, allows a greater understanding of the activation patterns of the muscle of interest. In particular, the propagation velocity of the action potential along the muscle fiber (muscle fiber conduction velocity, MFCV) is one of the physiological characteristics correlated to the derangement of neuromuscular function since it is directly related to sarcolemmal excitability/function (Merletti et al., 2003) with Sacchetti et al. (2013) reporting a decrease in the MFCV of the vastus lateralis muscle in diabetic patients during isometric contractions in comparison to healthy matched individuals.

The present study, thus, has been designed to understand to what extent qualities such as muscle strength and endurance are compromised in diabetic patients in the early phases of the disease, and whether an active lifestyle, combined with a limited number of training sessions (i.e. sustainable by all patients), is effective in preserving their neuromuscular function. Specifically, in this study a particular emphasis was paid to the characterization of the torque-velocity relationship, muscle fatigability and the myoelectric activity of diabetic individuals both pre and post training when compared to their age matched healthy counterpart.

METHODS

**Subjects**. Eight type 2 diabetic patients (T2D) and eight healthy control subjects (H) gave their informed consent to participate in the study, which was approved by the local ethics committee. All diabetic patients were treated with diet and oral hypoglycemic agents (metformin) but not insulin or other drugs, were free from clinical signs of diabetic peripheral neuropathy and had relatively short history of the diseases (mean diabetes duration of 5.2 ± 1.3 years). They were accepted for study only if they had total $HbA_{1c}$ levels <9% on therapy. Subjects' main characteristics are shown in table 1. None of the subjects were involved in a regular exercise program for at least 6 months before entering the study. All the age-matched healthy subjects had normal glucose tolerance (assessed by a 75-g oral glucose tolerance test), and none were taking any medication.

**Exercise training program.** All subjects underwent a 16-week exercise training program, designed following the ACSMs guidelines for exercise participation in individuals with type 2 diabetes (ACSM 2010). Exercise was performed 3 times weekly under the direct supervision of a sport scientist. Each session started with a warm-up consisting in 10-min low intensity endurance exercises on a cycle ergometer or a treadmill and 3 sets of 15 abdominal crunches separated by 2-min rest. The core of the training session incorporated aerobic training followed by the resistance training. Subjects rested for 4 minutes between the two modalities of training. At the end of the training, subjects performed also 10 minutes of cool down with stretching exercises. The aerobic training was performed on a treadmill or a bicycle ergometer. In order to equally distribute sessions between treadmill and bicycle ergometer, all subjects carried out 2 sessions on treadmill and 1 on bicycle ergometer in week 1 and *vice versa* 2 sessions on bicycle ergometer and 1 on treadmill in week 2. This alternation was repeated for the subsequent weeks. Participants progressed from 20 minutes per session at 40-60% of the heart rate reserve (HRR; weeks 1-8) to 40 minutes per session at 60-80% of the HRR (weeks 9-16). Heart rate monitors (Polar, Finland) were used to adjust the workload in order to achieve the target heart rate. For the resistance training, 1 repetition maximum (1-RM) was assessed twice on 5 different weight machines (leg press, leg extension, bench press, cable curl, cable pull down). The training loads were calculated with respect to the highest 1-RM value obtained at baseline and at week 9. Resistance training consisted of 3 sets of 10 repetitions at a load progressing from 60 to 80% of 1RM.

**Overview of the experimental protocol**. Each subject visited the laboratory on three occasions. In the first visit, subjects were familiarized with the experimental procedures. Participants then returned to the laboratory on two additional days, the first before the training period (PRE) and the second 5 days after the 16 weeks of training program (POST). The same experimental protocol was followed both PRE and POST. The elbow flexion (EF) and knee extension (KE) torques of the dominant limb were measured with a dynamometer (Kin-Com, Chattanooga, USA). Participants were seated comfortably on the dynamometer and stabilized by chest, waist and thigh straps. The elbow angle was fixed at 90° (180°, full extension) with the upper arm parallel to the trunk and the forearm in a neutral position (halfway between pronation and supination). The wrist was secured in a padded cuff attached to the load cell. The rotational center of the lever arm was aligned to the distal lateral epicondyle of the humerus. The knee joint was set at a 90° angle (180°, full extension) as well as the hip joint. The lower leg was attached to the lever arm of the dynamometer with the ankle secured in a resistance pad. The center of rotation of the lever arm was aligned to the lateral femoral epicondyle of the knee.

The surface electromyographic signals (EMG) were recorded with a linear array of four electrodes (silver bars 5 mm long, 1 mm thick, 10 mm apart; OTBioelettronica, Turin, Italy) from the biceps brachii (BB) and from the vastus lateralis (VL) muscles. These two muscles were considered as representative of upper and lower limbs muscle respectively as previously reported (Bazzucchi et al. 2004; Harwood et al. 2008; Theou et al. 2013). After gentle skin abrasion and cleaning with ethyl alcohol, electrodes were attached on the skin over the BB along the line connecting the acromion to the cubital fossa, and over the VL on the line from the anterior spina iliaca superior to the lateral side of the patella. The optimal position and orientation of the electrodes were determined to be conveniently distant from the innervation zone and the tendon after checking that there was clear propagation in one direction of the action potentials without change in shape.(Bazzucchi et al. 2005). A reference electrode was placed around the wrist and ankle of the contralateral limb, respectively. To ensure the same electrode placement throughout the two experimental sessions, individual maps of the upper arm were made on transparent plastic by marking the position of permanent skin blemishes with respect to the electrodes. Three EMG signals were detected in a single-differential mode. Two double-differentials were computed off-line and were used for further analysis. Signals were amplified (x1000), band-pass filtered (10 Hz to 450 Hz), sampled at 2048 Hz (EMG-USB2 amplifier, OTBioelettronica, Turin, Italy), recorded and stored on a personal computer.

**Experimental Tests**. During the test trial, the following parameters were evaluated: (1) maximal voluntary isometric contractions (MVIC); (2) isokinetic concentric contractions; (3) isometric fatiguing task.

1) MVIC. The joint angle was fixed at 90° (180°, full extension) for both the elbow and the knee. The MVIC task consisted of rapidly increasing the force exerted to a maximum. Visual feedback was provided to the subjects by setting a target line on the computer screen at a value 20% higher than the best MVIC. All subjects were verbally encouraged to exceed the target force, producing a maximal contraction ‘‘as hard as possible’’ and to maintain it for at least 2–3 s before relaxing. A minimum of three maximal attempts were performed separated by 4 min to recover from fatigue. Participants were asked to perform further attempts if the MVIC of their last trial exceeded the previous trials by at least 10%. However, in no instance the number of MVIC attempts exceeded four per subject.

2) Isokinetic Concentric Contractions. After the MVIC task, the torque–velocity curve was assessed. Angular velocity values were fixed at 15°, 30°, 60°, 120°, 180° and 240° $s^{-1}$, and subjects were requested to flex the elbow or to extend the knee ‘‘as hard as possible’’. The range of motion (ROM) for elbow flexion and knee extension was 40°-130° and 80°-170° respectively, which included the angle at which the maximal torque for each joint was reached. The order of the trials was randomized to minimize the effect of skill acquisition. Each contraction was followed by a 5-min rest to prevent cumulative fatigue. In each trial strong verbal encouragement was given by the test leader.

3) Isometric Fatiguing Task. An isometric contraction set at 80% of the maximum force value obtained during the MVIC was performed at the end of the session. A horizontal target band was displayed on a PC monitor. Participants were requested to match the target and to hold the force as long as possible (exhaustion). The end of the exercise was determined when the torque value dropped more than 10% below the target for 3 s. Trials were also interrupted if participants reported pain or any discomfort.

**Data Analysis.** All data collected during the experiments were analyzed off-line (OT BioLab, OTBioelettronica, Turin, Italy). For the MVIC task, the trial which showed the highest value for force was chosen for the analysis. For each contraction speed tested, subjects performed three repetitions, and the one that produced the highest torque value was used for analysis. Peak torques assessed during MVIC and isokinetic contractions were used to assess the torque–velocity relationship. EMG signals were recorded simultaneously to mechanical data. Trials chosen for MFCV estimation were selected on the basis of maximal force. Maximal MFCV was estimated from the two double-differentials over 250ms-windows by means of the cross-correlation technique (Sbriccoli et al. 2003; Bazzucchi et al. 2005). The cross correlation function technique was used to estimate the time delay between the two signals (i.e., the amount of time shift that must be applied to one signal to minimize the mean square error with the other). This time shift is the same, which maximizes the cross correlation between the signals (Naeije and Zorn 1982). Estimates of MFCV were accepted only when cross-correlation values were >0.8.

For the isometric fatiguing task, parameters of interest were the time to fatigue (TTF) and MFCV slope. A linear regression was applied to the scattered MFCV data. The rate of change of MFCV (% $s^{-1}$) was defined as the percentage ratio between the slopes of these regression lines and their initial values at time 0. The value at time 0 was calculated as the mean of the first three seconds (Sbriccoli et al. 2003).

**Reliability.** Previous test-retest reliability from our laboratory for Torque and MFCV calculated from isokinetic tests performed 2 to 10 days apart, indicated that the intraclass correlation coefficients (*ICC*) ranged from 0.89 to 0.96 and 0.74 to 0.93 respectively, with no significant ($p > 0.05$) differences between mean test vs retest values.

**Statistical analysis.** All statistical analyses were performed with PASW statistics 20.0 (SPSS Inc, Chicago, Illinois, USA). Standard methods of descriptive analysis were used for calculation of means and standard deviations (SD) and to test the normal distribution of variables. When the sphericity assumption was violated, the Greenhouse-Geisser adjustment was performed. Subsequently, a repeated-measures analysis of variance (RM-ANOVA) with limb [arm vs leg] and angular velocity [0 (MVIC), 15, 30, 60, 120, 180, 240°·$s^{-1}$] as within factors, was used to compare the dependent variables [torque and MFCV] obtained from the two groups [T2D vs H] following the 16-week training [PRE vs POST]. In addition, a one-way ANOVA with limb [arm vs leg] as a within factor was used to determine the effect of training on torque, MFCV, TTF and MFCV slopes obtained by the two groups of individuals during the isometric fatiguing task. When significant effects were found, T-tests with Bonferroni correction for multiple comparisons were performed as follow-up analyses. An alpha of $p<0.05$ was considered significant for all comparisons. An a priori analysis was used to determine a sample size that yielded power values of 0.80 or greater. Data are expressed as mean ± SE. Regression lines for individual data sets of torque vs angular velocity were computed using the least-squares method.

RESULTS

**Torque-velocity relationships**

Torque-velocity relationships of elbow flexors (EF) and knee extensors (KE) muscles of the two groups before and after the training period are depicted in fig. 1.

After the training program, maximal torque of EF in H and T2D was unchanged, in both static and dynamic conditions. Differently, a significant interaction was found among angular velocity, training and group for torque ($p=0.02$) values in KE in T2D. More specifically, KE torque-velocity relationship of T2D was shifted towards higher values after the training program, with a higher effect ($p<0.05$) observed during MVIC (+9.3±4%) and during dynamic contractions conducted at 15 (+22.9±8.5%) and 30° $s^{-1}$ (+25.2±8.2%).

*FIG.1 app. here*

**Muscle fiber conduction velocity**

MFCV values recorded during static and dynamic contractions are depicted in fig. 2. A significant interaction was found among angular velocity, training and group for MFCV ($p<0.05$) values in KE. After training significantly higher values of MFCV were found at MVIC and 30°$s^{-1}$ ($p<0.05$) in the EF and at 15, 30, 60, 90 °$s^{-1}$ ($p<0.01$) in KE of T2D group. In this group, the MFCV enhancement in KE following the training was +11.2±1.6% on average.

*FIG.2 app. here*

**Muscular Endurance**

Figure 3 shows time to fatigue (TTF) recorded during the isometric fatiguing contractions. TTF was 26.9±1.3 s for H and 20.1±0.7 for T2D with no effect of the muscle group (EF vs KE) and of training (PRE vs POST). A significant interaction was found between muscle group (EF vs KE) and condition (T2D vs H). In particular, T2D patient showed significant lower TTF values with respect to H subjects in both PRE and POST trials in KE muscles ($p<0.05$).

MFCV slopes calculated over the isometric fatiguing contractions are depicted in fig. 4. No significant differences were found between PRE and POST session in EF for both groups (H and T2D). For T2D group, a higher MFCV slopes was found after training in the KE muscles ($p<0.01$).

*FIG. 3 and 4 app. here*

# DISCUSSION

The present study aimed at comparing the effect of a 16-week whole-body combined endurance and resistance training on neuromuscular function of the upper and lower limb in type 2 diabetic patients. The main findings indicated that the training program was successful in increasing the maximal torque generated by the KE muscles at slow contraction velocities along with an associated increase in the MFCV in diabetic individuals. In addition, T2D patients showed lower TTF than H individuals during isometric fatiguing contractions of KE before and after training, with an associated increase in the MFCV slopes seen only after training.

*Muscle strength*

One of the most important functional consequences of diabetes is muscle weakness. Reduced muscle strength of the knee extensors muscles in T2D patients, has been reported during maximal isokinetic (Andersen et al. 1996; Park et al. 2007; Kalyani et al. 2013) and isometric tasks (Ijzerman et al. 2012) while a comparable isokinetic strength with respect to healthy controls has been found in muscles acting around the elbow (Andersen et al. 2004) and the wrist (Andreassen et al. 2006; Park et al. 2007). A greater detrimental effect of type II diabetes on the torque-velocity relationship of leg muscles with respect to arm muscles has been recently provided (Sacchetti et al., 2013). Moreover, in that study, using a cross-sectional design, it was found that trained diabetic patients showed a less pronounced neuromuscular impairment with respect to their sedentary counterparts, which highlighted the need for investigating the effect of exercise training programs on neuromuscular function of diabetic patients.

To the best of our knowledge the present is the first study focusing on the effect of exercise training on the torque-velocity relationship (and myoelectric activity) of upper and lower limb muscles of T2D patients.

In line with several previous investigations (Dunstan et al. 2002; Ibáñez et al. 2008; Kwon et al. 2010; Larose et al. 2010), our findings showed an improvement of muscle strength of T2D patients after training. However, in the present study we demonstrate that the training was only effective in isometric contractions and dynamic contractions of lower velocity. While many day-to-day functional tasks require force production at these low velocities, such as rising from a chair or walking up stairs, there may be occasions when faster velocity contractions are required such as recovering from a stumble or grab an object that is falling. This may be a reflection on the training modality in which the resistance training exercises where completed at the slower velocities rather than in an explosive movement. However, this is worthy of consideration for exercise practitioners developing a suitable training program for muscle function in type 2 diabetic individuals.

An interesting finding in the present study was the lack of improvement in the muscle function of the EF, despite an improvement in the KE. The upper and lower extremities have been previously shown to be affected by type 2 diabetes to different extents, with lower limbs showing a more pronounced impairment of strength and greater metabolic derangement (Andersen et al., 2004; Christer . et al., 2006; Ibáñez et al., 2008; Ijzerman et al., 2012; Won Park et al., 2006, 2007; Olsen et al., 2005; Sacchetti et al., 2005). The higher neuromuscular impairment in the KE could be responsible for a lower baseline muscular capacity compared to the EF and, thus, a greater "gap to fill" with training. This larger gap would make more evident the effect of a moderate training regime, as the one adopted in the present study. Indeed, the exercise modality also deserves consideration. The participants were involved in a combined endurance and resistance training program, with the aerobic exercise performed on a treadmill or on a cycle ergometer. Therefore, while resistance exercises were equally distributed between the upper and lower body districts, the aerobic training was mainly focusing on the lower body, representing an additional stimulus for the musculature of the lower limbs. This factor could have contributed to the greater response of the KE to the 16-week combined exercise training compared to the EF, which represents a further consideration for in the exercise prescription for these patients.

*Muscle fiber conduction velocity*

In the present study, we explored the modifications in the propagation velocity of the action potential along the muscle fibers during maximal isometric and isokinetic contractions before and after the 16-week exercise program. To the best of our knowledge, this is the first longitudinal study investigating the exercise-induced modifications of the torque-velocity relationship with a concomitant estimation of the MFCV in T2D patients.

MFCV depends, among other factors, on sarcolemmal excitability (Arendt-Nielsen and Zwarts 1989; Linssen et al. 1996; Chisari et al. 1998), morphological and functional characteristics of muscle fibers (Arendt-Nielsen and Zwarts 1989; Kupa et al. 1995; Almeida et al. 2008) and can be influenced by changes in neuromuscular recruitment strategies occurring independently of motor nerve dysfunction (Sacchetti et al., 2013). In particular, the T2D patients involved in the present study did not present clinical signs of neuropathy and their median duration of diabetes was very short, so it may be plausible that their baseline MFCV values were not much different from the ones of healthy subjects. Studies on the $Na^+/K^+$ pump function, in fact, demonstrated no significant differences between control subjects and T2D patients with no evidence of neuropathy at baseline and following normal pump activity (Arnold et al. 2013) and activity-dependent changes similar to those observed in healthy men in the post-contraction period. On the other hand, alterations in $Na^+/K^+$ pump function coupled with reductions in nodal $Na^+$ currents have been hypothesized to be responsible for the slower recovery following maximal voluntary contractions in diabetic neuropathy (Krishnan et al. 2008).

After the training period, an increase in MFCV values of diabetic patients in the VL was obtained, keeping with the increase of the knee extensors muscles' strength. To note, even if limited to the lowest contraction speeds, we also found an increased

MFCV in the BB muscle of T2D patients, which was not associated to changes in the torque-velocity curve of the elbow flexors after training. This points toward an exercise-induced restoration of neuromuscular function which is, again, more evident in the lower limb likely due to the greater impairment of muscle quality of those body regions (Park et al., 2006). This, together with the training-induced improvements in MFCV in the BB despite an unchanged torque, suggests that MFCV may be useful for unmasking early signs of neuromuscular dysfunction and reconditioning in diabetic patients.

*Muscle fatigue*

Besides the reduction of muscle strength, diabetic patients may suffer from a reduction in muscle endurance, and this higher muscle fatigability may have a negative impact on activities of daily living, such as carrying shopping bags or climbing a long set of stairs. The number of studies investigating muscle endurance in relation with diabetes is limited (Andersen 1998; Almeida et al. 2008; Shah et al. 2011; Ijzerman et al. 2012) and the results are conflicting partially due to the different testing procedure adopted (isometric vs concentric contractions), the limb tested (upper vs lower) and the diabetic population (type 1 vs type 2) considered.

In the present study, T2D patients showed a lower TTF during the isometric fatiguing contractions of KE muscles compared to H, both pre and post training. Of note, after the training period, this was also associated to higher MFCV slopes. In normal conditions, during sustained voluntary contractions MFCV gradually declines, which is related to modifications in muscle membrane excitability (Chisari et al. 1998). The time course of this MFCV decline has been shown to be higher in muscles with a higher proportion of type II muscle fibers (Kupa et al. 1995). Taken together, these findings of a higher fatigability and MFCV slope in T2D appears to support the previously reported shift in muscle fiber type composition with diabetes, with a higher proportion of fast-twitch fibers at the expenses of slow-twitch ones (Saltin et al. 1977; Krotkiewski and Bjorntorp 1986; Lillioja et al. 1987; Gaster et al. 2001;

Oberbach et al. 2006). The change in contractile properties is further described by animal studies reporting a more marked diabetes-induced strength loss in fast-twitch muscles (Cotter et al. 1989; Sanchez et al. 2005) and in skinned fast-twitch single fibers (Paulus and Grossie 1983; Sanchez et al. 2005) than in slow-twitch muscles. Thus, it is tempting to speculate that the KE muscles of our patients could have been characterized by a higher proportion of type II fibers with respect to the arm muscles in reason of a greater diabetes-induced impairment as suggested by some (Gaster et al., 2001; Hickey et al., 1995; Mårin et al., 1994; Mogensen et al., 2007; Oberbach et al., 2006; Segerström et al., 2011; Stuart et al., 2013) but not all (Andreassen et al., 2014; Cederholm et al., 2000; He et al., 2001; Leenders et al., 2013; Zierath et al., 1996) studies. This would be reflected by lower TTF due to the greater fatigability of glycolytic fibers, by the higher MFCV slopes during the fatiguing contractions, as well as by the greater training effect on the torque-velocity relationship.

The present study has several practical implications. The selective effect of our conventional training program on the torque-velocity relationship highlight the need for implementing specific exercise protocols adopting different contraction velocities to selectively counteract the diabetic-induced neuromuscular deficiencies. The present data support our previous suggestion of considering different angular velocities when testing neuromuscular function in diabetes patients, as well as the effect of specific training regimes. Finally, MFCV appears to be a sensitive parameter for describing some of the modifications induced on neuromuscular functions by type 2 diabetes, even at its early stage.

Conclusions:

In conclusion, the present training study adopting conventional exercise modalities for diabetic patients indicates that individuals at the initial stage of the disease show a higher improvement of neuromuscular function in the lower than in the upper limb muscles. The training effect appears to be angular velocity-specific, which calls for adopting specifically structured exercise modalities. Finally, the velocity of propagation of the action potential along the muscle fibers appears to be a more sensitive marker than torque in detecting the early signs of neuromuscular function reconditioning.

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CAPTIONS

**Fig.1.** EF (panel A and B) and KE (panel C and D) torque-velocity curves in H and T2D groups during PRE (closed circles) and POST (open circles) training. Data are expressed as percentage of the MVIC values recorded during the PRE trial. Exponential regression lines were fitted. *$p<0.05$ PRE vs POST.

**Fig. 2**. MFCV values recorded on biceps brachii (panel A and B) and vastus lateralis (panel C and D) muscles in H and T2D groups during PRE (closed circles) and POST (open circles) training. *$p<0.05$ PRE vs POST.

**Fig. 3**. TTF values recorded during the isometric fatiguing task for elbow flexion (panel A) and knee extension (panel B) in H and T2D group before (black bars) and after (white bars) the 16-week training program. #$p<0.05$ T2D vs H.

**Fig. 4**. MFCV slopes values recorded during the isometric fatiguing task for biceps brachii (panel A) and vastus lateralis (panel B) muscles in H and T2D group before (black bars) and after (white bars) the 16-week training program. *$p<0.05$ PRE vs POST.

**Table 1**. Anthropometric and metabolic variables of diabetic and control subjects before (PRE) and after (POST) the 16-week training program. Values are reported as mean ± SD *different from POST $p<0.05$.

*Author Biography



Ilenia Bazzucchi received her PhD in Sport Science and Health and she is currently an Assistant Professor in Human Physiology at the Department of Movement, Human and Health Sciences at University of Rome "Foro Italico", Italy. She has recently been part of the Organizing Committee of the XX Congress of ISEK, International Society of Electrophysiology and Kinesiology. Her research work mainly concerns the study of neuromuscular control by means of surface electromyography, non-invasive assessment of muscle damage, neuromuscular effects of exercise and nutritional interventions in healthy individuals, athletes and patients.

Professor Giuseppe De Vito, MD and Specialist in Sport Medicine earned a PhD in Human and Exercise Physiology at the University of Rome "Sapienza", Italy. He is currently the Head of School of Public Health, Physiotherapy and Population Sciences in University College of Dublin (UK) and he previously held academic positions at the University of Strathclyde in Glasgow (UK) and at the University of Rome "Foro Italico", Italy. He is a member of both British and Italian Physiological Societies and Associate Editor of the Journal of Aging and Physical Activity and Member of the Editorial Board of the Journal of Electromyography and Kinesiology. His main research topic concerns: neuro-mechanical adaptations of muscle, tendons and joints to aging and training; effect of muscle temperature on power production; neuromuscular control studied by surface EMG; assessment of essential tremor; study of sarcopenia in older and diabetic individuals.

Francesco Felici, MD and Specialist in Sport Medicine, is an Associate Professor of Human Physiology and Exercise Physiology at the University of Rome "Foro Italico" Italy. He has chaired the XX Congress of ISEK and is a member of the Italian Physiological Society of the Council of the International Society of Electrophysiology and Kinesiology, of the European College of Sport Sciences. He is an Associate Editor (Section Sport and Exercise) of the Journal of Electromyography. He has authored more than 100 papers and scientific communications and his research activity focuses mostly in the human movement area – from energetic to control - in collaboration with national and international institutions. The main topics are: neuromuscular control, non linear analysis of surface electromyograms, neuromuscular effects of exercise and sport, exercise physiology in healthy and pathological subjects.

Susan Dewhurst has an undergraduate degree in Sport and Exercise Science and a PhD in Exercise Physiology both from the University of Strathclyde in Glasgow. Prior to starting her lecturing career, she spent time as a researching fellow at Aalborg University in Denmark and the University of Rome "Foro Italico", Italy. Her research interest are: effects of various physical activity interventions on muscle performance in older individuals, postural stability and gait analysis in older individuals, neuromuscular control in different populations, effects of temperature on neuromuscular control.

Antonio Sgadari earned his MD degree and specialization in Geriatrics and Gerontology at the Catholic University of Sacred Heart, Rome. He is currently Aggregate Professor at the Department of Geriatrics, Neurosciences and Orthopedics and Chief of the Physical Activity and Functional Rehabilitation Unit of the same University. His research interests are mainly focused on the effects of physical exercise in the elderly and in special populations (patients with diabetes, obesity, cardiovascular diseases, movement disorders). He is also interested in the validation and adaptation to the elderly of cardiorespiratory tests as well as in the development of specific training programs for special populations.

Massimo Sacchetti earned an MSc and a PhD in Physiology at the University of Copenhagen. He is currently Associate Professor at the Department of Movement, Human and Health Sciences at University of Rome "Foro Italico". At present, his research interests include the neuromuscular and metabolic responses to specific exercise sessions and training protocols for health and fitness in young and older individuals as well as in diabetic patients. He is also interested in studying the physiological aspects related to training and performance in endurance sports, with a special focus on cycling.

*Author Bio Photo



Figure1
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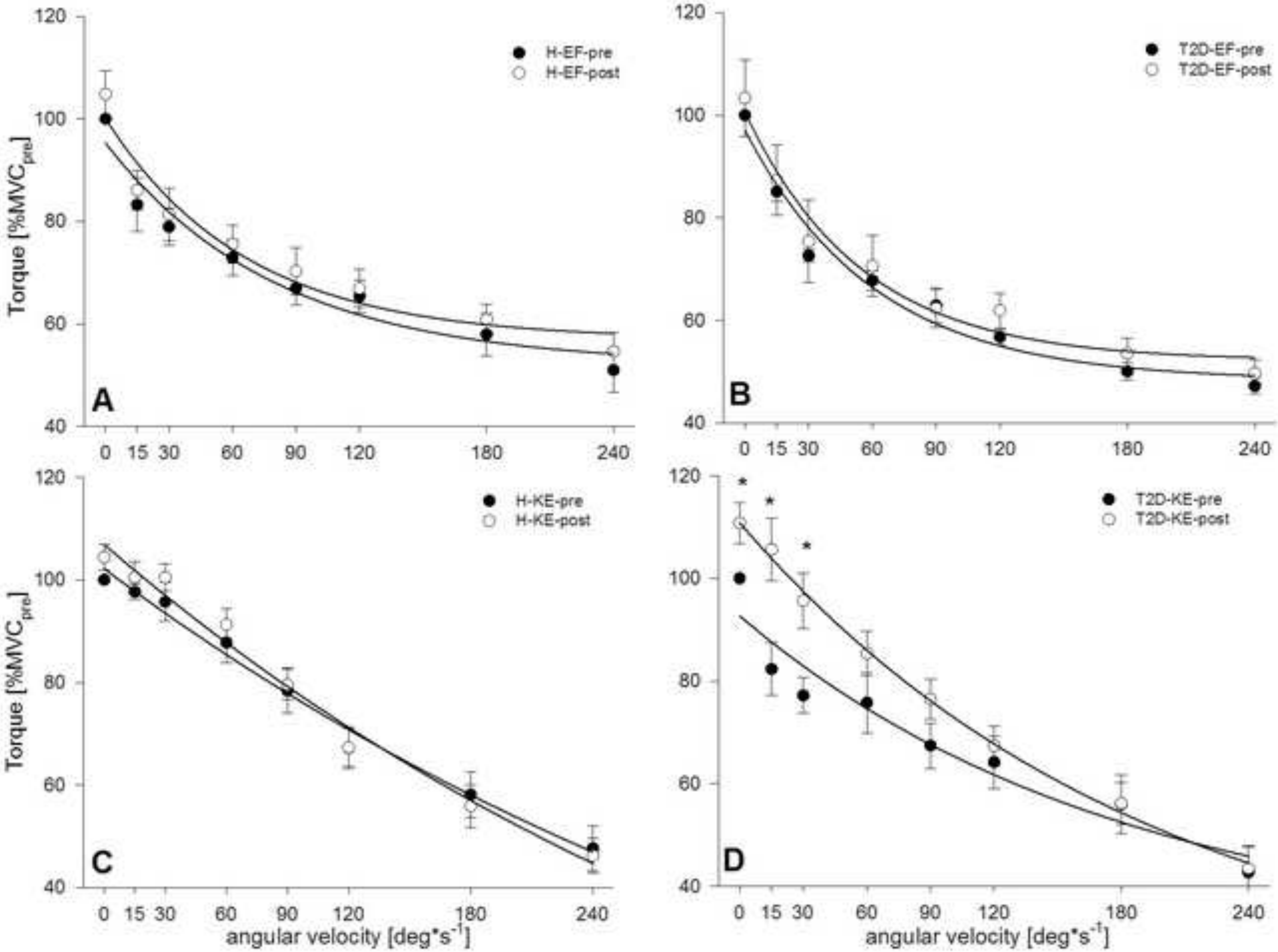

Figure2

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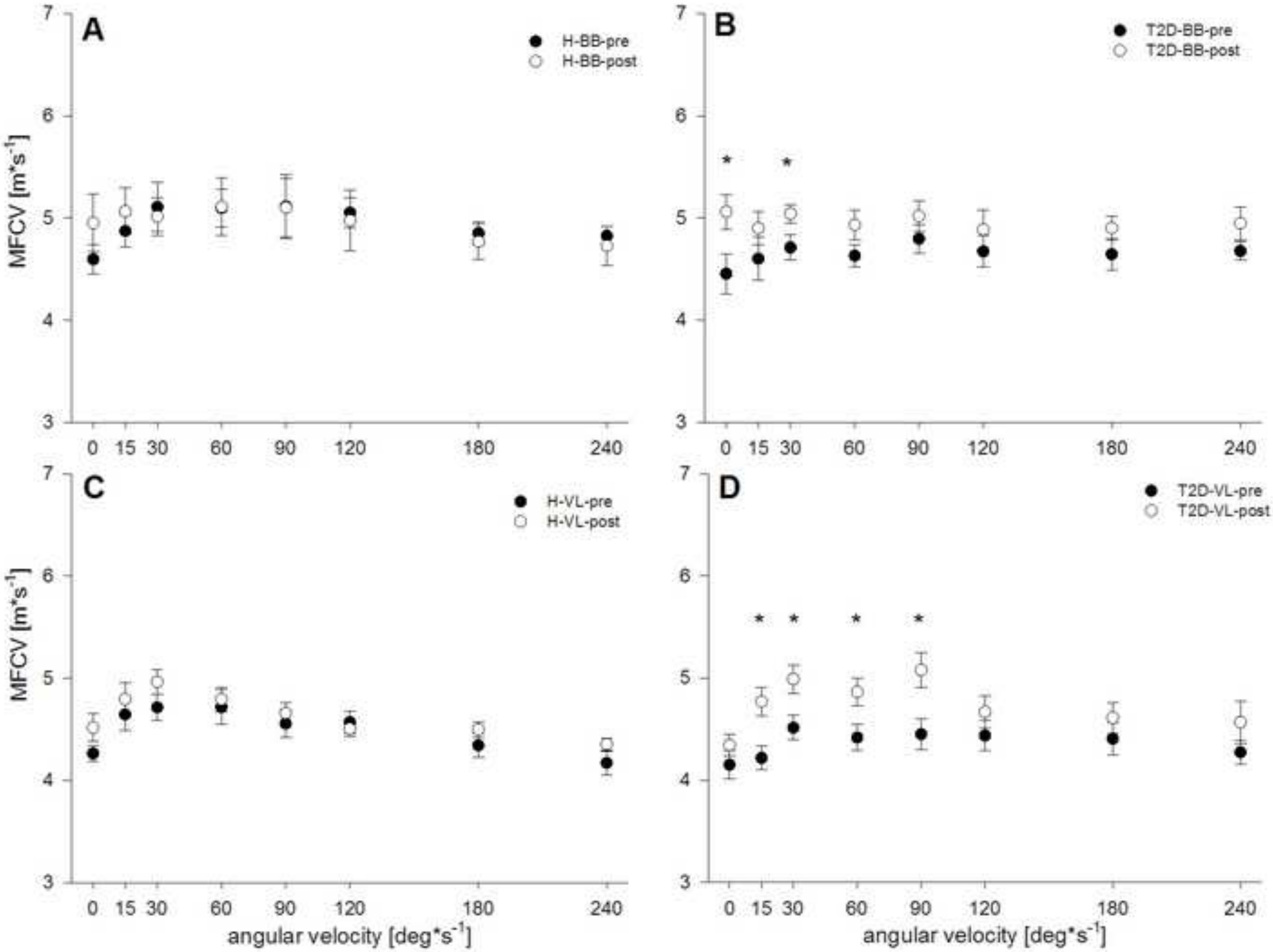
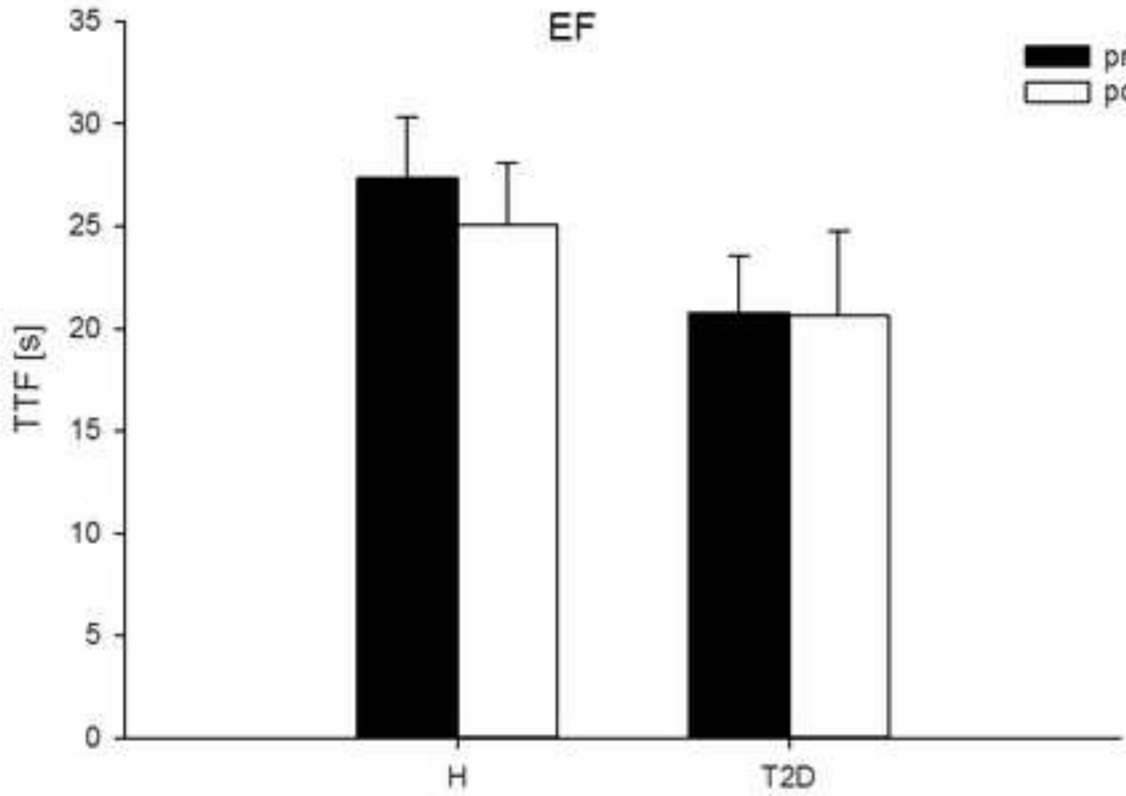


Figure3

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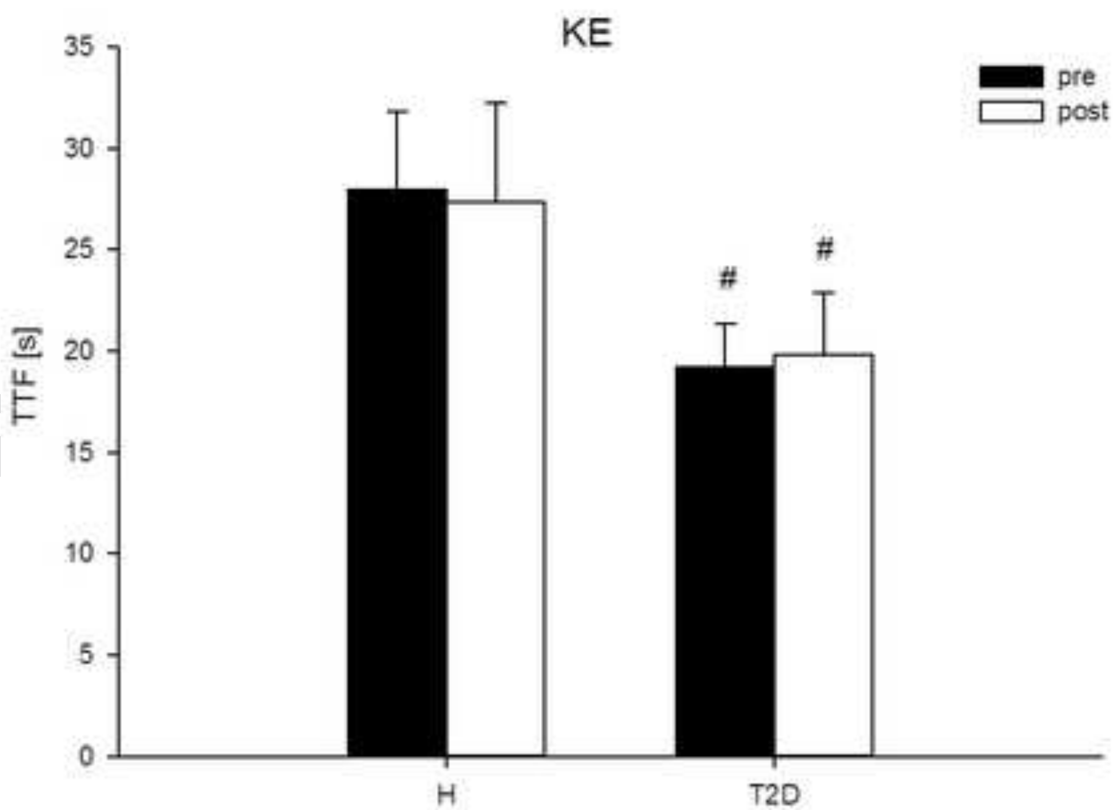
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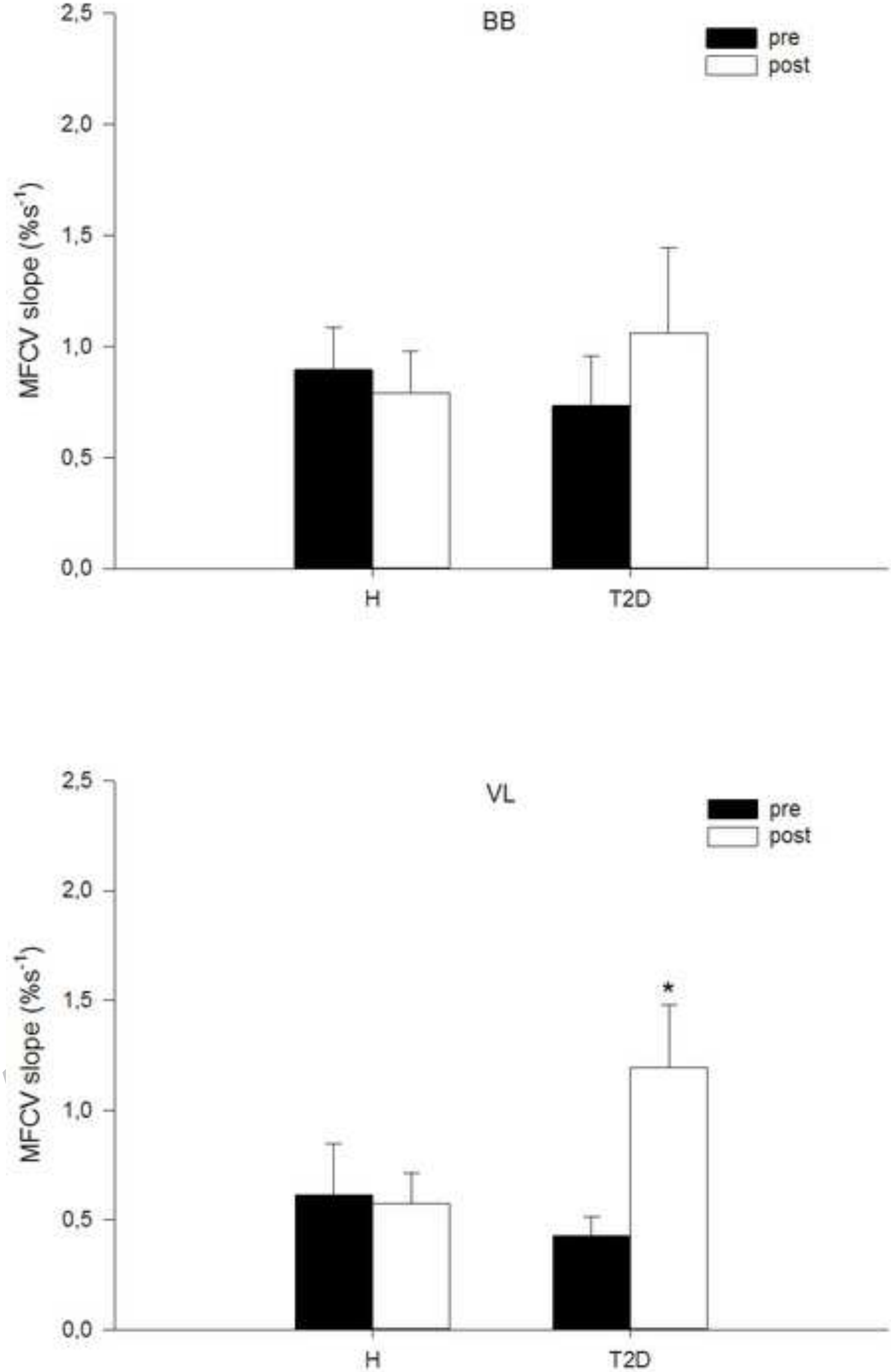
Figure4






BB
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post
MFCV slope (%s$^{-1}$)
2,5
2,0
1,5
1,0
0,5
0,0
H
T2D
VL
pre
post
MFCV slope (%s$^{-1}$)
*
2,5
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H
T2D

| | Diabetic subjects | | Control subjects | |
|---|---|---|---|---|
| | PRE | POST | PRE | POST |
| Age (years) | 61.5±2.8 | | 63.6±3.6 | |
| BMI ($kg*m^{-2}$) | 36.0±2.9 | 29.8±3.7* | 27.4±2.6 | 26.3±3.1 |
| BB Skinfold Thickness (mm) | 9.2±2.7 | 8.6±3.4 | 8.2±4.1 | 7.8±3.2 |
| VL Skinfold Thickness (mm) | 28.6±10.5 | 26.5±9.8 | 25.7±9.3 | 25.1±8.7 |
| HbA1C (%) | 6.9±0.6 | 6.3±0.7 | 5.7±0.1 | 5.6±0.2 |
| Total Cholesterol (mg*dl) | 194.0±19.3 | 178.4±18.0* | 189.6±21.7 | 181.1±1.0 |
| HDL (mg*dl) | 44.8±7.5 | 49.2±11.2 | 49.2±6.6 | 52.8±6.9 |
| LDL (mg*dl) | 180.0±23.9 | 139.0±22.8* | 163.0±21.6 | 149.2±15.2 |
| Triglycerides (mg*dl) | 153.8±29.0 | 118.6±32.9* | 113.0±10.1 | 104.3±11.0 |