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Skeletal muscle metabolic recovery following submaximal exercise in chronic heart failure is limited more by O₂ delivery than O₂ utilization

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ABSTRACT

Chronic heart failure (CHF) is associated with a prolonged recovery of skeletal muscle energy stores following submaximal exercise, limiting the ability to perform repetitive daily activities. The pathophysiological background of this impairment is not well established. The aim of this study was to investigate whether muscle metabolic recovery following submaximal exercise in patients with CHF is limited by O₂ delivery or O₂ utilization. Thirteen stable CHF patients (New York Heart Association class II-III) and 8 healthy subjects, matched for age and BMI were included. All subjects performed repetitive submaximal dynamic single-leg extensions in the supine position. Post-exercise phosphocreatine (PCr) resynthesis was assessed by ³¹P magnetic resonance spectroscopy. Near-infrared spectroscopy was applied simultaneously, using the rate of decrease in deoxygenated hemoglobin (HHb) as an index of post-exercise muscle re-oxygenation. As expected, PCr recovery was slower in CHF patients than in control subjects (time constant: 47±10 sec versus 35±12 sec, *P*=0.04). HHb recovery kinetics were also prolonged in CHF patients (mean response time: 74±41 sec versus 44±17 sec, *P*=0.04). In the patient group, HHb recovery kinetics were slower than PCr recovery kinetics (*P*=0.02), while no difference existed in the control group (*P*=0.32). In conclusion, prolonged metabolic recovery in CHF patients is associated with an even slower muscle tissue re-oxygenation, indicating a lower O₂ delivery relative to metabolic demands. Therefore, we postulate that the impaired ability to perform repetitive daily activities in these patients depends more on a reduced muscle blood flow than on limitations in O₂ utilization.

INTRODUCTION

Chronic heart failure (CHF) is associated with a prolonged recovery of skeletal muscle energy stores after submaximal exercise [1-4]. As daily life is characterized by repetitive submaximal activities, it can be assumed that this delayed recovery is an important contributor to exercise intolerance in these patients. Therefore, more insight into the physiological determinants of metabolic recovery is crucial for a better understanding of the pathophysiological basis of functional impairments in CHF patients and, moreover, it may help improving therapeutic approaches in these patients.

Factors influencing the rate of recovery of muscle energy stores are O₂ delivery and O₂ utilization. Whereas O₂ delivery is determined by muscle blood flow and arterial O₂ content, O₂ utilization is associated with oxidative capacity of skeletal muscles. Studies in healthy untrained individuals have provided evidence that metabolic recovery is limited by O₂ utilization, rather than O₂ delivery [5-7]. In CHF patients, both impairments of muscle blood flow [8,9] and muscle oxidative capacity [10,11] have been documented. To what extent these derangements contribute to the delayed muscle metabolic recovery in these patients, however, is not well established.

Near-infrared spectroscopy (NIRS) is a non-invasive method providing a continuous assessment of changes in tissue oxygenation. This technique is based on the principle that oxygenated (O₂Hb) and deoxygenated hemoglobin (HHb) have different absorption characteristics for near-infrared light. Assuming a constant O₂ content in arterial blood, changes in these parameters reflect changes in the difference between local O₂ delivery and O₂ uptake. Therefore, in combination with assessment of muscle metabolism, NIRS is potentially useful to investigate the relative influence of O₂ delivery and O₂ utilization on muscle metabolic recovery [12]. Provided that muscle acidosis is not severe, ³¹P magnetic resonance spectroscopy (³¹P-MRS) measurements of phosphocreatine resynthesis (PCr) can be used to evaluate the time course of the oxidative metabolic rate in skeletal muscles [13-15]. To our knowledge, only one study combined NIRS and ³¹P-MRS measurements during exercise recovery in CHF patients [1]. However, NIRS and ³¹P-MRS measurements were not performed simultaneously. In that study, CHF patients were found to have slower recovery of both PCr resynthesis and muscle tissue oxygenation. In contrast with healthy controls, PCr resynthesis was even slower than tissue re-oxygenation in the patient group, leading the authors to conclude that metabolic recovery in CHF is mainly limited by O₂ utilization.

The present study was conducted to quantify the delay in muscle metabolic recovery following submaximal exercise in moderately impaired CHF patients, and to examine the pathophysiological background of this delay by performing simultaneous measurements of ³¹P-MRS and NIRS in CHF patients and healthy individuals.

METHODS

Subjects

Thirteen patients with stable CHF (New York Heart Association class II-III and echocardiographic left ventricular ejection fraction \leq 40%) secondary to ischemic or dilated cardiomyopathy were recruited. Exclusion criteria were the presence of a pacemaker or implantable cardioverter defibrillator, claustrophobia, recent myocardial infarction (<3 months prior), significant symptomatic myocardial ischaemia, severe valvular heart disease, current involvement in a regular training program (\geq 2 times per week), mitochondrial disorders, peripheral vascular disease, significant chronic obstructive pulmonary disease and other disorders limiting the ability to exercise. The control group consisted of 8 age- and body mass index matched healthy subjects. These subjects were not receiving any

medication, and none were competitive athletes. Subject characteristics are listed in Table 1. The research protocol was approved by the local Research Ethics Committee, and all subjects provided written informed consent.

Exercise protocol

Exercise consisted of dynamic single leg extensions in the supine position. The right upper leg was immobilized with Velcro straps with the knee supported in approximately 90 degrees of flexion. Subjects were instructed to lift a lever resting on the lower leg which was attached to a weight via a pulley system. One contraction was performed every 1.5 s, paced by a digital metronome. All subjects performed exercise tests on 2 occasions within 1 week. During the first session, patients underwent an exercise test until exhaustion with 1 minute incremental steps. The initial weight applied and the incremental steps were set individually, aiming at a total test duration of 4 to 6 minutes. In addition to familiarizing subjects with the procedure, this test was used to determine the duration and workload during the second session. During this second visit, the exercise protocol was adjusted individually such that phosphocreatine (PCr) depletion approximated 50% at the end of the test (see ^{31}P magnetic resonance spectroscopy). In addition, a drop of intra-cellular pH below 6.8 was avoided in order to minimize the influence of muscular acidosis on PCr recovery kinetics [16-18]. Exercise was followed by a recovery period of at least 5 min, in which PCr recovery kinetics were assessed.

^{31}P magnetic resonance spectroscopy

During recovery from exercise, PCr is resynthesized purely as a consequence of adenosine triphosphate (ATP) generation, mainly by oxidation reactions within mitochondria. Because the creatine kinase reaction is much faster than ATP production, the PCr resynthesis rate is considered to reflect mitochondrial oxidative phosphorylation flux [13-15]. In the present study, ^{31}P magnetic resonance spectroscopy was performed with a 1.5-T whole-body magnet (Gyrosan S15/ACS, Philips Medical Systems, Best, The Netherlands). The spectroscopy procedures that were used have been described previously [18,19]. In brief, after the magnetic field homogeneity was optimized by localized shimming on the proton signal, ^{31}P signals were collected using a 6-cm diameter surface coil placed over the M. vastus lateralis of the right leg (mid thigh level). Data were acquired following a 90° adiabatic excitation pulse with a sweep width of 2 kHz and 1,024 data points. First, a fully relaxed spectrum was obtained at rest with a repetition time of 30 sec and 24 scans. During the exercise protocol, spectra were acquired with a repetition time of 3 sec. Zero- and first-order phase corrections were determined from the rest spectra and then also applied to the time series. Spectra were fitted in the time domain by using a nonlinear least-squares algorithm (AMARES) [20] in the jMRUI software package [21]. PCr, inorganic phosphate (Pi), ATP, and phosphodiester (PDE) signals were fitted to Lorentzian line shapes as described by Praet et al. [19]. Absolute concentrations of PCr were calculated after correction for partial saturation under the assumption that the ATP concentration is 8.2 mM at rest [22]. PCr depletion was defined as the difference between resting and end exercise PCr concentrations divided by the resting value. Intracellular pH was calculated from the chemical-shift difference between the Pi and PCr resonances as described previously [15]. For analysis of PCr recovery kinetics, data were averaged into 6 sec intervals (2 scans), and subsequently fit to a mono-exponential model:

$$[\text{PCr}]_{(t)} = [\text{PCr}]_{(EE)} + A * (1 - e^{-t/\tau})$$

where $[\text{PCr}]_{(t)}$ indicates the PCr concentration at time t , $[\text{PCr}]_{(EE)}$ indicates the value at the end of the exercise test, A is the amplitude of the post-exercise increase in $[\text{PCr}]$, and τ is the

time constant. The ‘goodness of fit’ of the model was determined by the coefficient of determination (R^2).

Near-infrared spectroscopy

Near-infrared spectroscopy is based on the O_2 dependency of absorption changes for near infrared light in hemoglobin and myoglobin, allowing a noninvasive estimation of concentration changes of oxygenated (O_2Hb) and deoxygenated hemoglobin (HHb). The theoretical principles and clinical utility of this measurement technique have been described previously [23,24]. In the present study, NIRS measurements were performed by a single channel continuous-wave near-infrared spectrophotometer (OXYMON, Artinis, Zetten, The Netherlands) with 2 wavelengths of emitting light (775 and 850 nm). The light source and detectors were connected to the leg with 2 nonmagnetic fiberoptic light guides. In order to obtain NIRS and ^{31}P MRS measurements from the same region in the *M vastus lateralis*, the light guides were integrated into the MRS-coil. Data were sampled at 50 Hz and stored for off-line analysis. Unlike other studies in CHF patients [1,25], we used deoxygenated hemoglobin (HHb) to evaluate the recovery kinetics of muscle oxygenation. This approach was chosen because it has been demonstrated that exercise-induced changes in total arterial blood volume under the NIRS probe significantly influence the kinetics of oxygenated hemoglobin (O_2Hb), irrespective of changes in tissue oxygenation [23,26,27]. Since the amount of HHb in arterial blood is low when assuming a normal arterial O_2 -saturation, changes in arterial blood volume can be expected to have a relatively low impact on HHb kinetics. Therefore, HHb kinetics are considered a more accurate marker of muscle tissue oxygenation than O_2Hb kinetics [23,26,27]. As demonstrated by Ferreira et al. [5], HHb recovery kinetics following submaximal exercise can be adequately assessed by the mean response time (i.e. time delay + time constant of mono-exponential decrease), approximating the time to reach 63% of the response. To calculate this mean response time (MRT-HHb), we first re-sampled the HHb data into 1 sec intervals. The time delay (Td_{HHb}) was defined as the time until HHb dropped more than 1 SD below the end-exercise HHb value [28]. End-exercise HHb was defined as the average value of the last 20 sec of exercise. The time constant of the subsequent HHb decrease (τ) was calculated by fitting a mono-exponential model to the data until 300 sec of recovery:

$$[HHb]_{(t)} = [HHb]_{(BL)} - A * (1 - e^{-(t - Td)/\tau})$$

where $[HHb]_{(t)}$ indicates the HHb concentration at time t , $[HHb]_{(BL)}$ indicates the baseline value at the point from which the data were fitted, A is the amplitude of the post-exercise decrease in $[HHb]$, Td is the time delay, and τ is the time constant.

The ‘goodness of fit’ of the model was assessed by R^2 . Finally, as already stated, MRT-HHb was calculated as $\tau + Td_{HHb}$.

Statistical analysis

Data were analyzed using SPSS 16.0 statistical software (SPSS Inc, Chicago, IL, USA). Continuous variables are presented as mean \pm SD, categorical variables as percentages. Because of the relatively small study populations, non-parametric tests were used for analysis of the data. Wilcoxon signed rank sum test was used for paired observations of continuous data, and Mann-Whitney U test for unpaired comparisons. Differences between categorical data were evaluated by the χ^2 test. Relations between variables were assessed by Spearman correlation coefficients (r_s). For all statistical comparisons, the level of significance was set at $P < 0.05$.

RESULTS

³¹P magnetic resonance spectroscopy

All subjects completed the exercise tests. Measurements obtained by ³¹P MRS at rest and at the end of exercise are shown in Table 2. Resting PCr concentrations were significantly lower in the control group. Whereas healthy controls achieved a higher absolute workload than CHF patients (4.8 ± 1.0 kg versus 3.0 ± 1.0 kg, $P=0.003$), there was no difference in PCr depletion during exercise, indicating that both groups exercised at the same relative exercise intensity. In addition, there were no significant differences in exercise duration (4.9 ± 1.5 min versus 4.6 ± 1.9 min, $P=0.94$) or intracellular pH at the end of exercise between patient and control groups (Table 2). The mean coefficient of determination (R^2) of the mono-exponential fits of PCr recovery was 0.96 (range: 0.92 – 0.98) in the patient group and 0.94 (range: 0.89 – 0.97) in the control group, indicating a good fit of the mono-exponential model to the data in both groups. Figure 1 shows representative examples of the time courses of PCr during recovery from exercise in a CHF patient (Figure 1A) and a healthy subject (Figure 1C). As shown in Figure 2, the time constant of PCr recovery (τ -PCr) in the patient group was significantly greater than in the control group (47 ± 10 sec vs 35 ± 12 sec, respectively, with $P=0.04$), indicating a slower muscle metabolic recovery in the patient group.

Near-infrared spectroscopy

NIRS data were successfully obtained and analyzed in all patients. In both groups, R^2 for the determination of the time constant of the post-exercise HHb decrease (τ -HHb) exceeded 0.90 in all cases (mean value 0.98 in the patient group and 0.98 in the control group). Representative examples of HHb recovery following exercise are shown in Figures 1B and 1D. Comparing patient and control groups, there were no significant differences in T_{dHHb} (19 ± 22 sec vs 5 ± 5 sec respectively with $P=0.37$) or τ -HHb (54 ± 38 sec vs 38 ± 15 sec respectively with $P=0.41$). However, MRT-HHb was significantly greater in the patient group (74 ± 41 sec vs 44 ± 17 sec, respectively, with $P=0.045$, Figure 2). As shown in Figure 2, MRT-HHb lasted longer than τ -PCr in the patient group (74 ± 41 sec vs 47 ± 10 sec, respectively with $P=0.02$), while there was no significant difference between these parameters in the control group (44 ± 17 sec vs 35 ± 12 sec respectively with $P=0.32$). There were no significant relations between MRT-HHb and τ -PCr in both groups (patient group: $r_s=0.35$, $P=0.25$; control group: $r_s=-0.14$, $P=0.74$).

DISCUSSION

To our knowledge, this is the first study to simultaneously assess the kinetics of skeletal muscle re-oxygenation and muscle metabolic recovery after submaximal exercise in patients with CHF. The main finding was that both PCr resynthesis and muscle re-oxygenation were delayed in CHF compared to healthy subjects. In addition, muscle re-oxygenation was slower than PCr recovery kinetics only in the patient group. These findings suggest that the observed delay in the recovery of muscle energy stores in CHF patients is determined by an impairment of O₂ delivery rather than O₂ utilization.

Considering ³¹P magnetic resonance spectroscopy measurements, we found slightly higher resting PCr concentrations in CHF patients than in healthy individuals, which is in contrast with other studies [1,3]. As it was shown that intracellular PCr concentrations are higher in type II muscle fibers than in type I muscle fibers [29], this finding may indicate that the included CHF patients had a higher % of type II muscle fibers than healthy controls, which is in line with other studies [10,30]. Furthermore we observed a slower PCr recovery

in CHF patients than in healthy subjects. This finding is in agreement with previous studies [1-4,31,32]. Only 2 of these studies applied a mono-exponential model to assess PCr recovery, both reporting greater time constants than in our study (75 ± 11 sec and 76 ± 30 sec vs 47 ± 10 sec respectively) [1,4]. This discrepancy can be explained by the fact that more severely impaired CHF patients were included in one study (mean peak $\dot{V}O_2$ 13.3 versus 19.5 $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) [4] and by a greater exercise-induced decrease in muscle pH in the other study (6.56 ± 0.01 versus 6.93 ± 0.04) [1].

Only few studies have examined the relative influence of impairments of local O_2 delivery and O_2 utilization on submaximal exercise capacity in CHF. Studies focusing on exercise-onset yielded conflicting results. Animal studies demonstrated a delayed exercise-related increase in skeletal muscle capillary blood flow [33] and a more rapid lowering in microvascular pO_2 in CHF as compared to healthy controls [34], pointing at a limiting role of O_2 delivery. In contrast, human studies showed that abnormalities in muscle metabolism are not associated with a reduced muscle blood flow during submaximal exercise in CHF patients [35,36]. The exercise protocols applied in these studies, however, involved small muscle groups (calf and forearm muscles respectively) and, therefore, the results of these studies may not be representative for exercise performed with larger muscle groups. Studies evaluating the physiological determinants of metabolic recovery from submaximal exercise in CHF patients are scarce. In a study with severely impaired CHF patients, Toussaint et al. showed that prolonged PCr recovery kinetics were associated with a reduction of reactive hyperemic blood flow, suggesting that local circulatory dysfunction contributes to the prolonged metabolic recovery in these patients [4]. The measurement techniques used in that study, however, did not permit simultaneous assessment of perfusion and metabolism in the same muscle area. Moreover, muscle perfusion could not be measured continuously during exercise recovery. In a study, using direct measurements of microvascular O_2 pressure in the exercising muscle of rats, McDonough et al. found a slower muscle re-oxygenation following submaximal exercise in CHF [37]. Using Near Infrared Spectroscopy (NIRS), we also found a delay in post-exercise muscle re-oxygenation in humans with CHF, which is in agreement with other studies in CHF patients [1,25]. From a physiological point of view, changes in tissue oxygenation are determined by changes in the difference between local O_2 delivery and O_2 uptake. Accordingly, the observed delay in post-exercise muscle re-oxygenation in CHF patients indicates a lower O_2 delivery relative to the metabolic demands in these patients, suggesting that an impairment of O_2 delivery plays an important role in the delay in metabolic recovery in moderately impaired CHF patients. This assertion is in line with the findings of other studies [38,39], that demonstrated an exaggerated vasoconstriction during and after exercise in CHF patients. Still, additional research is needed to establish a definite causal relationship between skeletal muscle underperfusion and impaired metabolic recovery following submaximal exercise, preferably by investigating the effect of experimental alterations of muscle blood flow on muscle metabolic recovery.

To our knowledge, only one study previously combined NIRS and ^{31}P -MRS measurements to investigate the physiological background of delayed metabolic recovery in CHF [1]. In agreement with our study, that study showed that both PCr and HHb recovery were delayed in CHF patients. However, in contrast with our study, Hanada et al. reported faster muscle re-oxygenation than PCr resynthesis in CHF patients, leading the authors to conclude that muscle metabolic recovery may depend primarily on the capacity of oxygen utilisation rather than on oxygen delivery. Several methodological differences may have contributed to this discrepancy with our results. First, the exercise protocol that we used was completely different from that used by Hanada et al. In our study, exercise involved a larger muscle group (quadriceps versus calf muscles) and, therefore, impairments of O_2 delivery may have had a greater influence on metabolic recovery. Also, we adjusted the exercise intensity based

on individual phosphocreatine depletion, therefore standardizing metabolic responses during recovery in patient and control groups. In contrast, Hanada et al. used a percentage of maximal workload to determine exercise intensity. This approach resulted in a marked end-exercise muscular acidosis in the patient group (pH: 6.56 ± 0.01 vs 6.93 ± 0.04 in the present study). Yet, previous studies showed that at these low pH values, the rate of PCr resynthesis cannot be used as reliable measure of mitochondrial function due to an increased proton efflux rate [16-18]. In fact, it may have lead to a substantial underestimation of the rate of recovery of mitochondrial oxidative metabolism in the patient group. Another important methodological difference with our study is the fact that Hanada et al. did not perform ^{31}P MRS and NIRS measurements simultaneously. This may have lead to differences in muscle sample areas. Yet, as shown recently, small differences in muscle sample areas may lead to considerable differences in microvascular oxygenation kinetics [40]. Finally, considering the analysis of the NIRS data, Hanada et al. did not include a time delay in the evaluation of the kinetics of muscle tissue re-oxygenation. However, our results showed that such a time delay can be of considerable magnitude in CHF patients (19 ± 22 sec) and should therefore be included in the overall kinetic analysis of muscle tissue oxygenation.

Clinical implications

This study investigated the pathophysiological mechanisms underlying the delayed muscle metabolic recovery in moderately impaired CHF patients. Although this issue has been previously addressed in the literature, the current study adds important new information. First, all CHF patients were on beta-blockers, reflecting a more contemporary clinical practice. Second, compared with previous studies, a larger muscles mass was evaluated and, therefore, the results may have implications to whole body exercise. From a clinical point of view, the results of this study imply that in order to increase the functional capacity of these patients, therapeutic interventions should primarily be aimed at increasing local skeletal muscle blood flow. This assertion is in accordance with the so called “muscle hypothesis”, which proposes that CHF is a vicious cycle where a disturbance in central hemodynamics triggers compensatory mechanisms that eventually result in chronic underperfusion of skeletal muscles [41], and, as a consequence, in an impaired exercise capacity. Therapeutic strategies that may be used to improve skeletal muscle perfusion include reducing local vasoconstriction or improving local endothelial function (e.g. by endurance training) [42], and improving the distribution of blood flow by reducing the metabolic demands in other tissues (e.g. by inspiratory muscle training) [43].

Study limitations

Before drawing definitive conclusions from this study, some limitations should be acknowledged. First, although we demonstrated a difference in the kinetics of muscle metabolic recovery and muscle re-oxygenation between CHF patients and healthy subjects at a group level, we did not observe a significant correlation between the kinetic variables. This may, at least in part, be attributed to the relatively small sample size of this study. Another explanation for the lack of correlation may be physiological heterogeneity in both patient and control groups. Therefore, studies with larger study populations are needed to identify subgroups with different physiological profiles and different underlying mechanisms of exercise tolerance. Second, due to the fact that ^{31}P MRS was used to estimate muscle metabolism, the exercise protocol involved single leg extensions in the supine position. It is, therefore, not certain whether the results of this study also apply to whole body exercise in an upright position. However, as the present study suggest that recovery from local exercise is already limited by muscle blood flow, it can be expected that this also applies to whole body exercise. Indeed, Belardinelli et al. demonstrated a slower recovery of muscle tissue

oxygenation following upright submaximal cycling exercise in CHF patients [25]. Nevertheless, future studies investigating the pathophysiological mechanisms of delayed metabolic recovery in CHF patients should also include whole body exercise.

Conclusions

The present study showed that muscle metabolic recovery following submaximal single leg extension is delayed in moderately impaired CHF patients. This prolonged metabolic recovery is associated with an even slower muscle tissue re-oxygenation, suggesting that recovery from submaximal exercise in these patients is limited by a reduced muscle blood flow, rather than an impaired O₂ utilization. This implies that, in order to increase the functional capacity of these patients, therapeutic interventions should primarily be aimed at increasing local skeletal muscle blood flow.

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Figure 1 Representative examples of the time course of phosphocreatine (PCr) and deoxygenated hemoglobin (HHb) during recovery from single leg extensions in a patient with chronic heart failure (A, B) and a healthy control subject (C, D)

(A,C) The curved lines represent the mono-exponential model fits of PCr recovery. Calculated values of the time constants (Tau-PCr) and the corresponding coefficients of determination (R^2) are shown in the figure. (B,D) The curved lines represent the mono-exponential model fits of HHb recovery. Calculated values of the time delays (TdHHb), the time constants (Tau-HHb), the coefficients of determination (R^2) and the mean response times (MRT-HHb) are shown in the figure.

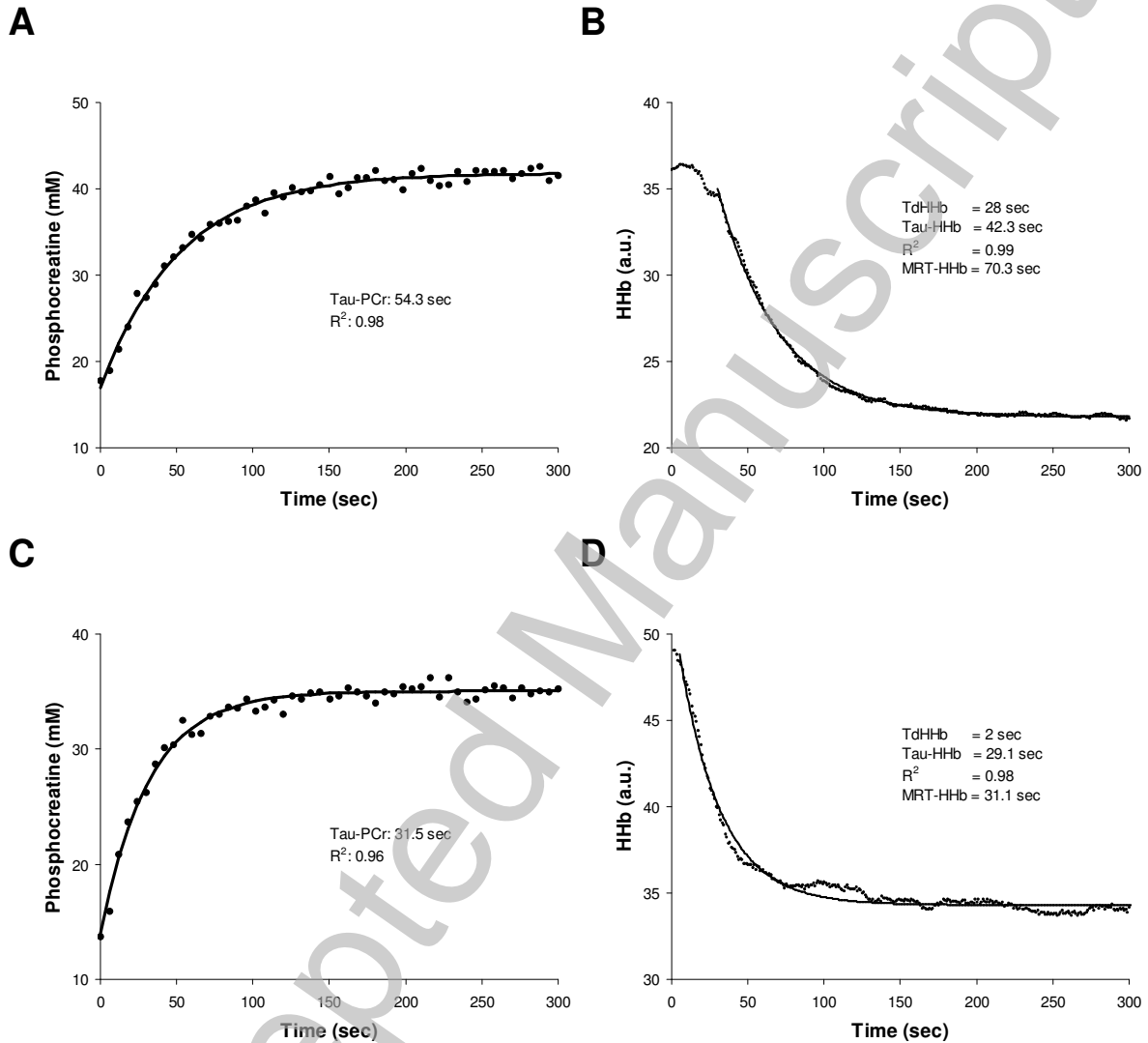


Figure 2 Kinetic parameters of phosphocreatine (time constant, Tau-PCr) and deoxygenated hemoglobin (mean response time, MRT-HHb) during recovery from submaximal single leg extension in chronic heart failure (CHF) patients ($n=13$) and healthy controls (Control, $n=8$)

* $P < 0.05$ between CHF patients and healthy controls

† $P < 0.05$ between Tau-PCr and MRT-HHb

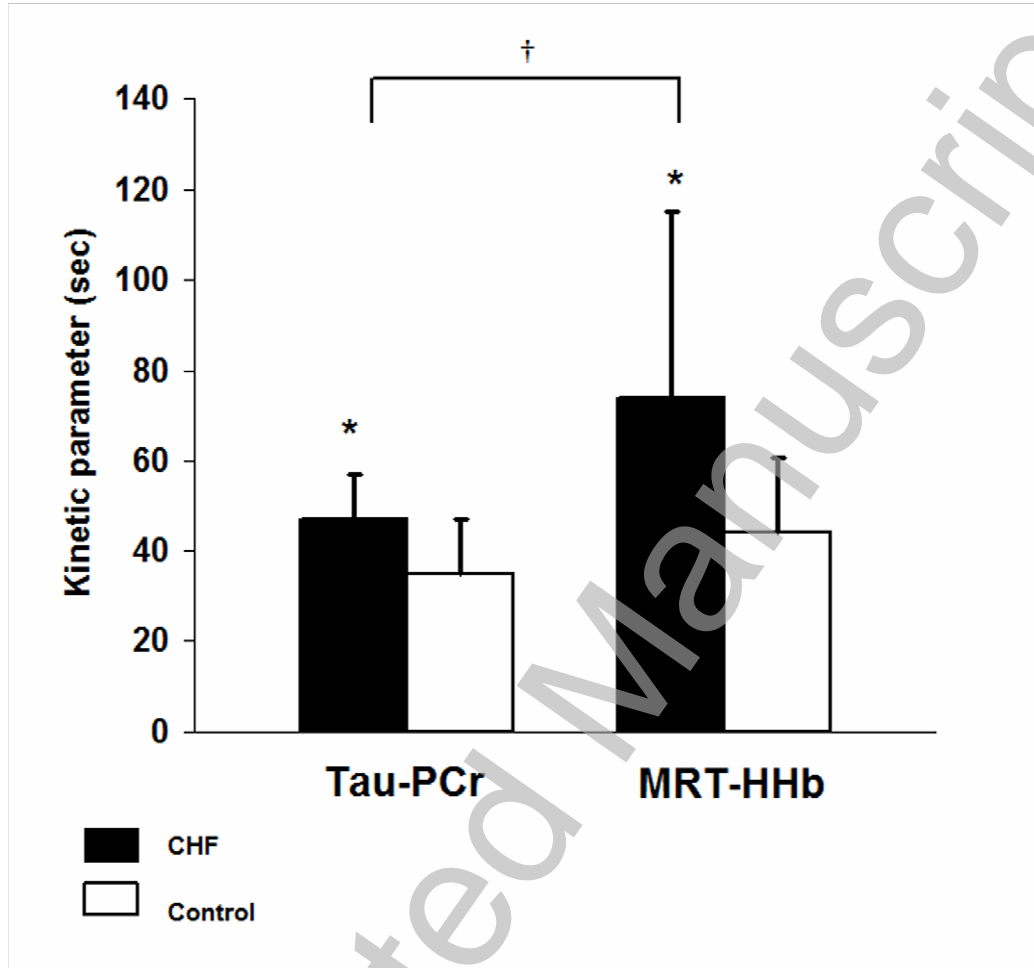


Table 1 Clinical characteristics of the study population

CHF = chronic heart failure; LVEF = left ventricular ejection fraction; ICM = ischemic cardiomyopathy; DCM = dilated cardiomyopathy; NYHA = New York Heart Association; ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker

Variable	CHF patients (n=13)	Control subjects (n=8)	P value
Age (years)	60 ± 14	59 ± 13	NS
Body mass index (kg/m ²)	28 ± 3	28 ± 4	NS
Male / female (%)	92 / 8	88 / 12	NS
Peak oxygen uptake (ml · kg ⁻¹ · min ⁻¹)	19.5 ± 4.9	36.7 ± 14.2	0.006
LVEF (%)	36 ± 5	-	
ICM / DCM (%)	46 / 54	-	
NYHA class II/III (%)	85 / 15	-	
Diuretics (%)	46	-	
Spironolactone (%)	39	-	
ACE inhibitor / ARB (%)	100	-	
Beta-blockers (%)	100	-	
Digoxin (%)	0	-	
Oral anticoagulation (%)	46	-	

Table 2 Parameters obtained by ³¹MRS and NIRS at rest and the end of exercise

CHF = chronic heart failure; PCr = phosphocreatine

Variable	CHF patients (n=13)	Control subjects (n=8)	P value
Rest			
PCr (mM)	38.6 ± 2.7	35.3 ± 2.6	0.03
pH	7.06 ± 0.02	7.07 ± 0.02	NS
Exercise			
PCr (mM)	19.7 ± 4.0	18.2 ± 4.6	NS
pH	6.93 ± 0.04	6.92 ± 0.05	NS
PCr depletion	0.49 ± 0.09	0.48 ± 0.13	NS