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REVIEW

Peripheral and respiratory muscles in chronic heart failure

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ABSTRACT: It is well-established that in patients with congestive heart failure (CHF), exercise is limited by fatigue and shortness of breath. The poor correlation between the fatigue and indices of central haemodynamic function might indicate that peripheral muscle alterations contribute to impaired exercise capacity. Intrinsic abnormalities of the skeletal muscles have been suggested as a possible explanation.

Since the shortness of breath correlates poorly with changes in lung function, changes in the respiratory muscles have been investigated. Studies have demonstrated diaphragmatic myopathy and atrophy similar, in part, to the changes in peripheral skeletal muscles. In CHF, type I (slow twitch) fibre atrophy is seen in respiratory as well as in peripheral muscles.

The mechanism of these alterations remains to be elucidated. Studies into the mechanism of muscle dysfunction in congestive heart failure are relevant to the prospect of treatment of the changes in peripheral and respiratory muscles.
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Muscle fatigue and dyspnoea are the major symptoms reported by patients with congestive heart failure (CHF) [1]. Several mechanisms, operating at different sites, may contribute to the development of these symptoms [2]. Animal as well as human studies have shown changes in contractile properties, histology and biochemistry of peripheral muscles as possible contributors to the reduced exercise performance [3, 4]. Recently, it was found that diaphragmatic structure and function are also compromised in CHF [5–7]. It has even been suggested that selective inspiratory muscle dysfunction may occur in CHF [8]. Diaphragmatic myopathy and reduced contractile function are the major findings in animal and human studies of respiratory muscles in CHF [5–7, 9]. The mechanism behind the muscle weakness and the contribution of the myopathy to the impaired exercise capacity and dyspnoea are not fully understood, nor are the clinical implications of these changes. Certainly, the peripheral muscle weakness leading to impaired exercise performance is disabling in daily life. The role of respiratory muscle weakness has not been completely elucidated. Whether it could contribute to failure to wean from mechanical ventilation [10] needs further research. This review summarizes data on the changes in peripheral and respiratory skeletal muscles seen in patients with heart failure. Changes in peripheral muscles are generally better documented than alterations in respiratory muscles. Only a few studies have so far addressed the changes produced in the diaphragm by CHF.

Factors contributing to exercise limitation

Failure of central motor drive to peripheral muscles might be a possible explanation for poor exercise capacity [2]. However, when central motor drive was quantified by delivering tetanic nerve stimulation during maximal voluntary contraction, the resulting increases in force were similar in CHF and control patients, and thus central motor failure could be excluded. The neuromuscular junction was examined by quantifying the amplitude of the compound action potential in response to a single nerve stimulus during fatigue. The amplitude of the motor response was not reduced in CHF patients. A significant correlation between the degree of muscle dysfunction and exercise capacity was, however, apparent in patients with CHF [2].

In the past, central haemodynamics and ventricular function were considered important determinants of exercise capacity. However, only poor relationships have been found between these measurements and exercise intolerance [11, 12]. Consequently, factors other than haemodynamics have been sought to explain the fatigue. More recently, it has been accepted that peripheral adaptive mechanisms play a significant role. Heart failure results not only in a fall in cardiac output but also in redistribution of blood flow favouring some regional vascular beds (brain and heart) at the expense of others (kidney and skeletal muscle) [13]. This is due to local peripheral vasoconstriction, mediated by increased sympathetic tone and activation of the plasma renin angiotensin system [13]. Acute heart failure elicits a sympathetic nervous response. This is less important in chronic heart failure, as the responsiveness to β-mimetic stimuli is attenuated due to receptor downregulation [14]. As a consequence of the chronically reduced blood flow, endothelium-mediated vasodilatation is reduced [14, 15]. In addition, fluid and sodium retention in heart failure and structural alterations of the vessel wall may contribute to increased vascular stiffness and changes

in local flow [14, 15]. It is important to note that a redistribution of blood flow is seen not only between the regional beds but also within the muscle itself [16]. DREXLER *et al.* [16] demonstrated, using the radiolabelled microsphere technique, that the flow to muscles with predominant white, glycolytic fibres (white portion of the vastus lateralis and white part of the gastrocnemius) is maintained in rats with CHF in contrast to the blood flow to muscles with predominantly oxidative fibres, such as the soleus and the red portion of the gastrocnemius. As blood flow is proportional to the oxidative capacity of muscle fibres [17, 18], it is possible that these findings support the interpretation that in heart failure a shift takes place from aerobic (oxidative) to anaerobic metabolism.

The importance of these haemodynamic factors has, however, been questioned by several studies. Acute improvements in haemodynamics caused by vasodilators could not be translated into an enhanced oxygen availability [15, 19]. Drugs which inhibit alpha-receptors and limit sympathetic-mediated vasoconstriction, or those that block the generation of angiotensin II, do not improve exercise tolerance immediately [15, 16]. Haemodynamic studies by WILSON and co-workers [20] showed that skeletal muscle underperfusion is not always a limiting factor in the exercise fatigue of CHF patients. They measured leg blood flow in CHF patients and showed that it was impaired in an important proportion of CHF patients. A quarter of the patients studied, however, did not show skeletal muscle underperfusion, as evidenced by normal leg blood flow. These findings may indicate that the influence of insufficient perfusion is minimal. Conversely, it is important to emphasize that long-term administration of angiotensin-converting enzyme (ACE) inhibitors and of vasodilators, both with venous and arterial effect, seems to restore exercise capacity, at least partially, due to their peripheral activity. This is likely to be related to their vasodilatory effect [15].

Release of cytokines in heart failure could affect skeletal muscle. It has been demonstrated by WILCOX *et al.* [21] that diaphragm contractility decreases in response to an infusion of tumour necrosis factor-alpha (TNF-α). As studies have shown elevated serum levels of TNF in chronic heart failure [22], the effects of this cytokine on limb muscle could explain part of the skeletal muscle failure in CHF.

Alterations in skeletal muscle

Skeletal muscle function

Measurements of skeletal muscle function in CHF patients have usually shown a tendency for a reduction in muscle strength, although some have not found a decrease. A marked reduction was regularly found in the static and dynamic endurance of large skeletal muscles, such as the quadriceps, as well as of smaller muscles, such as foot dorsiflexors [2, 20, 23, 24]. In a study by MINOTTI and co-workers [24] dynamic endurance, quantified as the decline in peak torque during 15 successive isokinetic knee extensions, was significantly reduced in the CHF group compared to controls (fig. 1). During aerobic

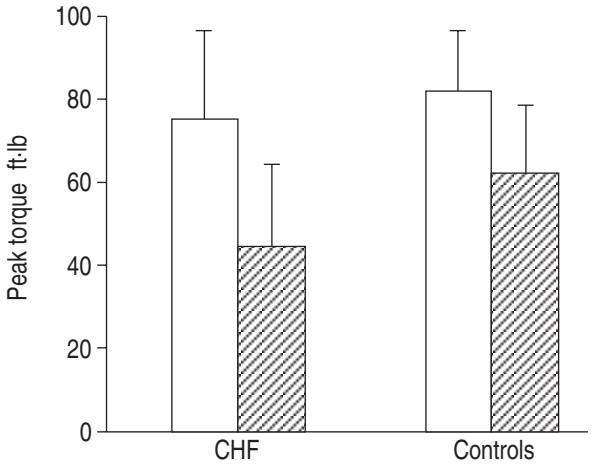

Fig. 1. – Values for peak torque of the knee extensors (mean±SD) during ischaemic isokinetic exercise at 90 degrees·s^{-1} in patients with congestive heart failure (CHF) and controls in the first three (▭) and final three repetitions (▭). The absolute peak torque (force) is lower and the peak torque decline is greater in the patients with CHF compared to controls. (From [24] with permission).

exercise the peak torque declined to 65% of the initial value in CHF patients compared to 86% in the control group during the isokinetic exercise at 90 degrees·s^{-1} ($p<0.002$). In addition, during ischaemic exercise a greater decline in peak torque was seen in CHF patients compared to controls (to 56 *vs* 76% of initial torque value; $p<0.01$). Static endurance, defined as the time required for force to decline to 60% of the maximum, during a sustained maximal voluntary contraction, was similarly reduced in the patients compared to controls (40±14 *vs* 77±29 s; $p<0.02$). Moreover, a close relationship between the degree of muscle dysfunction and exercise capacity, measured as peak oxygen consumption, was seen ($r=0.9$; $p<0.001$ for endurance determined at 90 degrees·s^{-1}, and $r=0.66$; $p=0.005$ for endurance at 180 degrees·s^{-1}) [24]. This finding suggests that impaired muscle endurance may play a role in determining exercise performance in these patients. One research group, however, found a reduced endurance in the quadriceps but not in the adductor pollicis [25]. This finding could suggest that deconditioning plays a role in the muscle weakness, as upper limbs seem to be less affected than lower limbs. Peripheral arterial insufficiency seems unlikely as an explanation for these differences. In contrast to heart failure, an inadequate blood flow without heart failure induces a decrease in glycolytic enzymes, whereas oxidative metabolism is relatively preserved. Mild peripheral arterial insufficiency even increases oxidative enzymes [26]. This makes it unlikely that chronically impaired nutritive muscle blood flow is sufficient to explain the changes observed.

Skeletal muscle metabolic abnormalities

Nuclear magnetic resonance (NMR) spectroscopy with ^{31}P permits noninvasive evaluation of intracellular metabolic responses to exercise, as it allows assessment of phosphocreatine (Pcr) utilization and intracellular pH [27]. The ratio of inorganic phosphate (Pi) to Pcr (Pi/Pcr) gives an estimate of adenosine diphosphate (ADP) concentration, as ADP is released from the breakdown

of the adenosine triphosphate (ATP) in amounts equal to those of Pi. As the ADP level is closely linked to mitochondrial respiration, the Pi/Pcr ratio provides an index of oxidative metabolism.

WILSON and co-workers [27] and MASSIE and co-workers [28] reported that repeated exercise at increasing workloads increased Pcr depletion and reduced pH more in patients with CHF than in control subjects. To exclude the possibility that the findings were due to a difference in relative workloads (controls in comparison with atrophic muscles of CHF patients), MASSIE and coworkers [29] normalized the workload to the maximal strength of each individual. The marked degree of acidification which was then found in CHF patients, indicates a greater dependence on glycolytic metabolism. It was demonstrated that these metabolic differences were independent of perfusion by measuring the blood flow by venous plethysmography [29], and by performing exercise under ischaemic conditions [23]. Moreover, Pcr recovery (which depends on oxidative phosphorylation) was not impaired. How this result relates to insufficient oxygen delivery is unclear. It is possible that the analysis of Pcr recovery used in this study was not sufficiently sensitive to detect impairment. ARNOLDA *et al.* [3] demonstrated similar changes in rats with heart failure. These NMR findings show that intrinsic changes are present in skeletal muscle in CHF. Their contribution to impaired exercise capacity needs to be elucidated further.

Histological and biochemical changes

Muscle biopsies have been performed in CHF patients in order to investigate the metabolic abnormalities. Histological and biochemical changes are summarized in table 1. Structural changes, such as increased lipid deposition and interstitial cellularity, as well as muscle fibre atrophy, have been described [4]. Reduction in oxidative enzyme capacity and maintained glycolytic and glycogenolytic enzyme function have been demonstrated. These results could be explained by the important finding of an increase in the percentage of type II (fast twitch) glycolytic fibres and a reduced proportion of type I (slow twitch) oxidative fibres [4, 30, 31]. Differentiation of the type II fibres showed the IIb fibres to be responsible for the increase in the percentage of type II fibres [30, 31]. SABBAH *et al.* [32] obtained similar results in the triceps muscle of dogs with heart failure. HOWELL *et al.* [9] could not demonstrate such a fibre shift in the latissimus dorsi of mini-pigs with CHF induced by supra-ventricular tachycardia, although a shift was found in the diaphragm.

Concerning fibre atrophy, variable results have been reported. SULLIVAN *et al.* [30] and HOWELL *et al.* [9] demonstrated type IIb atrophy, whereas MANCINI *et al.* [31] found atrophy both of IIa and IIb fibres. SABBAH *et al.* [32], on the contrary, found slight but comparable atrophy both of type I and type II fibres. BRUNOTTE *et al.* [33] found no histological alterations in the calf muscle of rats with CHF induced by coronary ligation, although biochemical changes were noted. In the rats examined by BRUNOTTE *et al.* [33] the infarction induced was, however, smaller than 46%. Haemodynamic alterations are seen only with infarctions greater than 46% [34]. The infarctions in the study by BRUNOTTE *et al.* [33] may have been too small to induce histological changes in the muscle. Findings with regard to capillary density have also been variable. DREXLER *et al.* [4] found that the number, size and ultrastructure of mitochondria were altered in CHF patients compared with control subjects (table 1). These changes are consistent with the above described ^{31}P NMR studies [31].

One research group measured a significant reduction in the concentration of membrane bound Na,K-adenosine triphosphatase (ATPase) in the skeletal muscle of patients with cardiac failure [35].

Notably, the changes are in contrast with the alterations seen in normal aging, where a shift to a lower percentage of type IIa and IIb fibres is seen with a corresponding increase in type I fibres [36].

The contribution of deconditioning to the skeletal muscle changes remains to be determined since, as in CHF, the type of fibre atrophy in deconditioning is not yet fully elucidated. Some studies have demonstrated type I atrophy during immobilization [37], but others suggest type II atrophy with disuse [38]. Moreover, the type of fibre atrophy seems to be dependent upon the cause of deconditioning [38], and on the initial fibre type distribution [39].

Table 1. – Histological and biochemical changes in peripheral skeletal muscle in CHF

Structural changes
Interstitial cellularity↑
Lipid content↑
Capillary density ↑ or =
Volume density mitochondria↓
Mitochondrial surface cristae↓
Glycogen↓
Enzyme activity
Oxidative enzyme activity
β-hydroxyacyl-CoA dehydrogenase↓
Citrate synthase↓
Succinate dehydrogenase↓
Cytochrome oxidase↓
Glycolytic enzyme activity
Phosphofructokinase=
Lactate dehydrogenase=
Membrane bound Na-K ATPase↓
Fibre type percentage
IIb↑
IIa=
I↓
Muscle function
Strength (↓)
Endurance↓

CHF: congestive heart failure; ATPase: adenosine triphosphatase; =: no change; ↓ : decrease; ↑ : increase; ( ): variable result.

Respiratory muscle involvement

Normal daily activities in patients with heart failure are limited not only by peripheral muscle fatigue, but also by dyspnoea. The pathophysiology of dyspnoea in heart failure has not been studied as extensively as the pathophysiology of peripheral muscle fatigue. The factors contributing to exertional dyspnoea seem to be more

numerous than those contributing to peripheral muscle fatigue. Firstly, in heart failure the work of the respiratory muscles is increased by several mechanisms. Minute ventilation is greater during exercise, due to the greater stimulation of the respiratory centre in the brain stem by metabolic changes in the skeletal muscles, and the consequent increased lactate release into the bloodstream [1, 20]. The circulating lactate is buffered by bicarbonate, resulting in the production of carbon dioxide, which stimulates the respiratory centres [1].

Mechanical phenomena also contribute to the increased workload of the respiratory muscles. Chronic intrapulmonary changes lead to a reduction in pulmonary compliance: congestion and resulting oedema make the lung stiffer [1]. It has also been shown that during exercise the physiological pulmonary dead space per breath almost doubles in patients with heart failure, whereas it remains relatively unchanged in normal subjects. The increase in dead space/tidal volume ratio is related to the rapid shallow breathing seen in patients with heart failure [40]. Not only is the workload increased in CHF, but there is also a decrease in function of the respiratory muscles as seen in altered contractile properties, reduced blood flow and histological and histochemical changes.

Alterations in contractile properties of the diaphragm

HAMMOND *et al.* [41] showed a marked reduction in maximal respiratory pressures, used as an index of respiratory force, whereas the handgrip force was less dramatically reduced. MCPARLAND *et al.* [8] suggested that in CHF inspiratory muscle weakness may occur even without peripheral muscle impairment (fig. 2), indicating that the respiratory dysfunction is not simply part of a generalized skeletal muscle weakness. In these studies, however, handgrip force was taken as an index of limb muscle strength and upper limbs have been shown to be less affected than lower limbs in CHF [25]. The influence of CHF on different characteristics of the respiratory muscles has been described in several animal and human studies.

Animal studies. SUPINSKI *et al*. [5] reported reduced diaphragmatic strength and increased diaphragmatic fatiguability in dogs, in which heart failure was induced by ventricular pacing. The tetanic force was significantly reduced as well as the twitch force. During the fatigue run, the rate of fatigue was substantially greater in dogs with heart failure despite similar phrenic blood flows in heart failure and control groups. CHEMLA *et al.* [6] and LECARPENTIER *et al.* [42] found a decreased mechanical performance of the diaphragm in Syrian hamsters, both in the twitch and tetanic modes. In addition, in our laboratory, research has been done on Syrian hamsters with congenital heart failure [43]. A reduction in diaphragmatic force (both tetanic and twitch) was found and this remained after normalization for the cross-sectional area, suggesting a myopathy of the diaphragm. The endurance was greatly impaired at 160 Hz but not at 25 Hz. The time-to-peak-tension appeared unaltered, in contrast to the half-relaxation-time, which was significantly reduced. In the force-frequency curve, a limited shift to the right was seen [43]. Similar alterations were found by HOWELL *et al.* [9] in a model of mini-pigs with CHF induced by pacing. The diaphragmatic force was reduced at all stimulation frequencies. CHF did not significantly alter the time-to-peak-tension but markedly shortened the half-relaxation-time. No low frequency (40 Hz) fatigue could be observed.

Human studies. Similar results were found by MANCINI *et al*. [7] in patients with CHF. They demonstrated a significant increase in the tension-time index at rest and throughout exercise in patients with heart failure compared with normal subjects ($p<0.05$). This index is calculated for each breath and is the product of transdiaphragmatic pressure/maximal transdiaphragmatic pressure ($P_{di}/P_{di,max}$) × duty cycle (t_I/t_{tot}) [44]. It describes the relationship between force of contraction and duration of contraction and is inversely related to endurance. The significant increase in the tension-time index resulted primarily from increased P_{di} as the duty cycle was comparable between the two groups. A significant correlation was found between the dyspnoea ratings assessed by the Borg scale and the tension-time index

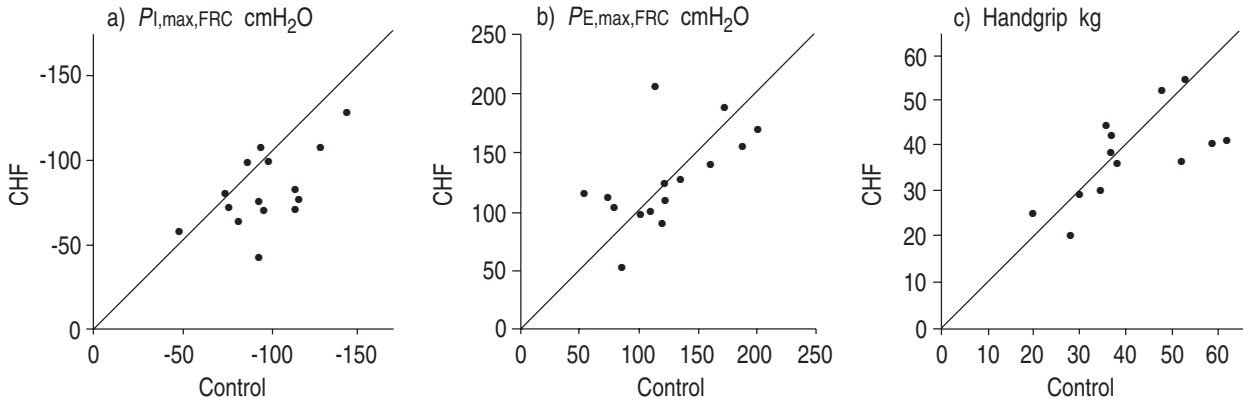

Fig. 2. – Relationship of matched controls to congestive heart failure (CHF) patients for: a) inspiratory muscle strength; b) expiratory muscle strength; and c) limb muscle strength. $P_{I,max,FRC}$: maximum inspiratory mouth pressure at functional residual capacity; $P_{E,max,FRC}$: maximum expiratory mouth pressure at functional residual capacity. Diagonal lines are the lines of identity. It can be seen that patients with CHF showed a reduction in $P_{I,max,FRC}$ compared with their matched control patients. Expiratory muscle strength and handgrip strength are not significantly different between the two groups. (From [8] with permission).

as a parameter of diaphragmatic work (p=0.009). Furthermore, a significant correlation was demonstrated between the dyspnoea index and forced expiratory volume in one second (FEV_1) (p=0.02), but not with other pulmonary function tests. Further relationships were present between the dyspnoea index and deoxygenation of the serratus anterior measured by near infrared spectroscopy (p=0.01), and between dyspnoea and maximal inspiratory pressure ($P_{I,max}$) (p=0.009). A weaker correlation was observed with maximal expiratory pressure ($P_{E,max}$) (p=0.03) as an index of respiratory muscle strength [7]. In the study by MANCINI *et al.* [7], patients with heart failure showed a significant decrease in $P_{E,max}$, but only a tendency to reduced $P_{I,max}$ at rest. Moreover, no low frequency fatigue could be induced by bilateral transcutaneous phrenic nerve stimulation at 1 Hz [7].

MCPARLAND *et al.* [45] demonstrated strong correlations between dyspnoea and $P_{I,max}$ and $P_{E,max}$, as indices of inspiratory and expiratory muscle strength, respectively. It was concluded that inspiratory muscle strength accounted for most of the variance in the dyspnoea-index in heart failure at functional residual capacity (FRC). Addition of expiratory muscle strength to the regression model did not significantly enhance the explained variance. This is in contrast with the findings of MANCINI *et al.* [7]. In contrast to other authors [7, 40], MCPARLAND *et al.* [45] could not demonstrate significant reductions in spirometric values. In view of the known relationship between vital capacity and $P_{I,max}$, the reduction in inspiratory muscle force was not very severe [46]. Moreover, the potential clinical consequences of the respiratory weakness observed remain unclear. AMBROSINO *et al.* [47] observed a significant reduction both of $P_{I,max}$ and $P_{E,max}$ in combination with a slight but significant increase in respiratory frequency in CHF.

Changes in blood flow and oxygenation

During exercise, MUSCH [48] determined the response of blood flow to muscles involved in respiration, in rats with CHF induced by occlusion of the left main coronary artery. He detected a significantly greater blood flow to the diaphragm during exercise in rats with CHF. The blood flow to other respiratory muscles remained similar. Whether this increase in blood flow to the diaphragm observed in the infarcted group of rats is a response to an increase in energy demands remains to be determined. The arterial oxygen tension (P_{a,O_2}) and arterial carbon dioxide tension (P_{a,CO_2}) were unchanged during exercise in the rats with CHF and in a sham-operated group of rats, suggesting the same effective alveolar ventilation. In patients with CHF compared with controls at rest, AMBROSINO *et al.* [47] found a similar P_{a,O_2} but a reduced P_{a,CO_2}. By near infrared spectroscopy, MANCINI *et al.* [7] demonstrated that the deoxygenation (of haemoglobin) of the serratus anterior (an accessory respiratory muscle) during exercise appeared to be more marked in CHF compared to controls, although the total blood volume of this muscle remained unchanged.

Histological and histochemical alterations

As noted previously, alterations in skeletal muscle fibre type, size and enzyme content have been demonstrated in peripheral skeletal muscle. It might be expected that the respiratory muscles, which are also skeletal muscles, would be affected in the same manner. However, LINDSAY *et al.* [49], who investigated 14 CHF patients undergoing cardiac transplantation, could not fully confirm this hypothesis. They did not find the same alterations as described in peripheral muscles, although they found structural abnormalities in some of the patients. Histological examination of the diaphragm of Syrian hamsters with CHF in our laboratory showed type I atrophy in combination with an increase in proportion of type I fibres (unpublished data). Histological studies of the diaphragm of mini-pigs revealed atrophy of type I fibres but also of type IIa and IIb fibres, as well as an increase in the proportion of type I fibres and a decrease in the proportion of type II fibres [9].

These changes are not similar to those found in peripheral muscles, which could imply different pathophysiological mechanisms in the two muscle groups. The mechanism of these changes and of the differences between the two muscle groups remains to be elucidated. The observation of a difference between respiratory and peripheral skeletal muscle could potentially be explained by a more important contribution of deconditioning to changes in peripheral muscle. The workload on the respiratory muscles is not diminished in heart failure and may even be enhanced by increased ventilation and reduced compliance [1, 40]. Another difference between the two muscle groups could be the fact that perfusion is differently affected. Also, a difference in receptors for humoral factors, influencing skeletal muscles (for example the cytokines) between respiratory and peripheral muscles may have to be taken into account. These hypotheses need further examination.

Are skeletal muscle abnormalities reversible?

STRATTON *et al.* [50] trained the forearm muscles of 10 males with CHF. They found an increased endurance and Pcr resynthesis, suggesting improvement of oxidative capacity by training and the possibility of partial reversal of the skeletal muscle metabolic abnormalities. In addition, it was shown that selective respiratory muscle training, improved respiratory muscle endurance and strength, with a subjective improvement of dyspnoea [51]. These findings raise the important question of whether alterations in skeletal muscle in patients with CHF result from deconditioning. There is, however, considerable evidence against deconditioning as the sole explanation of the metabolic changes observed. Lack of exercise can hardly be accepted as a cause of respiratory muscle weakness, as ventilation is actually increased in CHF [40]. Moreover, in patients with the chronic fatigue syndrome, who are certainly deconditioned, similar abnormalities could not be demonstrated by ^{31}P NMR during exercise testing [52]. In addition, lack of exercise decreases hexokinase and increases

lactic dehydrogenase [53]. These metabolic changes were not found in rats with CHF [3]. The fact that the same abnormalities are present in small postural muscles, which are less prone to disuse [2], as in large muscles, and that the same abnormalities are seen in patients with CHF who remain active suggests that the changes cannot be attributed solely to disuse.

Acute improvements in haemodynamics by means of therapy with vasodilators, ACE inhibitors or positive inotropic agents cannot induce an enhanced oxygen consumption [16, 19, 54]. Chronic treatment with vasodilators or positive inotropic agents also fails to produce a sustained beneficial effect on exercise performance, even though some exert marked haemodynamic effects [54]. Chronic treatment with ACE inhibitors increases blood flow to the exercising muscle and improves peak oxygen consumption. These protracted effects of ACE inhibitors might be due to an effect on the vessel wall [54], or to an improvement in the oxidative capacity of the working muscle. The same effects of ACE inhibitor therapy are seen in the respiratory muscles of Syrian hamsters, in which early therapy helps to preserve diaphragmatic contractility [6, 42].

STRATTON *et al.* [55] demonstrated that the metabolic abnormalities in skeletal muscle in patients with CHF persist in large part after successful heart transplantation. NMR spectroscopy with ^{31}P could not demonstrate any improvement in the alterations seen in the skeletal muscle of patients during the first 6 months after transplantation. Late after transplantation (> 6 months), the only significant improvement seen was in Pcr resynthesis. Other parameters (submaximal exercise pH, submaximal exercise Pcr/(Pcr+Pi), exercise duration, end exercise ADP concentration) remained altered, compared to controls. No adequate explanation has been found for these findings. They indicate that a reduced blood flow cannot fully explain the alterations seen in CHF. Moreover, as already mentioned, studies in patients with peripheral vascular disease suggest that chronic underperfusion of working skeletal muscle produces an increase in muscle oxidative capacity [26], rather than a decrease as found in CHF.

In conclusion, congestive heart failure is known to influence peripheral skeletal muscles and, probably even more so, respiratory skeletal muscles. Alterations in contractile properties, histology and biochemistry have been documented. More studies are needed on the mechanism of these changes produced by congestive heart failure in ventilatory and peripheral muscles.

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