

## Diaphragmatic function after intense exercise in congestive heart failure patients

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*Diaphragmatic function after intense exercise in congestive heart failure patients. T.J. Kufel, L.A. Pineda, R.G. Junega, R. Hathwar, M.J. Mador. ©ERS Journals Ltd 2002.*

**ABSTRACT:** Respiratory muscle strength and endurance is reduced in patients with congestive heart failure, making these patients susceptible to diaphragmatic fatigue during exercise.

In order to determine whether or not contractile fatigue of the diaphragm occurs in patients with congestive heart failure following intense exercise, twitch transdiaphragmatic pressures (twitch  $P_{tdi}$ ) were measured during unpotentiated and potentiated cervical magnetic stimulation (CMS) of the phrenic nerves before and at intervals after cycle endurance exercise.

Ten patients aged  $65.7 \pm 6.0$  yrs (mean  $\pm$  SD) with an ejection fraction of  $31.2 \pm 9.8\%$  performed a constant-load symptom-limited exercise test at 60% of their peak work capacity. Twitch  $P_{tdi}$  at baseline were  $15.9 \pm 6.3$  cmH<sub>2</sub>O (unpotentiated CMS) and  $28.8 \pm 10.7$  cmH<sub>2</sub>O (potentiated CMS) and at 10 min postexercise were  $16.4 \pm 4.7$  cmH<sub>2</sub>O (unpotentiated CMS) and  $27.6 \pm 10.1$  cmH<sub>2</sub>O (potentiated CMS). One patient demonstrated a sustained fall in twitch  $P_{tdi}$  of  $\geq 15\%$ , considered potentially indicative of diaphragmatic fatigue.

Contractile diaphragmatic fatigue is uncommon in untrained patients with congestive heart failure following high-intensity constant-workload cycle exercise. Therefore, diaphragmatic fatigue is an unlikely cause of exercise-limitation during activities of daily living in heart failure patients.

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Exercise intolerance due to dyspnoea and fatigue is a frequent and disabling symptom in patients with congestive heart failure (CHF). Some investigators believe that inspiratory muscle fatigue might be an important mediator of dyspnoea during exercise in CHF [1]. Conclusive data showing that intense exercise causes diaphragmatic fatigue in patients with CHF are not available.

The limb muscles of patients with heart failure undergo changes that predispose them to reduced endurance and contractile fatigue [2]. Similar changes might occur in the inspiratory skeletal muscles. Studies have found respiratory muscle weakness [3] and reduced respiratory muscle endurance [4] in patients with CHF. In addition, patients with heart failure show an increased ventilatory response to exercise [5], further exacerbating the imbalance between inspiratory muscle capacity and load. Therefore, it is reasonable to hypothesise that diaphragmatic fatigue may occur in patients with CHF when stressed by exercise.

The limited studies investigating respiratory muscle fatigue in patients with CHF after exercise are inconclusive. MANCINI *et al.* [1] failed to demonstrate evidence of diaphragmatic fatigue after exercise using transcutaneous electrical stimulation of the phrenic

nerves. However, the negative results may be explained partially by the fact that they failed to account for twitch potentiation, obtaining twitch measurements immediately after exercise [6]. Furthermore, the work of LEVINE and HENSON [7] suggests that an incremental exercise protocol, as used by MANCINI *et al.* [1], is of insufficient intensity and duration to result in diaphragmatic fatigue. Recently, HUGHES *et al.* [8] demonstrated a slowing of the inspiratory muscle relaxation rate (MRR) in CHF patients after exercise, implying that inspiratory muscle loading is excessive during exercise and the inspiratory muscles are in a potentially fatiguing pattern of contraction. However, this does not confirm that overt muscle fatigue is present since slowing of the MRR precedes overt muscle fatigue. Furthermore, TIKUNOV *et al.* [9] found an increased proportion of type I (slow-twitch fatigue-resistant) fibres and an increase in oxidative enzyme activity in the diaphragm of patients with CHF, suggesting that the diaphragm of heart failure patients may be more fatigue-resistant. These findings and the methodological problems described above prohibit definitive conclusions and warrant further investigation using new techniques and different methodology. Magnetic stimulation of the phrenic nerves is an accepted

alternative to electrical stimulation and is a nonvolitional, simple and reproducible technique of assessing inspiratory muscle function that reduces the difficulties encountered with electrical stimulation [10].

The purpose of the present study was to determine whether or not contractile fatigue of the diaphragm occurs in patients with moderately severe heart failure following intense exercise. Accordingly, transdiaphragmatic twitch pressure (twitch  $P_{tdi}$ ) was measured during supramaximal cervical magnetic stimulation (CMS) before and after high-intensity endurance cycle exercise to the limits of tolerance in a group of patients with CHF.

## Methods

### Subjects

Ten male patients with CHF aged  $65.7 \pm 6.0$  yrs (mean  $\pm$  SD), of height  $1.77 \pm 0.09$  m and weight  $89.7 \pm 15.7$  kg, volunteered for the present study. The diagnosis of CHF was based on a history of dyspnoea on exertion, fluid retention, fatigue and a left ventricular ejection fraction of  $\leq 35\%$ . All patients were clinically stable at the time of the study and free from overt pulmonary, musculoskeletal or neurological disease that could affect exercise performance. Patients with peripheral vascular disease, a pacemaker, uncontrolled hypertension, or abnormal electrolyte or haemoglobin levels were excluded. The aetiology of the CHF was ischaemic in nine of the patients and idiopathic in the remaining patient. The medications taken included digoxin ( $n=2$ ), diuretics ( $n=9$ ), angiotensin-converting enzyme inhibitor ( $n=10$ ), nitrates ( $n=6$ ) and  $\beta$ -blockers ( $n=2$ ). Four patients were in New York Heart Association functional Class II and six in Class III. The appropriate institutional review boards approved the study and informed consent was obtained from all subjects.

### Study design

The resting left ventricular ejection fraction was obtained by gated cardiac blood pool study. Pulmonary function was measured using standard techniques according to American Thoracic Society recommendations [11]. Maximal inspiratory pressure ( $P_{I,max}$ ) was measured as previously described [12]. Cardiac and pulmonary function measurements are shown in table 1.

A maximal symptom-limited incremental cycle exercise test was performed to determine the peak work capacity ( $W_{peak}$ ) of each subject as previously described [12]. Several days after the incremental exercise test, subjects performed constant-workload exercise at 60% of  $W_{peak}$  until they were no longer able to maintain a pedalling frequency of  $>50$  revolutions per minute despite verbal encouragement. All exercise tests, calculations of peak and mean inspiratory pressure swings, and measurement of arterialised lactate levels were performed as described previously [12]. Immediately after exercise

Table 1. – Cardiac and pulmonary function measurements

	Absolute value	Percentage of predicted value <sup>#</sup>
LVEF %	31.2 $\pm$ 9.8	
FEV <sub>1</sub> L	2.70 $\pm$ 0.48	77.3 $\pm$ 7.8
FVC L	3.54 $\pm$ 0.55	78.6 $\pm$ 6.8
FEV <sub>1</sub> /FVC %	75.6 $\pm$ 4.0	
TLC L	6.11 $\pm$ 0.92	89.0 $\pm$ 14.5
RV L	2.46 $\pm$ 0.56	103.1 $\pm$ 29.2
$DL_{CO}$ mL $\cdot$ min <sup>-1</sup> $\cdot$ mmHg <sup>-1</sup>	22.27 $\pm$ 8.0	81.0 $\pm$ 25.0
$P_{I,max}$ cmH <sub>2</sub> O	94 $\pm$ 21	87.1 $\pm$ 18.0
MVV L $\cdot$ min <sup>-1</sup>	109.1 $\pm$ 21.0	82.2 $\pm$ 11.4

Data are presented as mean  $\pm$  SD. LVEF: left ventricular ejection fraction; FEV<sub>1</sub>: forced expiratory volume in one second; FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume;  $DL_{CO}$ : diffusing capacity of the lung for carbon monoxide;  $P_{I,max}$ : maximal inspiratory pressure; MVV: maximum voluntary ventilation. <sup>#</sup>: from [13–16].

was discontinued, patients were asked to choose the symptom that they felt was most responsible for stopping exercise.

CMS of the phrenic nerve was achieved using a commercial magnetic stimulator (Magstim 200; Magstim Co. Ltd., Whitland, UK) and a 90-mm coil ( $n=10$ ) [9]. The technical details of this procedure have been described previously [12]. Recent work suggests that the potentiated twitch may be a more sensitive index of fatigue [17, 18]. Therefore,  $P_{tdi}$  twitch force (twitch  $P_{tdi}$ ) was measured using CMS 5 s after a 5-s maximal Mueller manoeuvre against an occluded airway in eight patients.

Diaphragmatic compound muscle action potentials (M-wave) were recorded with surface electrodes. The technical details of this procedure have been described previously [12]. Magnetic stimulation often results in a large shock artefact that obscures the initial portion of the M-wave. However, with repositioning of the surface electrodes and ground before initial measurements, satisfactory M-waves were obtained before and after exercise in five subjects.

Twitch  $P_{tdi}$  was defined as the peak amplitude above the immediately preceding  $P_{tdi}$  baseline. Approximately eight twitches by CMS and five potentiated twitches were obtained before and 10, 30 and 60 min after exercise. In order to prevent twitch potentiation, the unpotentiated twitches were obtained prior to measuring the potentiated twitch. Individual twitches were rejected from analysis using previously defined criteria [19].

### Statistical analysis

Changes in variables over time were analysed by repeated-measures analysis of variance. If the result of the analysis of variance was significant, measurements after exercise were compared to baseline using a paired t-test with Bonferroni correction. For each individual patient, a fall in twitch  $P_{tdi}$  after exercise of  $\geq 15\%$  at 10 and 30 min was considered potentially indicative of diaphragmatic fatigue. Before the study

Table 2. – Cardiopulmonary parameters during endurance exercise

	Resting	Mid-exercise <sup>#</sup>	End-exercise
$V'O_2$ L·min <sup>-1</sup>	0.34±0.04	1.36±0.30	1.39±0.21 (62.2±13.4)
$f_c$ beats·min <sup>-1</sup>	76.1±15.0	128.4±12.0	131.4±16.4 (85.2±11.2)
$V'E$ L·min <sup>-1</sup>	12.3±1.74	41.9±7.66	50.9±9.1 <sup>*</sup>
$V_T$ L	0.68±0.16	1.47±0.46	1.49±0.39
$f_R$ breaths·min <sup>-1</sup>	18.6±3.4	31.3±11.2	33.4±11.9
$t_I$ s	1.32±0.24	0.99±0.36	0.93±0.32
$t_I/t_{tot}$	0.40±0.24	0.46±0.03	0.47±0.03
$P_{tdi}$ cmH <sub>2</sub> O	9.57±3.31	17.78±4.93	17.76±4.04
$T_{tdi}$	0.021±0.007	0.048±0.011	0.049±0.014
$T_{toes}$	0.016±0.007	0.064±0.030	0.066±0.034
$PTP_{di}$ cmH <sub>2</sub> O·s <sup>-1</sup> ·min <sup>-1</sup>	127.6±50.0	300.8±77.0	301.5±64.2
$PTP_{oes}$ cmH <sub>2</sub> O·s <sup>-1</sup> ·min <sup>-1</sup>	86.7±34.1	325.8±86.0	331.2±94.7
Lactate mEq·L <sup>-1</sup>	1.6±0.6		5.1±1.4

Data are presented as mean±SD with the percentage of the predicted value in parentheses.  $V'O_2$ : oxygen consumption;  $f_c$ : cardiac frequency;  $V'E$ : minute ventilation;  $V_T$ : tidal volume;  $f_R$ : respiratory frequency;  $t_I$ : inspiratory time;  $t_I/t_{tot}$ : duration of total breathing cycle;  $P_{tdi}$ : transdiaphragmatic pressure;  $T_{tdi}$ : tension/time index of the diaphragm;  $T_{toes}$ : tension/time index of the oesophagus;  $PTP_{di}$ : pressure/time product of the diaphragm;  $PTP_{oes}$ : pressure/time product of the oesophagus. <sup>#</sup>: p=0.002 versus resting; <sup>\*</sup>: p=0.03 versus mid-exercise.

was performed, a power analysis was conducted assuming a normal distribution, an  $\alpha$  level of 0.05 and a power of 0.95. Using a within-subject between-trial coefficient of variation of 8%, it was found that a sample size of seven would be required to detect a 15% decrease in mean value (one-tailed). Data are expressed as mean±SD.

## Results

### Cardiopulmonary parameters during exercise

The peak oxygen consumption ( $V'O_2$ ) measured during incremental exercise was  $1.29\pm 0.31$  L·min<sup>-1</sup> or  $14.4\pm 2.3$  mL·kg<sup>-1</sup>·min<sup>-1</sup>, which was  $59\pm 18\%$  of the predicted maximum. The  $W_{peak}$  was  $95\pm 17$  W ( $64\pm 19\%$  of the predicted maximum). During incremental exercise, peak ventilation was  $53\pm 14$  L·min<sup>-1</sup>, which represented  $49\pm 15\%$  of the 12-s maximum voluntary ventilation (MVV) and the peak cardiac frequency was  $134\pm 22$  beats·min<sup>-1</sup> ( $87\pm 1\%$  of the predicted maximum).

Cardiopulmonary parameters measured during the constant-load endurance test are shown in table 2.

The patients exercised for a mean of  $10.1\pm 3.4$  min during the constant-load test at a workload of  $57\pm 11$  W ( $60\pm 2\%$  of  $W_{peak}$ ). The peak  $V'O_2$  during constant-load exercise was  $1.39\pm 0.21$  L·min<sup>-1</sup>, which was  $111\pm 16\%$  of the peak  $V'O_2$  obtained during the incremental exercise test. The peak ventilation attained during constant-load exercise was  $51\pm 9$  L·min<sup>-1</sup>, representing  $48\pm 14\%$  of the 12-s MVV. Peak cardiac frequency was  $131\pm 16$  beats·min<sup>-1</sup> ( $85\pm 11\%$  of the predicted maximum). At the end of exercise, four patients cited "shortness of breath" as the cause of exercise termination and six stopped exercise because of "leg fatigue".

### Diaphragm twitch force

Twitch  $P_{tdi}$  (unpotentiated and potentiated) was not significantly different from baseline at any time after exercise (fig. 1). Gastric and oesophageal twitch pressures (table 3) were also not significantly different

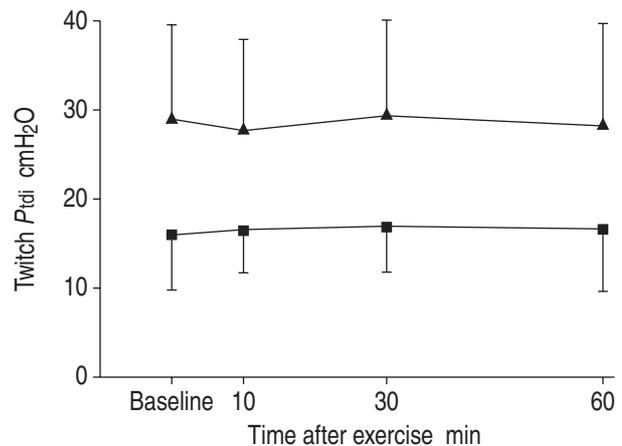


Fig. 1. – Unpotentiated (■; n=10) and potentiated (▲; n=8) twitch transdiaphragmatic pressures (twitch  $P_{tdi}$ ) before and 10, 30 and 60 min after exercise. Twitch  $P_{tdi}$  was not significantly different from baseline at any time after exercise. Data are presented as mean±SD.

Table 3. – Unpotentiated twitch pressures

	Baseline	Post-exercise		
		10 min	30 min	60 min
$P_{oes}$ cmH <sub>2</sub> O	11.6±4.3	12.2±4.1	12.4±4.1	12.7±4.8
$P_{ga}$ cmH <sub>2</sub> O	6.7±2.2	7.2±2.1	7.2±1.9	6.8±2.5

Data are presented as mean±SD.  $P_{oes}$ : oesophageal pressure;  $P_{ga}$ : gastric pressure.

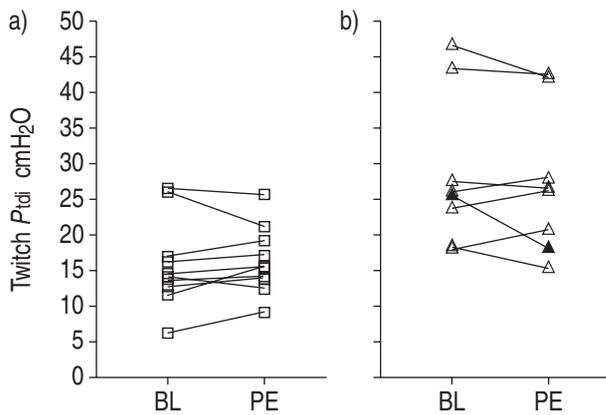


Fig. 2. – a) Unpotentiated and b) potentiated twitch transdiaphragmatic pressure (twitch  $P_{tdi}$ ) before (baseline (BL)) and 10 min after high-intensity cycling at 60% of maximal work capacity to volitional exhaustion (post-exercise (PE)) in each subject. Patients who displayed a  $\geq 15\%$  reduction in twitch  $P_{tdi}$  after exercise that persisted for 30 min were considered to have demonstrated diaphragmatic fatigue ( $\blacktriangle$ ); patients who did not meet these criteria were considered nonfatiguers ( $\% \square$ ,  $\% \triangle$ ).

from baseline at any time after exercise. One patient demonstrated a sustained fall in potentiated twitch  $P_{tdi}$  after exercise (fig. 2).

A diaphragmatic electromyogram was recorded for all subjects. Diaphragmatic M-wave amplitude was not significantly different from baseline at any time after exercise in the five subjects in whom it could be accurately measured at all times points. In the five subjects for whom M-waves could be obtained, there was no significant change in twitch  $P_{tdi}$  at any time after exercise compared with baseline.  $P_{I,max}$  was  $94 \pm 21$  cmH<sub>2</sub>O at baseline and  $93 \pm 25$  cmH<sub>2</sub>O immediately after exercise ( $p=NS$ ).

#### Breathing pattern during exercise

Mean inspiratory  $P_{tdi}$ , oesophageal pressure ( $P_{oes}$ ) and minute ventilation ( $V'E$ ) are shown in figure 3. Mean inspiratory  $P_{tdi}$  reached peak values early in exercise.  $V'E$  increased substantially early in exercise and more gradually as exercise progressed until a plateau was reached near the end of exercise. The mean inspiratory  $P_{oes}$  reached a plateau near mid-exercise. The pressure/time products and tension/time indices are shown in table 2.

#### Lactate measurements

Lactate concentration increased from  $1.6 \pm 0.6$  mEq·L<sup>-1</sup> at baseline to  $5.1 \pm 1.4$  mEq·L<sup>-1</sup> immediately after exercise ( $p=0.001$ ) and had recovered to  $2.9 \pm 0.7$  mEq·L<sup>-1</sup> at 30 min after exercise ( $p=NS$ ).

#### Discussion

The major conclusion of the present study is that contractile fatigue of the diaphragm is uncommon in untrained patients with moderately severe CHF.

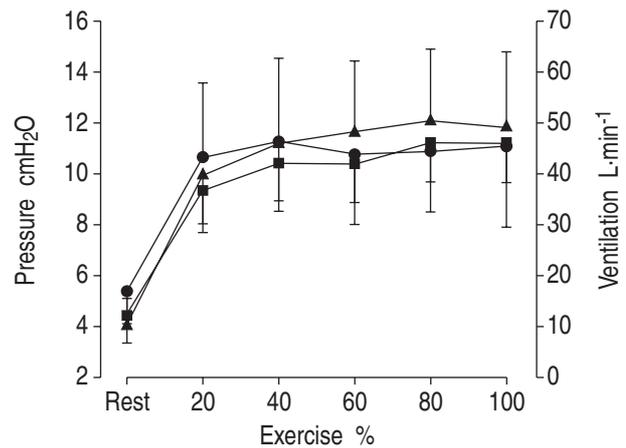


Fig. 3. – Mean inspiratory transdiaphragmatic ( $P_{tdi}$ ; ●) and oesophageal ( $P_{oes}$ ; ▲) pressures and minute ventilation ( $V'E$ ; ■) at rest and during exercise. After 20% of the exercise time,  $P_{tdi}$ ,  $P_{oes}$  and  $V'E$  reached 97, 83 and 81% of their maximal value, respectively.

#### Critique of methods

Unpotentiated CMS was used to detect diaphragmatic fatigue in a group of patients with CHF. The authors' laboratory has considerable experience with CMS and transcutaneous electrical stimulation in normal subjects and patients [6, 12, 19–22]. CMS was utilised in the present study because this method is well tolerated and technically easier to perform than transcutaneous electrical stimulation. Furthermore, congruent changes in twitch  $P_{tdi}$  were demonstrated with CMS and transcutaneous electrical stimulation in patients with chronic obstructive pulmonary disease (COPD) before and after high-intensity exercise [12]. Unlike electrical stimulation, CMS can potentially detect both ribcage and diaphragmatic fatigue [23], and fatigue of either muscle group would be clinically relevant. Thus, it was felt that CMS was ideal for the proposed experiments.

Patients were exercised at 60% of their peak workload based on prior studies performed in the authors' laboratory. Normal subjects demonstrated evidence of diaphragmatic fatigue after voluntary hyperpnoea at a  $V'E$  of 60% MVV sustained for  $\sim 8$  min [21]. Furthermore, diaphragmatic fatigue was found in normal volunteers after endurance exercise in which subjects exercised for a mean of 8 min at a  $V'E$  that was 50% of their MVV [22]. JOHNSON *et al.* [24] suggested that high-intensity exercise should be sustained for  $\geq 10$  min in order to produce significant diaphragmatic fatigue. Therefore, it was felt that a workload of 60%  $W_{peak}$  would be tolerated by patients and probably result in an exercise  $V'E$  of sufficient intensity ( $\sim 50\%$  MVV) and duration (8–10 min) to cause diaphragmatic fatigue. The subjects exercised for 10 min at a  $V'E$  of 48% of 12-s MVV. Thus they attained levels of ventilation and exercise duration similar to those previously shown to result in diaphragmatic fatigue.

Twitch potentiation [6] and lung volume changes [25] are important variables that can influence twitch

$P_{tdi}$ . A vigorous voluntary contraction can increase twitch  $P_{tdi}$  amplitude (twitch potentiation). It has previously been shown that diaphragmatic twitch potentiation decays exponentially with the greatest change occurring within the first 2 min and was minimal (<4% above baseline) 8 min after a vigorous muscle contraction [6]. Therefore, the first set of post-exercise twitch measurements were obtained 10 min after exercise and subsequent sets of unpotentiated twitches were obtained  $\geq 15$  min after any potentiation manoeuvre. End-expiratory lung volume is known to increase during exercise in patients with CHF [26]. It rapidly returns to baseline after stopping exercise in patients with COPD [27]. Patients with CHF should behave similarly.

Some may argue that significant recovery could occur during the 10-min period after stopping exercise that was allowed in the present study for the effects of twitch potentiation to resolve. However, reductions in twitch force after a fatiguing task reflect low-frequency fatigue that is known to recover very slowly. LAGHI *et al.* [17] demonstrated a reduction in twitch  $P_{tdi}$  after resistive loading that did not return to baseline levels when measured  $\sim 20$  h after task failure. Therefore, complete recovery from diaphragmatic fatigue within 10 min of terminating exercise, would not be expected.

#### *Diaphragmatic fatigue and exercise*

No change was found in twitch  $P_{tdi}$  obtained by two different methods after high-intensity cycle exercise in a group of patients with moderately severe CHF (fig. 1). None of the patients demonstrated a sustained fall of 15% in unpotentiated twitch  $P_{tdi}$ . LAGHI *et al.* [17] suggested that the potentiated twitch might be a more sensitive method for evaluating small changes in diaphragmatic contractility. In order to investigate the possibility that the unpotentiated twitch missed some patients with a small amount of diaphragmatic fatigue, potentiated twitch was measured in eight patients. One patient demonstrated a persistent fall in potentiated twitch  $P_{tdi}$  suggestive of fatigue. The changes in potentiated twitch  $P_{tdi}$  for that patient were greater than but consistent with those observed with the unpotentiated method. The within-subject between-trial coefficient of variation in the authors' laboratory for CMS is  $6.1 \pm 1\%$  [19]. A persistent 15% reduction (which is greater than twice the mean variability) in twitch  $P_{tdi}$  was chosen as being potentially indicative of diaphragmatic fatigue. A 10% cut-off would have identified two patients by the unpotentiated and potentiated methods. Interestingly, the two subjects that met the less rigid criteria identified dyspnoea as the cause of terminating exercise. It is possible that diaphragmatic fatigue is more common in those patients who identify dyspnoea as the single factor limiting exercise performance. However, as reported by HAMILTON *et al.* [28], isolated dyspnoea as the cause of premature termination of exercise is found in <15% of cardiac patients. Further study in this select group may be warranted; however, the aim of the present study was to determine

whether or not diaphragmatic fatigue occurs in a representative group of heart failure patients. There were no apparent differences between the subject who might have developed diaphragmatic fatigue after exercise and the remainder of the group in terms of left ventricular function, medication, pulmonary function, baseline exercise data or work performed during exercise.

Recently, data on 10 healthy elderly subjects aged 68.3 yrs were reported [20]. These subjects exercised at  $\sim 70\%$  of their predetermined peak workload for nearly 18 min and generated an exercise ventilation of 50% MVV. Similar to the heart failure patients presented in the current report, no change was seen in twitch  $P_{tdi}$  from baseline at any time after exercise using CMS, bilateral anterolateral magnetic stimulation or the potentiated technique. At end-exercise, the pressure/time products of the oesophagus and diaphragm for the healthy elderly were  $316 \pm 29$  and  $311 \pm 28$   $\text{cmH}_2\text{O} \cdot \text{s}^{-1} \cdot \text{min}^{-1}$  (mean  $\pm$  SEM), respectively. The end-exercise tension/time indices of the oesophagus and diaphragm were  $0.057 \pm 0.005$  and  $0.044 \pm 0.004$ , respectively. None of these values were significantly different from those obtained in the present heart failure patients. Comparisons of the study in the healthy elderly to the current study in heart failure patients is legitimate despite the fact that the healthy elderly subjects exercised slightly more intensely (70% of peak workload). Despite exercising at a greater workload for a longer duration, the healthy elderly did not attain greater ventilation than the heart failure patients (mean  $\pm$  SEM  $58.8 \pm 4.7$  versus mean  $\pm$  SD  $50.9 \pm 9.1$   $\text{L} \cdot \text{min}^{-1}$ , respectively;  $p = \text{NS}$ ) and did not demonstrate diaphragmatic fatigue despite exercising for a longer period of time. Since the healthy elderly normal subjects did not demonstrate diaphragmatic fatigue at a workload greater than that used in the present heart failure study, they would not be expected to demonstrate diaphragmatic fatigue if exercised at a lesser workload.

The present authors and others have observed diaphragmatic fatigue after endurance exercise in young healthy adults [22, 24]. Why might healthy young people develop diaphragmatic fatigue after exercise while older patients with CHF do not? It is felt that exercise-induced diaphragmatic fatigue requires a high level of sustained diaphragmatic work and an unspecified exercise-dependent factor [29]. The present subjects sustained exercise for a sufficient duration to result in fatigue. However, was the diaphragmatic work of high enough intensity to result in diaphragmatic fatigue? The pressure/time product and tension/time index were measured as estimates of inspiratory muscle work during exercise. In the present authors' laboratory, the peak pressure/time product of the oesophagus for young sedentary subjects who demonstrated diaphragmatic fatigue after exercise was significantly greater than that achieved by the patients with CHF ( $585 \pm 52$   $\text{cmH}_2\text{O} \cdot \text{s}^{-1} \cdot \text{min}^{-1}$  (mean  $\pm$  SEM),  $p < 0.001$ ) [22]. However, maximal inspiratory muscle strength was lower in the elderly CHF patients than in subjects of the previous study of younger healthy subjects [22]. Thus, the tension/time index of the oesophagus in the heart failure patients was not

significantly different from that observed in the young sedentary subjects ( $0.066 \pm 0.01$  versus  $0.083 \pm 0.009$ ,  $p = \text{NS}$ ). This suggests that the heart failure patients performed similar amounts of inspiratory muscle work relative to their capacity, and, despite exercising intensely for sufficient duration, the majority of patients did not display evidence of diaphragmatic fatigue after exercise.

Could the present subjects have attained higher levels of inspiratory muscle work? The heart failure patients were highly motivated and exercise data indicate that they terminated exercise at their physiological limits. At the end of endurance exercise, peak  $\dot{V}O_2$  was  $111 \pm 16\%$  of the peak  $\dot{V}O_2$  obtained during the incremental maximal exercise test, and peak cardiac frequency was  $85 \pm 11\%$  of the predicted maximum. The peak lactate levels generated by the heart failure patients were significantly lower than those observed in the healthy elderly (mean  $\pm$  SD  $5.1 \pm 1.4$  versus mean  $\pm$  SEM  $6.8 \pm 0.6$  mEq·L<sup>-1</sup>;  $p = 0.03$ ) [20], but was not significantly different from that observed in a group of patients with COPD (mean  $\pm$  SEM  $4.8 \pm 0.5$  mEq·L<sup>-1</sup>;  $p = \text{NS}$ ) [30]. Thus, the present subjects appear to have exercised maximally. The rationale for getting patients to exercise at 60% of their incremental  $\dot{W}_{\text{peak}}$  is reviewed above. A greater workload could have resulted in greater inspiratory muscle work, although peak exercise ventilation was similar during the endurance and maximal incremental exercise tests, but it is unlikely that patients with heart failure would be capable of sustaining higher workloads for very long. It is possible that the present subjects could not attain higher levels of inspiratory muscle work because they were forced to stop exercise because of peripheral leg muscle fatigue. It has previously been shown that quadriceps muscle fatigue occurs following endurance exercise in elderly patients [20] and in patients with COPD [30]. This possibility deserves further investigation in heart failure patients. The present data are consistent with the increased proportion of type I (slow-twitch fatigue-resistant) fibres and increase in oxidative enzyme activity in the diaphragm of patients with CHF demonstrated by TIKUNOV *et al.* [9]. Perhaps the increased work of breathing observed in patients with CHF trains the respiratory muscles as postulated for patients with COPD. These adaptations make the diaphragm more fatigue-resistant and offer an attractive explanation for the present findings.

It is well known that ageing and chronic disease result in a reduction in physical activity, deconditioning and a reduction in maximal work capacity. Exercise training in patients with CHF is increasing in popularity and has been shown to increase exercise capacity, reduce mortality and improve quality of life [31]. Whether a trained heart failure patient can perform enough work during exercise to develop diaphragmatic fatigue remains to be determined.

### Conclusion

Contractile diaphragmatic fatigue is uncommon in untrained patients with moderately severe heart

failure after a bout of constant workload exercise of greater intensity than is commonly expected during the activities of daily living for such patients. Thus, diaphragmatic fatigue is unlikely to be an important cause of exertional symptoms and exercise limitation in the majority of untrained patients with heart failure.

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