



Diaphragm function in patients with cervical cord injury or prior poliomyelitis infection

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Diaphragm function was evaluated in cervical cord injury patients (CCI), 1–3 years after injury (CCI_{1–3}) and 10 years or more after injury (CCI_{≥10}), as well as in a group of prior poliomyelitis infection patients (PPI), requiring intermittent positive pressure ventilation (IPPV) for about 6 h per night. Measurements included transdiaphragmatic pressure swings (ΔP_{di}) at rest, during maximal inspiratory efforts against closed airways ($\Delta P_{di_{max}}$) and during sniff manoeuvres (ie maximal inhalation through the nose, $\Delta P_{di_{sniff}}$), vital capacity normalized to age and height (VC_{%pred}), tidal volume (V_t), relative inspiratory time (Ti/T_{tot}), breathing frequency (f_b), and the tension-time index of the diaphragm (TTdi = $\Delta P_{di} / \Delta P_{di_{max}} \times Ti / T_{tot}$). The median VC_{%pred} was 50% in the CCI_{1–3} group and 57% in the CCI_{≥10} group, but only 28% in the PPI group. $\Delta P_{di_{max}}$ values were similar for the CCI_{1–3} (11.8 kPa) and CCI_{≥10} (11.9 kPa) groups, but were lower (7.1 kPa) in the PPI group. Due to the reduction in $\Delta P_{di_{max}}$, the PPI group had higher $\Delta P_{di} / \Delta P_{di_{max}}$ values than the CCI groups, however, the TTdi was similar amongst the different groups studied. A submaximal exercise test in five cervical cord injury patients and in five polio patients with similar $\Delta P_{di_{max}}$, $\Delta P_{di_{sniff}}$ and TTdi values at rest revealed clear group differences with respect to force development, in that CCI patients showed significant increases in TTdi, while PPI demonstrated only minor changes. In CCI patients, an increase in ventilation was accompanied by an increase in $\Delta P_{di} / \Delta P_{di_{max}}$ while in contrast, the PPI patients showed no increase in $\Delta P_{di} / \Delta P_{di_{max}}$. We conclude that CCI patients, both recently and previously injured, have a similar maximal inspiratory force and are less impaired than the PPI patients. The TTdi at rest is similar in all groups, but the PPI patients react to inspiratory loads with little increases in TTdi, while the CCI patients increase their TTdi above fatiguing (0.15) levels. The different behaviours may be linked to loss of sensory pathways in the CCI patients.

Keywords: respiratory muscles; ventilatory failure; tetraplegia; poliomyelitis

Introduction

Neuromuscular disease often involves weakness of the respiratory muscles. If breathing strategies remain unaltered, this weakness presents an increasing load on the inspiratory muscles. Braun *et al.*¹ suggested that patients with neuromuscular disorders who have paresis of the inspiratory muscles might fatigue their inspiratory muscles, which will then lead to further weakness, and subsequently to chronic hypercapnia. In these patients, periodic mechanical ventilation improved the patients' chronic hypercapnia, and was suggested to be due to rest of the respiratory muscles.¹ More recent evidence derived from experiments on respiratory muscle loading in healthy humans,² in

obstructive sleep apnea patients,³ in awake and anaesthetized animals,^{4,5} and in patients with severe chronic obstructive⁶ pulmonary disease (COPD),¹ suggests that subjects avoid fatigue of the respiratory muscles by hypoventilating. Afferent information from the over-exerted muscles may reduce the central drive in order to preserve muscle integrity.

The complex interplay between the time course of the force required to breathe and the maximal inspiratory force available is well described by the tension-time index of the diaphragm, TTdi.^{7,8} This index is the product of the transdiaphragmatic pressure expressed as a fraction of the maximal transdiaphragmatic pressure, and the duty cycle. The latter quantity represents the ratio between the time for inspiration (Ti) and the time for one total respiratory cycle (T_{tot}). In neuromuscular disorders,

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the force reserve (maximal force available minus force used ie maximal transdiaphragmatic pressure-tidal transdiaphragmatic pressure) of the diaphragm has clinical relevance. Neuromuscular patients with weak respiratory muscles are often referred to the Intensive Care Unit (ICU) because of ventilatory failure following a lung infection.⁹ Establishing the force reserve of the diaphragm is also of vital importance for patients who progressively deteriorate towards chronic respiratory insufficiency. In such patients, the clinical course may be decelerated, halted or even reversed by intermittent assisted ventilation.^{10,11,12} However, clear indications for the onset of treatment are not established.

Not all reductions in force reserve are expected to be compensated equally. If afferent information limits the force development, it is expected that cervical cord injury patients with abolition of sensory pathways may handle extra loads on inspiration differently than chronic poliomyelitis patients, where sensory pathways are intact.

This study set out to compare the pressure (force) developed by the diaphragm at rest and during exercise in two well-defined groups of patients with neuromuscular disorders: patients with cervical cord injuries (CCI) not receiving respiratory related treatment, and patients with prior poliomyelitis infection (PPI) treated with night-time assisted ventilation. In addition, we sought to evaluate the effects of time elapsed after injury on diaphragm function by comparing newly and chronically injured CCI patients. The respiratory response to exercise was compared in 5 CCI and 5 PPI patients with similar force reserves and resting diaphragm load. We wanted to identify the mechanical factors which operate in compensating the diaphragm during incipient ventilatory insufficiency.

Methods

Patients

Twenty-one male patients with motor deficits corresponding to clinically diagnosed complete cervical cord injuries at the C5 to C8 levels (CCI), and six male patients with prior poliomyelitis infection (PPI) being treated chronically with intermittent positive pressure ventilation (IPPV) for approximately 6 h every night were included in this study. Eight CCI patients had been injured for 1 to 3 years (CCI₁₋₃) and thirteen CCI patients for 10 years or more (CCI_{≥10}). Two PPI patients had received ICU treatment for acute respiratory insufficiency and one PPI patient had a history of chronic elevation of arterial carbon dioxide tension (PaCO₂) levels. All PPI patients had kyphoscoliosis (scoliosis angles ranged from 60° to 120°) and three patients wore corsets. All patients gave their informed consent and the study was approved by the Ethical Committee at Sahlgrenska University Hospital, Gothenburg, Sweden.

Procedures and protocol

Gastric (Pga) and esophageal (Pes) pressures were obtained with two latex balloons attached to a modified quadruple-lumen Swan Ganz Pacing-TD catheter (93-200H-7F, American Edwards Laboratories), 110 cm in length.¹³ Each balloon was 10 cm in length, 3.5 cm in circumference and 0.12–0.15 mm in thickness (AE Medical Corporation). A third balloon was attached (proximal end 6.5 cm below the distal end of the esophageal pressure balloon) to the catheter, and was used as an anchor. The catheter was connected to two differential pressure transducers (SCM-Screenmate-spezial, Erich Jaeger GmbH & Co. KG) with the reference sides open to atmosphere. Ventilatory flow was measured at the mouth with a pneumotachograph (Jaeger Screenmate, 1/E 0586, resistance 36 Pa/l/s, Erich Jaeger GmbH & Co.KG) mounted on a moveable lever. After analogue to digital conversion, the data was processed and stored in a digital computer (PDP-11/70, Digital Equipment Corporation). Ti/Ttot was calculated from ventilatory flow. Volume was obtained by the numerical integration of flow.

The transdiaphragmatic pressure was obtained by subtracting Pes from Pga. The thin lumen catheter used in the present study had a filtering effect on the recorded pressure signal, the dominating influence being that of a low-pass filter.¹⁴ The low-pass filtering due to the catheter's size was corrected by adding a portion of the pressure's time differential to the signal. In order to suppress the increased influence of noise due to this process, a low-pass filter was added. The cut-off frequencies of the two compensating filters were determined by minimizing the difference between the modified pressure signal and a 'true' pressure signal obtained at the same time through a thick walled wide lumen catheter (1.2 mm internal diameter and of the same length as the modified Swan Ganz catheter). The characteristic frequencies obtained were 1.4 Hz for the differentiating filter and 8.7 Hz for the noise suppressing filter. Subtraction of the corrected pressure signal (modified Swan Ganz catheter) from the pressure signal obtained at the same time through a wide lumen catheter, during panting manoeuvres interrupted by coughs and sniffs, did not result in peak differences larger than 2% of the wide lumen catheter signal.

For each breath, the swing in transdiaphragmatic pressure was calculated as the difference between transdiaphragmatic pressure at end-inspiration and transdiaphragmatic pressure at end-expiration, and will subsequently be referred to as ΔP_{di} . The maximal inspiratory ΔP_{di} ($\Delta P_{di_{max}}$) was obtained by measuring maximal inspiratory efforts against a closed airway (Mueller manoeuvre). $\Delta P_{di_{max}}$ was calculated as the difference between the peak transdiaphragmatic pressure and the mean end-expiratory transdiaphragmatic pressure during tidal breathing. The sniff transdiaphragmatic pressure swing ($\Delta P_{di_{sniff}}$) was obtained during maximally forced inspirations

through the nose and was corrected for end-expiratory pressure, as described for ΔPdi_{max} . TTdi was calculated for each breath as the product of $\Delta Pdi/\Delta Pdi_{max}$ and $Ti/Ttot$.

Prior to the test, patients ate a small standardized breakfast. All tests were performed with the patients sitting comfortably in their own wheelchairs with no support for the arms. In three PPI patients, the test procedure was also performed with arm support.

The catheter was inserted into the nose, swallowed, and passed down into the esophagus to a distance of 30 cm from the nares. The anchoring balloon was then inflated and the catheter was withdrawn until it was anchored against the cardia of the stomach. The anchoring balloon was fixed in place by attaching a counterweight to the catheter just proximal to the nose.

In order to empty the esophageal and gastric balloons, a syringe was emptied until a negative pressure of 2 kPa was obtained,¹⁵ since the Valsalva manoeuvre could not be performed by the CCI patients. Then, 0.5 ml and 2.5 ml of air were injected into the esophageal and the gastric balloons, respectively.¹⁵ The esophageal balloon technique was verified by the dynamic occlusion test in most patients,¹⁶ and invariably showed negligible differences between mouth and esophageal pressure swings.

Measurement of static respiratory parameters at rest

Once the patients were at ease with the catheter, ΔPdi_{max} and ΔPdi_{sniff} were measured. In order to improve the subjects' motivation, a video monitor was

used to display the highest acquired ΔPdi_{max} and ΔPdi_{sniff} which the patients could achieve from a series of at least three reproducible maximal attempts. Following these measurements, three vital capacity manoeuvres (VC) were performed at low levels of flow. The highest values were recorded and stored in the computer. Some PPI patients argued that they were not able to perform VC, ΔPdi_{max} and ΔPdi_{sniff} manoeuvres satisfactorily without arm support. These patients were therefore allowed to repeat the manoeuvres with arm support.

Measurement of dynamic respiratory parameters at rest

Ten to 15 min following the maximal ΔPdi tests, flow and pressures were recorded for approximately 1 min of tidal breathing. No attempts were made to standardize the breathing pattern during this period and the patients remained naive about these specific measurements.

Measurement of dynamic respiratory parameters during exercise

Five CCI and five PPI patients with similar ΔPdi_{max} (CCI=8.5, 6.0–11.6 kPa; PPI=7.1, 6.2–8.7 kPa, median and range), ΔPdi_{sniff} (CCI=5.1, 3.9–8.0; PPI=4.4, 2.7–4.8), and resting TTdi values (CCI=0.07, 0.06–0.08; PPI=0.07, 0.06–0.08) performed a submaximal exercise test. These two groups will subsequently be referred to as CCI_{exer} and PPI_{exer}. In order to determine the submaximal work load, subjects performed a pre-test consisting of a series of 4 min of arm or leg exercise with a crank rate of

Table 1 Median values and significance levels for CCI₁₋₃, CCI_{≥10} and PPI group variables

	CCI ₁₋₃ Median	CCI _{≥10} Median	PPI Median	CCI ₁₋₃ -CCI _{≥10}	CCI ₁₋₃ -PPI	CCI _{≥10} -PPI
Age (years)	26	41	46	**	**	**
Height (cm)	180	185	168	ns	**	**
Weight (kg)	68	70	64	ns	ns	ns
Time after injury/ infection (years)	2	17	42	ns	**	...
Level of injury	6.5	6.5		ns	-	ns
Vt (l)	0.6	0.6	0.4	ns	ns	***
VC (l)	2.8	3.3	1.3	ns	**	***
VC _{%pred} (%)	50	57	28	ns	**	**
Pdi _{max} (kPa)	11.8	11.9	7.1	ns	*	*
Pdi _{sniff} (kPa)	8.0	7.9	4.4	ns	*	ns
ΔPdi (kPa)	1.2	1.4	1.4	ns	ns	*
$\Delta Pdi/\Delta Pdi_{max}$	0.11	0.13	0.17	ns	*	ns
Ti (s)	1.6	1.6	1.2	ns	ns	ns
Ttot (s)	3.8	3.6	2.8	ns	ns	ns
Ti/Ttot	0.42	0.45	0.39	ns	ns	ns
TTdi	0.05	0.06	0.07	ns	ns	ns

P* < 0.05, *P* < 0.01, ****P* < 0.001. Abbreviations: CCI = cervical cord injuries; CCI₁₋₃ = 1–3 year after injury; CCI_{≥10} = 10 years or more after injury; PPI = prior polio infection; Vt = tidal volume at normal breathing; VC = vital capacity; VC_{%pred} = vital capacity in per cent of predicted value; ΔPdi_{max} = the highest transdiaphragmatic pressure swing obtained during a maximal inspiratory manoeuvre against a closed airway; ΔPdi_{sniff} = the highest transdiaphragmatic pressure swing obtained during a maximal forced inspiration through the nose; ΔPdi = transdiaphragmatic pressure swing during a normal tidal breath; Ti = inspiratory time; Ttot = total time for one breath; TTdi = the product of $\Delta Pdi/\Delta Pdi_{max}$ and $Ti/Ttot$

60 rpm. The patient was given a 5 min rest between each work load. The initial work load was 10 watt (W) and the work load was successively increased by 10 W until the 4 min period could no longer be endured. The highest load that could be sustained for 4 min will subsequently be referred to as Wmax. The degree of perceived effort of respiration and work in the extremities was determined by the subject on a 6–20 degree rating scale of perceived exertion (RPE) every 30 s.¹⁷

One week following the pre-test, subjects returned to perform the main protocol which included the recording of respiratory parameters. Before the start of the exercise test, each subject sat still while holding his hands on the arm ergometer. The patient was provided with a noseclip and breathed through the pneumotachograph. In patients with poor grip function the hands were secured onto the hand-grips with an elastic bandage. The exercise test started with 30 s of breathing at rest, and was followed by a 120 s warm-up period at approximately 20% of Wmax. The load was then increased to Wmax, and the exercise continued until exhaustion.

Electromyographic (EMG) measurements

Qualitative determination of voluntary intercostal muscle EMG activity was performed with a bipolar surface EMG electrode. The electrode was successively positioned in the first to the seventh intercostal space in the midclavicular line parasternally. For each intercostal space, the patients were urged to make at least three maximal inspirations. As a criterion for the loss of voluntary muscle activity, we used total absence of phasic inspiratory myoelectric activity.

Statistical methods

Group values are presented as medians and ranges. Comparison of the different groups was performed by nonparametric statistics (Wilcoxon rank-sum test). To analyze the relationships between the different variables, we used simple linear and multiple regression analyses. Statistical significance was expected if the probability for rejection of the null hypothesis exceeded 95% (ie $P < 0.05$).

Results

Group median anthropometric data and median values of ΔPdi_{max} , ΔPdi_{sniff} , $\Delta Pdi/\Delta Pdi_{max}$, Ti , $Ttot$, $Ti/Ttot$, VC and $VC\%_{pred}$ (VC related to height and age) obtained at rest for CCI_{1-3} , $CCI_{\geq 10}$ and PPI patients are presented in Table 1.

Static respiratory parameters

$VC\%_{pred}$ values were reduced to 50%, 57% and 28% in the CCI_{1-3} , $CCI_{\geq 10}$, and PPI groups, respectively. ΔPdi_{max} and ΔPdi_{sniff} values were similar for the CCI_{1-3} , and $CCI_{\geq 10}$ groups, but significantly lower for the PPI patients (Table 1). The contribution of ΔPes and ΔPga to ΔPdi_{max} in each subject is illustrated in

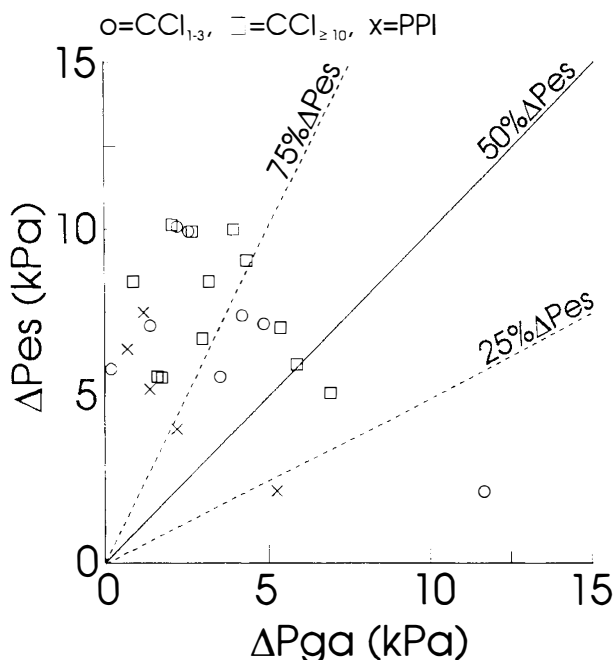


Figure 1 ΔPes and ΔPga contribution to ΔPdi_{max} in CCI_{1-3} (circles), $CCI_{\geq 10}$ (squares) and in PPI (crosses) patients. In most patients, ΔPdi_{max} was dominated by the increase in ΔPes . Although, in three patients, (2 CCI and 1 PPI) the ΔPga contribution to ΔPdi_{max} was higher than the ΔPes . In the two CCI patients, the higher ΔPga values could be explained by a reduction in abdominal compliance. However, in the PPI patient no such explanation was found indicating that ΔPdi_{max} mainly consisted of an expulsive abdominal contraction

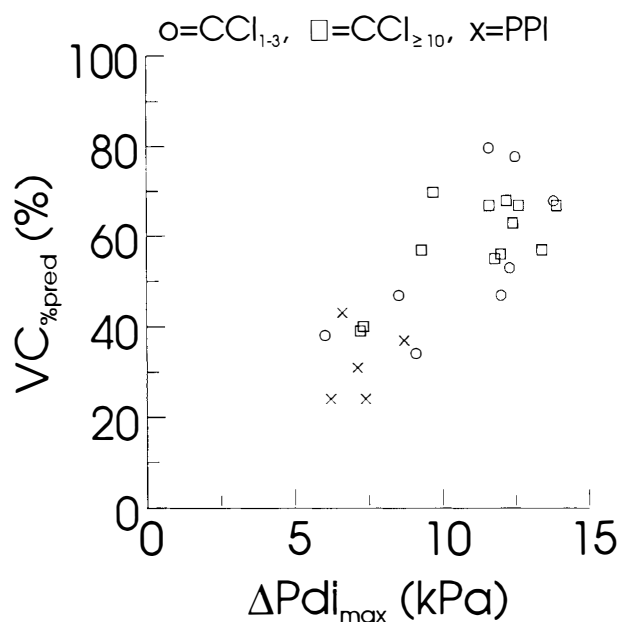


Figure 2 In all patients $VC\%_{pred}$ was dependent of ΔPdi_{max} ($r = 0.77$) and followed the regression line $VC\%_{pred} = 2.0 + \Delta Pdi_{max} \times 4.9$ ($P < 0.0001$). Circles = CCI_{1-3} , squares = $CCI_{\geq 10}$ and crosses = PPI patients

Figure 1. In the PPI patients, who argued that their performance of VC, ΔPdi_{max} and ΔPdi_{sniff} were improved with arm support, the use of the arms during these manoeuvres did not reveal any substantial benefit.

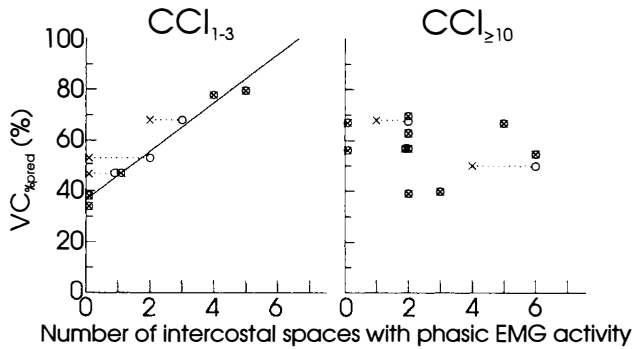


Figure 3 The left panel of the diagram illustrates the high correlation ($r=0.98$) between the $VC_{\%pred}$ and the number of left (circles) and right (crosses) side intercostal muscles with maintained inspiratory EMG activity in CCI_{1-3} patients. The regression line indicates that $VC_{\%pred}$ will be between 35 to 40% in patients with no intercostal muscle function and 100% in patients with muscle function in seven intercostal spaces, as determined by EMG. No such relationship was found in $CCI_{\geq 10}$ patients as illustrated in the right panel

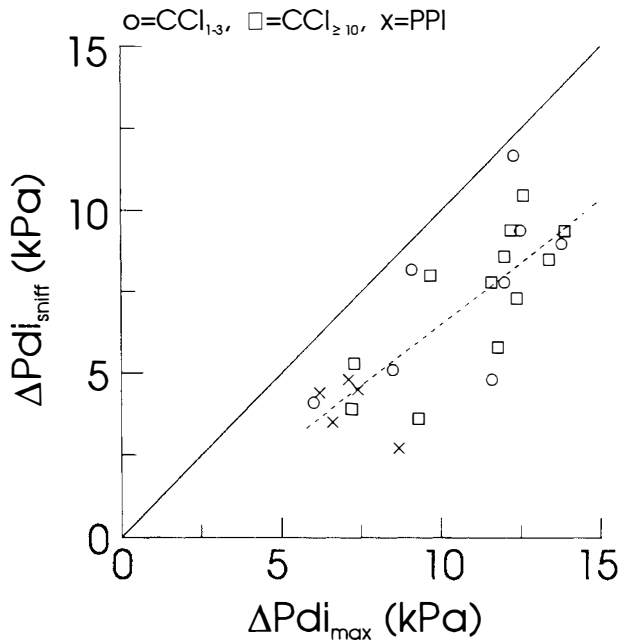


Figure 4 Correlation between ΔPdi_{max} and ΔPdi_{sniff} ($r=0.79$). The progressive increase in the difference between the regression (dashed) line and the line of identity (solid) indicates that, in the studied interval, there is an increase in difference between the two measures with increasing diaphragmatic force. CCI_{1-3} =circles, $CCI_{\geq 10}$ =squares and PPI=crosses

In all patients, the $VC_{\%pred}$ was dependent on ΔPdi_{max} ($r=0.77$), as illustrated in Figure 2. In CCI_{1-3} patients, $VC_{\%pred}$ strongly correlated ($R=0.98$) to the number of intercostal spaces producing EMG activity, as illustrated in Figure 3 (left panel). In the patients with older injuries, $CCI_{\geq 10}$, the strong dependence of $VC_{\%pred}$ on maintained intercostal function was no longer evident (Figure 3, right panel). No correlation was found between $VC_{\%pred}$ and the clinically determined motor level of lesion in any of the two CCI groups. ΔPdi_{max} correlated weakly ($r=0.57$) with the motor lesion level in the $CCI_{\geq 10}$ group, but not in the CCI_{1-3} . For all the data (ie pooling both CCI groups and the PPI group), the correlation between ΔPdi_{max} and ΔPdi_{sniff} was high ($r=0.79$) as depicted in Figure 4. ΔPdi_{sniff} was always smaller than ΔPdi_{max} by a magnitude of 15 to 20%.

Dynamic respiratory parameters measured at rest

The median TTdi values were similar for the three groups, ranging from 0.05 to 0.07 (Table 1). Compared to PPI patients, the median $\Delta Pdi/\Delta Pdi_{max}$ ratio was 35% lower in the CCI_{1-3} patients and 24% lower in the $CCI_{\geq 10}$ patients. The lowest Ttot was found in the PPI group, giving a median f_b of 22 breaths/min, compared to 16 and 17 breaths/min, respectively, in the CCI_{1-3} and $CCI_{\geq 10}$ patients. A similar pattern was found for Ti and was confirmed by a very high correlation between Ti and Ttot ($r=0.94$). No significant differences in Vt, ΔPdi , and Ti/Ttot were found between the CCI_{1-3} and $CCI_{\geq 10}$ and PPI groups.

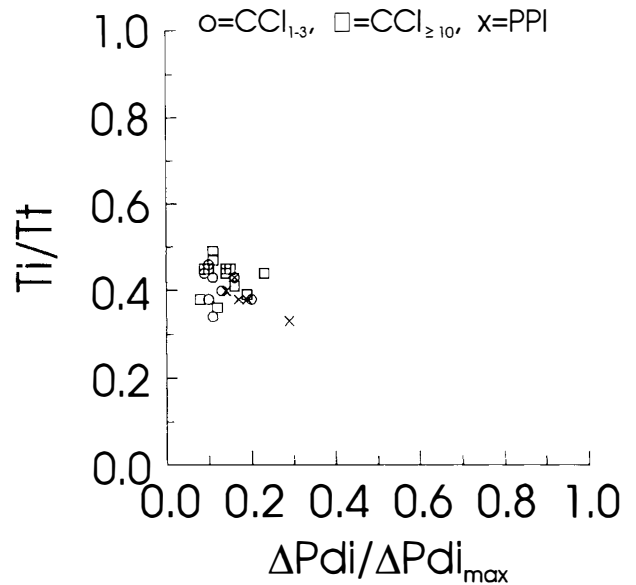


Figure 5 The contribution of $\Delta Pdi/\Delta Pdi_{max}$ and $Ti/Ttot$ to TTdi in the CCI_{1-3} (circles), $CCI_{\geq 10}$ (squares) and in the PPI (crosses) patients. As depicted in the diagram no clear distinctions were found between the CCI groups and ventilator treated PPI group

Figure 5, depicting the T_i/T_{tot} and $\Delta P_{di}/\Delta P_{di_{max}}$ contributions to the TT_{di} , illustrates that several CCI_{1-3} and $CCI_{\geq 10}$ patients had values overlapping those of the PPI patients.

Dynamic respiratory parameters measured during exercise

In contrast to the results of dynamic respiratory parameters measured at rest, the exercise test revealed

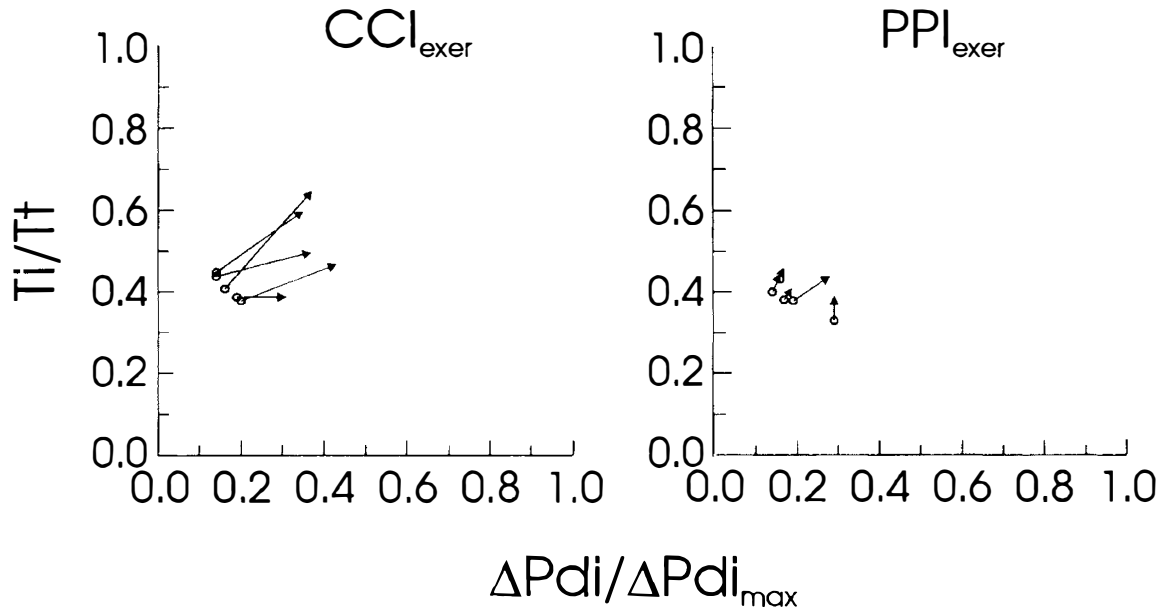


Figure 6 In the CCI_{exer} group (left panel), the changes in $\Delta P_{di}/\Delta P_{di_{max}}$ and T_i/T_{tot} from rest to the end of exercise resulted in clear increases in TT_{di} . Corresponding changes in $\Delta P_{di}/\Delta P_{di_{max}}$ and T_i/T_{tot} were not found in the PPI_{exer} group (right panel) who only showed minor changes in TT_{di}

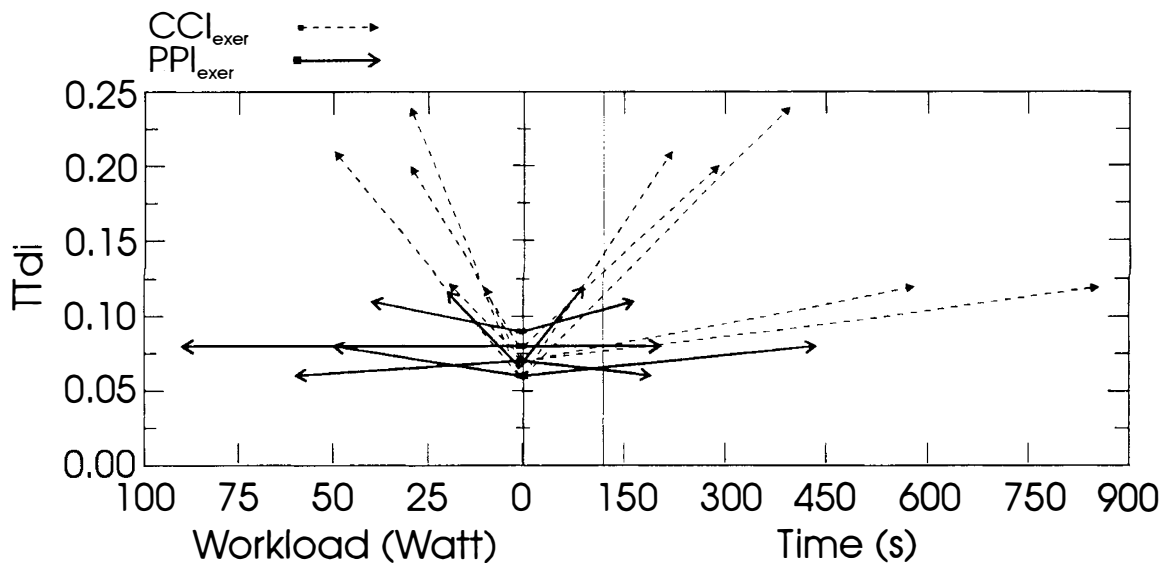


Figure 7 Description of the exercise-induced changes in TT_{di} from rest to end of exercise, in relation to workload and time of exercise in the CCI_{exer} (dashed lines and circles) and PPI_{exer} (solid lines and crosses) patients. The vertical solid line at 120s indicates the end of the warm-up period

clear differences between CCI_{exer} and PPI_{exer} patients for TTdi. Figure 6 depicts the contribution of $\Delta Pdi/\Delta Pdi_{max}$ and $Ti/Ttot$ during 1 min of rest and during the last 30 s of exercise in the CCI_{exer} patients (left panel) and the PPI_{exer} patients (right panel). During exercise, all the PPI_{exer} patients except one showed little or no increase in $\Delta Pdi/\Delta Pdi_{max}$, while all the CCI_{exer} patients showed clear increases in $\Delta Pdi/\Delta Pdi_{max}$. Each patient's change in TTdi from rest to the end of exercise, in relation to endurance time and workload, is illustrated in Figure 7.

Compared to the CCI_{exer} patients, the PPI_{exer} patients seemed to have higher perceived respiratory efforts than perceived efforts in the extremities. The $\Delta Pdi/\Delta Pdi_{max}$ obtained at end of exercise was not related to the perceived respiratory effort obtained during the pre-test (right panel of Figure 8). However, the perceived respiratory effort was inversely related (not significant for the CCI patients) to the change in $\Delta Pdi/\Delta Pdi_{max}$ from rest to end of exercise, as depicted in the left panel of Figure 8. During exercise, CCI_{exer} patients demonstrated higher increases in $\Delta Pdi/\Delta Pdi_{max}$ with a perception of lower respiratory effort, compared to the PPI_{exer} patients.

Despite the differences in development of $\Delta Pdi/\Delta Pdi_{max}$ during exercise in the CCI_{exer} and the PPI_{exer} groups, no clear differences were observed between the

groups regarding changes in f_b , Vt and mean inspiratory flow (Vt/Ti). As illustrated in Figure 9a and 9b (left panels), CCI_{exer} and PPI_{exer} patients demonstrated clear increases in f_b and Vt/Ti during exercise. In each group, the patient with the highest Vt/Ti at rest, showed a reduced Vt during exercise. The right panels of Figure 9a and b illustrate that, during exercise, the increase in Vt and Vt/Ti was accompanied by increases in the $\Delta Pdi/\Delta Pdi_{max}$ in the CCI_{exer} group. In the PPI_{exer} group, the increase in Vt and Vt/Ti was not associated with an increase in $\Delta Pdi/\Delta Pdi_{max}$. From rest to the end of exercise, most PPI_{exer} patients demonstrated shifts in the major axis of the Pes-Pga curve, as illustrated in Figure 10 for one breath obtained at rest and one breath obtained during the last minute of exercise in one PPI_{exer} patient.

Discussion

The ΔPdi_{max} values obtained during a Mueller manoeuvre in normal male subjects range from 10 to 14 kPa. The median ΔPdi_{max} values obtained for the cervical cord injured patients (CCI₁₋₃ = 11.8 kPa and CCI_{≥10} = 11.9 kPa) indicate that the diaphragmatic force in most CCI patients is close to normals. However, about 20% of the CCI patients have

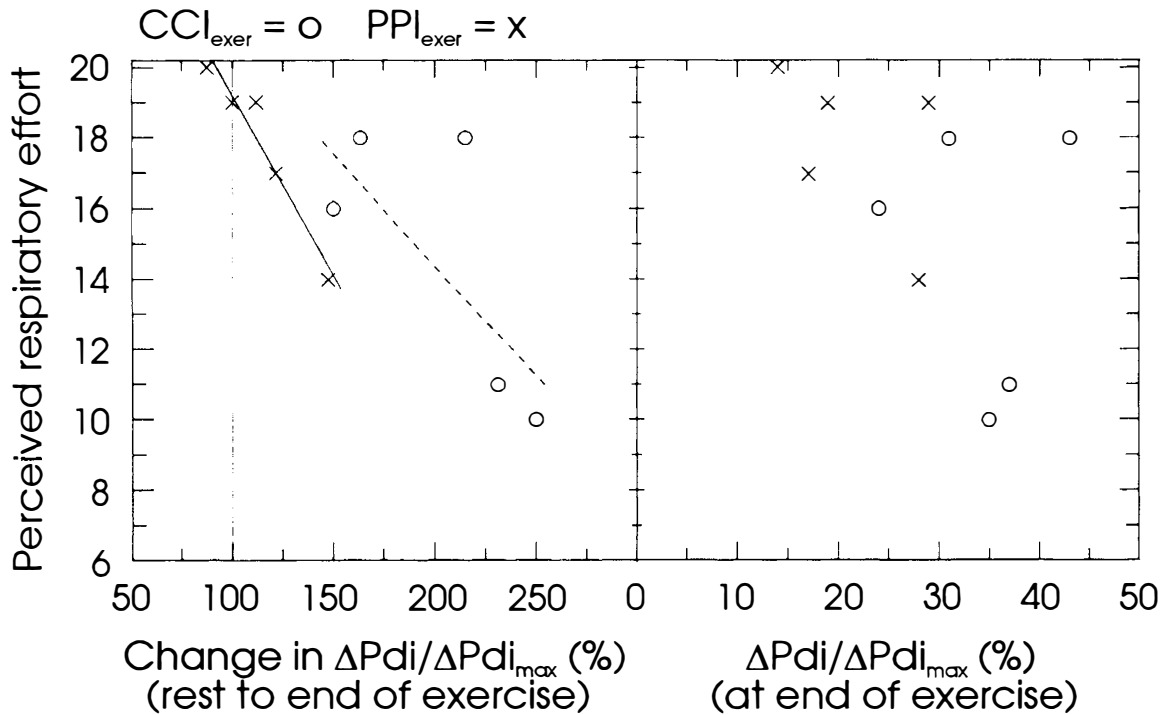


Figure 8 As depicted in the left panel, the PPI patients (crosses) showed an inverse relationship between the perceived respiratory effort, as reported during the last minute of exercise at W_{max} in the pre-test, and the change in $\Delta Pdi/\Delta Pdi_{max}$ ratio (100% indicate resting level) in the second test. In CCI patients with similar TTdi at rest (circles), the increases in $\Delta Pdi/\Delta Pdi_{max}$ were substantially higher for any given recording of perceived respiratory effort, compared to the PPI group. The right panel show that no correlation was found between the perceived respiratory effort in and the $\Delta Pdi/\Delta Pdi_{max}$ at the end of exercise, suggesting that the RPE scale relates better to the changes in force than the actual force developed

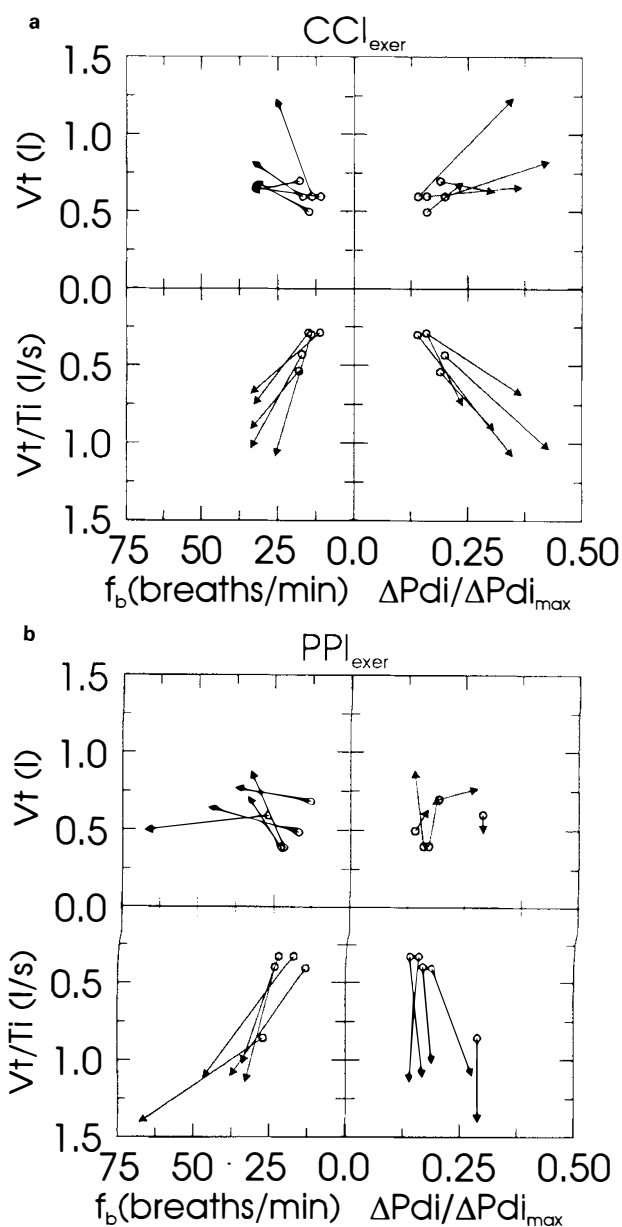


Figure 9 (a, b) The ventilatory response to exercise was similar in the CCI_{exer} (a, left panels) and PPI_{exer} (b, left panels) regarding changes in Vt, Vt/Ti, and f_b. However, in the CCI_{exer} group (a, right panels) the increase in Vt and Vt/Ti were related to increases in ΔPdi/ΔPdi_{max} ratios. In contrast, increases in Vt and Vt/Ti in the PPI_{exer} group (b, right panels) were not characterized by such an increase in ΔPdi/ΔPdi_{max}

reduced ΔPdi_{max} and ΔPdi_{sniff} values comparable to those of the PPI patients. In the PPI patients, the median ΔPdi_{max} value of 7.1 denotes a clear reduction (notice that the median age is higher in the PPI group). The contribution of ΔPes and ΔPga to ΔPdi_{max} was dominated by ΔPes similar to the findings reported for the Mueller manoeuvre in patients with pulmonary

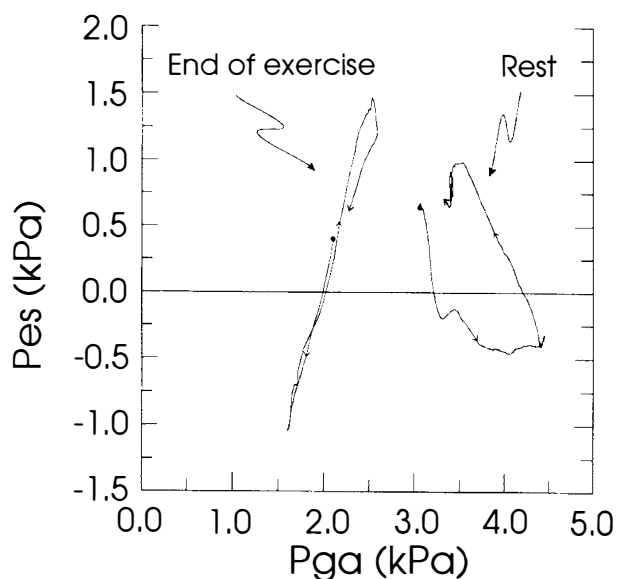


Figure 10 Illustration of a typical shift in the major axis of the Pes-Pga curve. As illustrated, the proportional relationship between Pes and Pga found at rest is replaced by an inversely proportional relationship during exercise with a clear reduction in the loop hysteresis. Also, the mean absolute Pga is decreased and the peak Pes values are higher during exercise. Solid circles indicate start of the loop

fibrosis.¹⁸ One PPI and two CCI patients showed higher ΔPga than ΔPes contribution to ΔPdi_{max} as shown in Figure 1. One of the CCI patients used an abdominal binder, the other had undergone an anterior rhizotomy, giving signs of decreased abdominal compliance. No support for such an explanation was found for the PPI patient, indicating that he probably performed the Mueller manoeuvre in combination with an abdominal expulsive effort.

Miller *et al.*²⁴ reported a mean ΔPdi_{sniff} value of 14 kPa in normal male subjects, which is clearly higher than our findings of 8 kPa in the CCI groups. In contrast to the results in our study, the ΔPdi_{sniff} values in their study exceeded the ΔPdi_{max} values obtained during a Mueller manoeuvre. However, in the study of Miller *et al.*²⁴ the ΔPga contribution to the ΔPdi was clearly lower during ΔPdi_{max} (Mueller manoeuvre) than during ΔPdi_{sniff}. In patients with paralyzed abdominal muscles, as the CCI patients in the present study, this artifact of abdominal expulsive contractions is not present. Hence, similar to the limb muscles, the force generated decreases in proportion to the velocity of the shortening of the muscle. Fitting *et al.*²⁵ showed that there is a linear relationship between mean Vt/Ti and mean velocity of diaphragmatic shortening during tidal breathing in dogs. Previous investigators have shown that both in humans^{26,27} and in animals,^{28,29} the maximal inspiratory pressures decrease as inspiratory flow increases. As indicated by the results of a 30% lower ΔPdi_{sniff} compared to ΔPdi_{max} in the present study, a dynamic contraction with shortening

of the diaphragm is expected to generate lower forces than an isometric contraction. Miller *et al.*²⁴ reported a tendency for a correlation between ΔPdi_{sniff} and ΔPdi_{max} . In contrast, our study showed a high linear correlation between ΔPdi_{max} and ΔPdi_{sniff} ($r=0.79$), where ΔPdi_{sniff} is proportional to, but lower than ΔPdi_{max} . In the transition region between these two dependencies, a linear regression following the equation, $\Delta Pdi_{sniff} = -1.08 + \Delta Pdi_{max} \times 0.76$ ($P < 0.0001$), describes the relation quite well. The dispersion of ΔPdi_{sniff} with respect to ΔPdi_{max} among subjects was however high.

Forner³⁰ reported an average $VC_{\%pred}$ of 51% in 48 CCI patients injured at C5–C8 which is similar to the median values of $VC_{\%pred}$ in the present study (50% in the CCI_{1–3} group and 57% in the CCI_{≥10} group). In the CCI and PPI patients, $VC_{\%pred}$ was strongly dependent on ΔPdi_{max} suggesting that the reduced VC is due to muscular impairment. A clear correlation between inspiratory muscle force and $VC_{\%pred}$ has also been observed in patients with other neuromuscular disorders.¹

In the present study there was a positive correlation between $VC_{\%pred}$ and the levels of intercostal muscle function, as assessed with the EMG electrodes in the CCI_{1–3} patients. In the CCI_{≥10} group, no such correlation was found. Estenne and De Troyer³¹ described that rib cage motion in CCI patients (C4–C7), injured 4 months to 26 years previously and with no signs of inspiratory related intercostal muscle EMG activity, is dependent on the function of the accessory muscles. In general, they found that the lower rib cage expanded more than the upper. Paradoxical antero-posterior (AP) movements of the upper rib-cage dominated in these patients with silent or continuous spastic scalenes. In patients with functioning scalenes, no movement or small increases in the AP diameter were found. The authors also described two patients injured 9 and 26 years previously as having paradoxical upper chest wall AP movements. This was not found in two patients 3 and 5 months after injury. Still, no clear association between rib cage mechanics and time since injury has been established. De Troyer and Heilporn³² showed that longstanding paralysis (2.5 to 10 years) of intercostal muscles in CCI patients (C5–C7) resulted in marked alterations of lung compliance and a reduction in the passive outward recoil of the chest wall. Normal functional residual capacity and compliance of the respiratory system was found in only two patients with maintained inspiratory intercostal EMG activity. Thus, it seems that the activity of the intercostal and scalene muscles is important in preserving the respiratory mechanics during the first decade following injury.

Fugl-Meyer and Grimby³³ reported a low correlation between lung volume and the clinically determined lesion level in 14 CCI patients (C4–C8) injured for less than 6 years. In our data, there was no such correlation in the CCI groups, whereas a low correlation between ΔPdi_{max} and the motor level of

injury was found in the CCI_{≥10} group. These results imply that the motor level of injury is a weak predictor of the respiratory function in low cervical cord injuries (C5–C8).

The exercise test showed that PPI_{exer} patients had no or modest increases in TTdi upon exertion. One patient even demonstrated a reduced TTdi from rest to the last minute of exercise. In the PPI_{exer} patients who increased their TTdi, the increase was mainly due to an increase in $Ti/Ttot$ and was associated with an increase in ventilation. In contrast, the CCI_{exer} patients had a substantial increase in TTdi from rest to the last minute of exercise with increases in ventilation similar to those found in PPI_{exer} patients. In PPI_{exer} patients, shifts of the major axis in the Pes-Pga curve and increases in Pes denote a synergistic coordination of the inspiratory and expiratory muscles in order to increase ventilation (Figure 10). Despite the similarity in $\Delta Pdi/\Delta Pdi_{max}$ values at rest and small or no increases in $\Delta Pdi/\Delta Pdi_{max}$ during exercise in the PPI_{exer} group, those patients clearly perceived higher respiratory efforts during the pre-test. The divergent response to exercise in the PPI_{exer} group, with the perception of strenuous respiration, the inability to increase force, and the differences in ventilatory strategy, strongly suggests a reduced force reserve. However, it should be noted that the force reductions observed in kypho-scoliotic PPI patients is due to a combination of mechanical disadvantage and diaphragm paralysis. The earlier history of hypercapnic respiratory insufficiency in two of the PPI_{exer} patients having no or almost no increase in TTdi during the exercise is in accordance with previous findings that hypercapnia is preferred to respiratory muscle fatigue.^{2, 6}

In summary, the major findings of this study are: (1) vital capacity is related to maximal inspiratory muscle force in CCI and PPI patients, (2) the static respiratory force parameters are similar in the recently and the long-time injured CCI groups, but lower in the PPI group, (3) the TTdi during breathing at rest is similar for all groups, (4) the PPI patients respond to intrinsic inspiratory loads with much smaller changes in TTdi than the CCI patients with similar ΔPdi_{max} , ΔPdi_{sniff} , and resting TTdi. We speculate that preserved afferent neural pathways in PPI patients are responsible for the difference in inspiratory muscle output upon exertion.

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