

**A Randomised Crossover Study of Pressure and Volume Non-Invasive Ventilation  
in Chest Wall Deformity**

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## **Abstract**

### **Background**

Non-invasive ventilation is an established treatment for chronic respiratory failure due to chest wall deformity. There are few data available to inform the choice between volume and pressure ventilators. The aim of this study was to compare pressure and volume targeted ventilation in terms of diurnal arterial blood gas tensions, lung volumes, hypercapnic ventilatory responses, sleep quality and effect on daytime function and health status, when ventilators were carefully set to provide the same minute ventilation.

**Methods.** 13 patients with chest wall deformity underwent a 4-week single blind randomised crossover study using the Breas PV403 ventilator in either pressure or volume mode with assessments made at the end of each 4-week period.

**Results.** Minute ventilation at night was less than that set during the day with greater leak, for both modes of ventilation. There was more leak with pressure than volume ventilation ( $13.8 \pm 1.9$  v  $5.9 \pm 1.0$  l·min<sup>-1</sup>,  $p=0.01$ ). There were no significant differences in sleep quality, daytime arterial blood gas tensions, lung mechanics, ventilatory drive, health status or daytime functioning.

**Conclusions.** These data suggest that pressure and volume ventilation are equivalent in terms of the effect on nocturnal and daytime physiology, and resulting daytime function and health status.

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### **Keywords:**

Positive pressure ventilation, Hypercapnic responses

Health related quality of life, Chronic respiratory failure

Chest wall deformity, non-invasive ventilation

## Introduction

Domiciliary non-invasive positive pressure ventilation (NIV) is an established treatment in chronic respiratory failure due to chest wall deformity (CWD). It is beneficial in terms of improvements in symptoms, daytime function, arterial blood gas tensions, and sleep quality.[1-3] There is also evidence for improved quality of life and survival.[4] A recent Cochrane systematic review including four eligible studies with a total of 51 patients confirmed improvements in symptoms of hypoventilation, daytime hypercapnia and nocturnal oxygenation.[5]

### *Pressure vs. Volume Ventilation*

Most ventilator modes are either pressure or volume targeted, each with potential advantages and disadvantages. Volume ventilation by definition includes a predetermined set tidal volume, however in the presence of interface leak, the set volume is not guaranteed which, theoretically at least, is a problem, particularly during sleep when NIV is conventionally applied.[6] Also if the impedance to inflation is increased, airway pressures may be high. This may be transient if for instance the patient swallows or coughs and may be uncomfortable for the patient. Conversely pressure targeted ventilators deliver a preset airway pressure, but variable tidal volume depending on chest wall compliance, airway resistance and patient effort. The constant airway pressure even during swallowing may explain the trend towards better tolerance of pressure targeted ventilation in some studies.[7] Any differences between the method of delivery of ventilation may have a consequential effect on nocturnal ventilation, sleep quality and daytime physiology and psychometric function.

Epidemiological data suggest that there is an increasing preference to pressure ventilation when NIV is used for home mechanical ventilation [8], but clinical studies are divided on which, if either, is the better mode of ventilation in terms of gas exchange or overnight oximetry. Short term studies have shown either equivalence [9][10], benefit of pressure [11] or benefit of volume [12] whilst longer term studies have also been conflicting or have used heterogeneous groups of patients.[13][14] In all these studies, the ventilator settings were not equivalent in terms of minute ventilation and therefore were not really comparing the *mode* of delivery of the ventilation. Furthermore these studies have evaluated physiological outcomes, but none have assessed outcomes that are important to patients, such as daytime functioning and health status.

The aim of this study was therefore to compare volume and pressure non-invasive ventilation when carefully controlled for minute volume, in terms of nocturnal ventilation and leak, sleep quality, and their impact on gas exchange, daytime function and health status. The hypothesis was that pressure ventilation is superior to volume ventilation due to better leak compensation.

## Methods

The study protocol was approved by the Local Research Ethics Committee. Patients gave written consent to participate.

### *Patients*

An a priori power calculation suggested that a sample size of 10 would have 90% power to detect a difference in mean arterial oxygenation of 1 kPa using a paired t-test at 95% significance level. 13 patients with chronic respiratory failure due to chest wall deformity were invited to participate in the study. All were established on and compliant with nocturnal NIV (Mean duration (standard error) of NIV 32 (8) months) and had been stable for at least six weeks. All patients had been using the NIPPY 1 ventilator (B & D Medical, Stratford upon Avon, UK). These ventilators provide pressure-controlled ventilation. None were using oxygen or humidification at home.

### *Ventilator Settings*

The Breas PV403 (Mölnlycke, Sweden) was chosen because this ventilator offers both pressure support and volume ventilation as an option within the same machine and was therefore useful in reducing patient bias. Like the NIPPY 1, it uses an exhalation valve and does not provide positive end expiratory pressure. During a daytime titration period using the patient's usual nasal mask, ventilator settings (set tidal volume and inspiratory time) were altered during volume ventilation to obtain the highest comfortable tidal volume with a set ventilator back up rate of 15 breaths per minute. Inspiratory pressure was then altered during pressure ventilation to obtain the same expired minute ventilation as that delivered during volume ventilation (see online appendix for further explanation). Inspiratory trigger sensitivity was set to  $-0.1$  cmH<sub>2</sub>O in both modes, expiratory trigger to 50% of maximal flow, and rise time to the shortest available (pressure ventilation only). Adequacy of ventilation was confirmed by comparison with the daytime minute ventilation obtained with the patients 'usual' ventilator and pulse oximetry. Minute ventilation was at least equivalent to that achieved with the patient's usual ventilator.

### *Study Design (see figure 1)*

The study design was a 4-week crossover with 2-week washout during which time the patients used their usual ventilator. Patients were randomised to receive either pressure targeted or volume targeted ventilation using settings as above, which were concealed from the patient. Check overnight oximetry was performed in the home after one week. At the end of each four-week period, patients returned for full polysomnography, using the ventilator in the same mode, and daytime measurements as described below. A washout period of two weeks followed during which the patient used their usual established ventilator before a further four weeks using the alternate ventilatory mode.

### *Measurements*

Polysomnography was performed using the Alice 4 System (Respironics, Murrysville, PA, USA) and scored according to standard criteria.[15] Overnight flow and pressure waveforms were recorded. (model 3700 pneumotachometer, Hans Rudolph). Minute leak was calculated as the difference between inspired and expired tidal volumes, multiplied by the respiratory rate. Ventilator compliance (hours used) was downloaded from the ventilator to a personal computer the following day. Arterial blood gas tensions were measured off ventilation the following morning using a radial artery puncture.

Patients underwent a series of physiological and psychometric measurements including resting minute ventilation and occlusion pressure at 100ms (p0.1), hypercapnic ventilatory responses[16], spirometry, maximal (plateau) inspiratory and expiratory mouth pressures (from FRC and total lung capacity respectively), and sniff nasal

inspiratory pressures (SNIP).[17] Psychometric measures included a battery of tests sensitive to changes due to chronic hypoxia and sleep deprivation. [18-21] Health status was assessed by validated disease specific (MRF-28)[22] and generic (SF-36v2)[23] questionnaires together with the Hospital Anxiety and Depression Scale.[24] The SF-36 was transformed to United Kingdom population norm scores (z score).[25] Physical activity at home was measured using a pedometer in the final week of each treatment period. Patient comfort during ventilation was assessed by visual analogue scales (VAS).

### Statistical Analysis

The primary outcome measures were the daytime arterial blood gas tensions during spontaneous breathing. Secondary endpoints included patient orientated outcomes such as daytime function, quality of life and health status. Data was compared using paired student t-tests. The crossover analysis was considered valid provided that no significant order effect was noted from the two treatment periods. The Hochberg procedure was used to adjust for multiple secondary endpoints.[26]

### Results

13 patients started the study. 1 patient discontinued the study after 1 month due to intervening (unrelated) medical problems. Baseline data at the time of recruitment are given in table 1. This group represent a population with severe restrictive lung diseases (FEV<sub>1</sub>/FVC ratio 87% ± 3%) with mean FVC 0.69 ± 0.05 litres. There was no significant order effect and therefore data from both treatment periods were used.

	<b>Baseline</b>
Number (male)	13 (6)
Age (years)	60.5 (12.7)
Height (m)	1.56 (0.09)
Diagnosis (n)	
Post polio	4
Early onset kyphoscoliosis	7
Pott's disease	1
Thoracoplasty	1
BMI (kg·m <sup>-2</sup> )	25.3 (5.3)
FEV <sub>1</sub> (l)	0.60 (0.04)
FVC (l)	0.69 (0.05)
IPAP (cmH <sub>2</sub> O)	23.0 (1.3)
pH *	7.38 (0.01)
HCO <sub>3</sub> <sup>-</sup> (mmol·l <sup>-1</sup> ) *	28.6 (0.68)
P <sub>a</sub> O <sub>2</sub> (kPa) *	8.83 (0.26)
P <sub>a</sub> CO <sub>2</sub> (kPa) *	6.42 (0.09)
SaO <sub>2</sub> (%)*	91.7 (0.7)

Table 1 Patient demographics, anthropometric measures and established ventilator settings (mean ± SEM) \*Unassisted ventilation taken at 8am. BMI: body mass index; FEV<sub>1</sub>: forced expiratory volume in one second; FVC: forced vital capacity. IPAP: set inspiratory positive airways pressure; P<sub>a</sub>O<sub>2</sub>, P<sub>a</sub>CO<sub>2</sub>: arterial oxygen and carbon dioxide tensions; HCO<sub>3</sub><sup>-</sup>: bicarbonate; SaO<sub>2</sub>: oxygen saturation.

*Initial Settings and nocturnal ventilation (table 2)*

The modes of ventilation were closely matched as intended during the daytime in terms of expired minute ventilation and leak. Similarly at night, there was no difference in expired minute ventilation between pressure and volume modes, although both were significantly lower than during the daytime titration periods ( $p < 0.01$ ). The same expired minute volume was achieved with a significantly lower mean inspiratory pressure ( $IP_{\text{mean}}$ ) during volume ventilation (14.8 vs. 20.9 cmH<sub>2</sub>O,  $p = 0.008$ ). There was significantly greater leak at night during pressure ventilation (13.8 vs. 5.9 l·min<sup>-1</sup>,  $p = 0.01$ ).

	<b>Pressure</b>	<b>Volume</b>	<b>p</b>
Set pressure (cmH <sub>2</sub> O)	25.0 (1.1)	-	
Set tidal volume (ml)	-	749.2 (34.5)	
Set volume (ml·kg <sup>-1</sup> )	-	11.9	
Set Ti (s)	-	1.2 (0.1)	
Set backup rate	15	15	
Measured MVe (l·min <sup>-1</sup> )	12.14 (0.65)	12.18 (0.63)	0.93
Measured Leak (l·min <sup>-1</sup> )	2.43 (0.52)	2.22 (0.35)	0.71

Table 2 Initial Daytime Set Parameters (mean ± SEM). Ti: inspiratory time; MVe: expired minute ventilation.

*Diurnal arterial blood gas tensions and hypercapnic ventilatory responses (table 3)*

There was no significant difference in arterial blood gas tensions or oxygen saturation between pressure or volume ventilation. Resting daytime minute ventilation was identical (10.8 l·min<sup>-1</sup>) and ventilatory drive, as measured by  $P_{0.1}$ , was similar in both groups. There was no consistent change in the slope of the ventilatory or  $P_{0.1}$  hypercapnic responses. The different modes of ventilation had no impact on spirometry, mouth or sniff nasal pressures.

Outcome	Pressure	Volume	p	p <sub>c</sub>
pH *	7.38 (0.01)	7.38 (0.01)	0.56	0.56
HCO <sub>3</sub> <sup>-</sup>	28.6 (0.68)	29.5 (0.66)	0.07	0.28
P <sub>a</sub> O <sub>2</sub> (kPa)	9.00 (0.23)	8.68 (0.36)	0.18	0.36
P <sub>a</sub> CO <sub>2</sub> (kPa)	6.38 (0.12)	6.61 (0.16)	0.09	0.27
SaO <sub>2</sub>	92.3 (0.75)	90.7 (1.17)	0.04	0.20
Pi,max (cmH <sub>2</sub> O)	-36.3 (5.1)	-38.5 (4.9)	0.47	1.00
Pe,max (cmH <sub>2</sub> O)	66.2 (10.6)	72.1 (10.7)	0.31	1.00
SNIP (cmH <sub>2</sub> O)	-36.0 (5.3)	-37.7 (5.8)	0.66	1.00
FEV <sub>1</sub> (l)	0.60 (0.04)	0.61 (0.04)	0.57	0.86
FVC (l)	0.72 (0.06)	0.76 (0.06)	0.86	1.00
<b>Spontaneous Ventilation</b>				
VTe (ml)	439 (26)	396 (34)	0.29	0.58
RR <sub>spn</sub> (bpm)	25.4 (2.1)	28.4 (2.2)	0.09	0.36
Mve (l·min <sup>-1</sup> )	10.8 (0.5)	10.8 (0.6)	0.80	0.80
P <sub>0.1</sub> (cmH <sub>2</sub> O)	-1.53 (0.17)	-1.26 (0.11)	0.18	0.54
<b>Hypercapnic responses</b>				
ΔVE/ΔpCO <sub>2</sub> (l·min <sup>-1</sup> ·kPa <sup>-1</sup> )	2.87 (0.41)	3.59 (0.63)	0.15	0.31
MVe @ 8 kPa (l·min <sup>-1</sup> )	14.6 (1.2)	13.7 (1.0)	0.45	0.45
ΔP <sub>0.1</sub> /ΔpCO <sub>2</sub> (cmH <sub>2</sub> O·kPa <sup>-1</sup> )	-0.91 (0.17)	-0.72 (0.12)	0.07	0.21
P <sub>0.1</sub> @ 8 kPa (cmH <sub>2</sub> O)	-2.60 (0.44)	-1.90 (0.35)	0.008	0.03
<b>Polysomnography</b>				
SaO <sub>2</sub> (mean, %)	92.8 (0.9)	91.8 (1.1)	0.20	1.00
SaO <sub>2</sub> < 90% (minutes)	73 (32)	107 (40)	0.11	1.00
RDI (hr <sup>-1</sup> )	0.7 (0.7)	0 (0)	0.29	1.00
TcCO <sub>2</sub> (mean, KPa)	4.3 (0.8)	4.7 (0.6)	0.76	1.00
VTe (ml)	548 (75)	546 (78)	0.98	1.00
MVe (l·min <sup>-1</sup> )	8.34 (0.91)	8.38 (1.3)	0.58	1.00
Minute Leak (l·min <sup>-1</sup> )	13.80 (1.93)	5.87 (1.03)	0.001	0.01
Peak inspiratory flow (l·min <sup>-1</sup> )	149 (21)	152 (21)	0.85	1.00
RR <sub>vent</sub> (bpm)	15 (0.3)	15.6 (0.3)	0.19	1.00
IP <sub>peak</sub> (cmH <sub>2</sub> O)	24.2 (1.1)	23.4 (1.1)	0.85	1.00
IP <sub>mean</sub> (cmH <sub>2</sub> O)	20.9 (1.1)	14.8 (0.8)	0.001	0.008
Ti (s)	1.53 (0.10)	1.33 (0.05)	0.07	0.56
Te (s)	2.30 (0.13)	2.38 (0.10)	0.58	1.00
Ti/Ti <sub>TOT</sub>	0.40 (0.03)	0.36 (0.02)	0.11	0.75
Total Sleep Time (TST) (min)	394 (16)	416 (13)	0.10	1.00
Latency (min)	52 (10)	41 (8)	0.38	1.00
Efficiency (%)	77 (8)	85 (2)	0.24	1.00
REM (% TST)	12 (2)	13 (2)	0.52	1.00
NREM 1+2 (% TST)	55 (6)	54 (6)	0.85	1.00
NREM 3+4 (% TST)	26 (6)	25 (5)	0.68	1.00
Respiratory arousals (/hr)	0.8 (0.4)	0.0 (0.0)	0.10	1.00
Non-respiratory arousals (/hr)	16.0 (2.2)	18.4 (4.6)	0.44	1.00
Ventilator hr (/night @ home)	8.1 (0.7)	8.4 (1.1)	0.25	0.25

Table 3 Daytime arterial blood gas tensions and spontaneous ventilation, hypercapnic responses and polysomnography (mean ± SEM) after 4 weeks of each of pressure and volume ventilation. \*unassisted ventilation. p: raw probability; p<sub>c</sub>: Hochberg correction for multiple endpoints. Pi,max: maximal inspiratory mouth pressure; Pe,max: maximal expiratory mouth pressure; SNIP: sniff nasal inspiratory pressure; VTe: expired tidal volume; RR<sub>spn</sub>: spontaneous respiratory rate; MVe: expired minute ventilation; P<sub>0.1</sub>: pressure at mouth 100ms after an occluded inspiratory effort; ΔVE/ΔpCO<sub>2</sub>: slope of ventilatory response curve to inspired carbon dioxide; ΔP<sub>0.1</sub>/ΔpCO<sub>2</sub>: slope of P<sub>0.1</sub> against inspired carbon dioxide; RDI: respiratory disturbance index, number of apnoeas and hypopnoeas per hour of sleep; TcCO<sub>2</sub>: transcutaneous carbon dioxide; RR<sub>vent</sub>: respiratory rate during assisted ventilation; IP<sub>peak</sub>: peak inspiratory pressure; IP<sub>mean</sub>: mean inspiratory pressure; Ti: measured inspiratory time; Te: measured expiratory time; TST: total sleep time; REM: rapid eye movement sleep; NREM: non-rapid eye movement sleep.

### *Sleep Quality (table 3)*

Compliance was excellent and patients used the ventilators for similar durations over each of the 4 week periods (pressure:  $8.07 \pm 0.69$  hrs/night, volume:  $8.40 \pm 1.10$ ). Total sleep time, sleep efficiency and the proportion of sleep spent in each stage were identical (table 3). In both groups the majority of arousals were non-respiratory (i.e. not associated with periods of desaturation or respiratory events). There was no difference at the end of each four weeks in terms of patient reported ventilator comfort, sleep quality and subjective sensation of breathlessness.

### *Health Status and physical activity (table 4)*

There were no differences between the two ventilatory modes in either measure of health status. The overall scores for the Hospital Anxiety and Depression Scale were raised indicating 'possibly abnormal', but there were no differences between the two modes. The norm-based SF-36 data reflects very poor physical functioning (physical component score pressure:  $14.8 \pm 3.9$ , volume  $15.5 \pm 3.3$ ) compared to the UK normal population ( $50 \pm 10$ ). Mental health was measured as close to the UK norm (pressure  $53.7 \pm 3.6$ , volume  $56.3 \pm 3.6$ ). There were no differences in daily activity as measured by the pedometer.

### *Psychometric Tests*

There were no differences in terms of performance in the psychometric test battery between pressure and volume modes.



<b>Outcome</b>	<b>Pressure</b>	<b>Volume</b>	<b>p</b>	<b><i>p<sub>c</sub></i></b>
<b>Health Status</b>				
<b>MRF-28</b>				
Daily activity	50.3 (19.8)	49.1 (17.0)	0.57	1.00
Cognitive function	29.2 (22.4)	25.0 (19.1)	0.81	1.00
Invalidity	33.3 (16.2)	26.7 (13.1)	0.44	1.00
<i>Total</i>	39.3 (13.1)	36.8 (12.7)	0.99	1.00
<b>SF-36</b>				
Physical functioning	19.0 (3.1)	20.1 (3.2)	0.81	1.00
Role physical	29.8 (2.6)	32.9 (3.4)	0.28	1.00
Body pain	23.9 (4.1)	23.9 (4.1)	0.99	0.99
General Health	21.5 (3.2)	21.4 (2.9)	0.99	1.00
<i>Physical Component Summary</i>	14.8 (3.9)	15.5 (3.3)	0.91	1.00
Vitality	43.0 (2.3)	45.6 (2.7)	0.38	1.00
Social Functioning	38.6 (3.1)	41.7 (3.6)	0.36	1.00
Role Emotional	41.7 (4.2)	44.3 (4.1)	0.61	1.00
Mental Health	50.1 (3.0)	51.7 (2.9)	0.69	1.00
<i>Mental Component Summary</i>	53.7 (3.6)	56.3 (3.6)	0.51	1.00
<b>HAD</b>				
Anxiety	6.5 (1.3)	6.3 (0.4)	0.21	0.42
Depression	4.1 (0.2)	3.8 (0.2)	0.81	0.81
Physical Activity (steps/day)	1216 (277)	1734 (761)	0.3	0.3
<b>Psychometric Tests</b>				
Serial Boxes (s)	16.1 (0.5)	15.8 (0.6)	0.77	0.77
Trailmaking B-A (s)	39.6 (6.3)	43.2 (6.9)	0.64	1.00
Rey List Learning	50.2 (3.5)	47.3 (2.9)	0.21	1.00
AMIPB – Info. processing	39.9 (4.3)	35.6 (1.9)	0.19	1.00
AMIPB – Design learning	36.5 (1.8)	33.0 (2.0)	0.08	0.64
Digit Span	3.5 (0.3)	3.7 (0.2)	0.58	1.00
SCOLP (no correct)	61.6 (5.5)	58.6 (5.6)	0.40	1.00
STROOP C (no correct)	99.4 (5.2)	95.4 (5.7)	0.19	1.00
<b>Visual Analogue Scales</b>				
Ventilator comfort	6.0 (1.9)	6.7 (1.4)	0.57	1.00
Sleep quality	6.5 (1.5)	6.1 (2.1)	0.79	0.79
Breathlessness	6.3 (0.9)	5.7 (1.8)	0.59	1.00

Table 4 Health Status, Psychometric Tests and Visual Analogue scales after 4 weeks of each of pressure and volume ventilation; mean  $\pm$  SEM). p: raw probability; *p<sub>c</sub>*: Hochberg correction for multiple endpoints. MRF-28; Mageri Foundation Respiratory Failure Questionnaire-28; SF-36: Short Form 36 z scores; AMIPB: The Adult Memory and Information Processing Battery; SCOLP: Speed and capacity of language processing test; STROOP: Stroop color-word test

## Discussion

In this carefully controlled randomised crossover study in patients with chest wall deformity, we have demonstrated that there was no significant difference between either pressure or volume modes of non-invasive ventilation in terms of daytime arterial blood

gas tensions and a range of psychological, sleep, health status and daytime functioning measures during one month of ventilation with either pressure or volume targeted ventilation.

This study improves upon the design of, previous studies comparing pressure and volume ventilation. Earlier studies were short term, performed at most over a few hours during the daytime.[9-11][27] However NIV is usually delivered each night during sleep over a prolonged period of time. More recent studies have tended to be longer term and have included either physiological, functional or health status outcome measures, but not the combination of all three as in the current study. [13][14][28][29] In a 1-month crossover study of patients with kyphoscoliosis, pressure and volume modes were equally effective in terms of gas exchange, sleep quality and comfort but no assessment was made of ventilatory drive, patient function or health status.[13] In another crossover study of pressure vs. volume in a heterogeneous sample of 10 patients with COPD and CWD, no difference was identified except for an excess of gastrointestinal side effects in the volume group.[14] This study did not control for minute ventilation and did not assess health status or daytime function. Uniquely we established identical *volumes* of delivered ventilation with the two modes, and have therefore studied differences in the *way* that ventilation is delivered. Additionally, our study evaluated end points likely to be of immediate importance to patients, e.g. health status, cognitive function, and daily activity.

A further strength of our study is that we compared ventilator modes just in patients with chest wall deformity. Most other studies looked at mixed groups of patients. The needs of patients with different conditions from a ventilator will vary and studying heterogeneous patient groups may mask differences important to some patient groups. However these data cannot be extended to ventilator users with other conditions. Indeed, a particular ventilator mode may be better suited in some conditions for other reasons, e.g. volume ventilation in severe neuromuscular disease, allowing patients with impaired cough to breath stack.

Patient selection was not random, but only patients who were already established on NIV and agreeable to participate were recruited. These were likely to represent the 'best' patients in terms of compliance, and it is not surprising that they had minimal hypercapnia at the start of the study. Most patients on home NIV will become experienced users over time so it is important to test for any differences in these patients. The study does not address whether one mode is easier for patients when they first start NIV; this would have required a parallel group study design with larger numbers of patients. Additionally because some patients present acutely unwell and require NIV immediately, it would not have been possible to perform such a comprehensive series of evaluations.

All patients were previously established on a (different) pressure ventilator, which may have biased the results favouring pressure ventilation. We think this unlikely, since patients were blinded and anecdotally could not identify which mode was pressure targeted. Again, uniquely, the same ventilator was used to provide both modes of ventilation to avoid bias and preference for the patients' usual ventilator.

One of the potential concerns in the design of this study, as with similar comparisons of pressure and volume ventilation, was that ventilator settings were titrated during the daytime.[14][29] A further strength of this study is that ventilation was *also* measured during sleep and although expired minute ventilation was significantly less at night than during the day, this difference was seen with both modes of ventilation.

Ventilators differ in methods and sensitivity of both inspiratory and expiratory triggers and the way in which flow is delivered. The results of this study are based on just one ventilator, and therefore should not necessarily be extrapolated to other machines. The difference in waveform between pressure and volume is a likely explanation for equivalent overnight minute ventilation with quite different mean inspiratory pressures. The PV403 does not provide positive end-expiratory pressure (PEEP), which is available in most pressure targeted ventilators. While benefit has been shown from the addition of extrinsic PEEP in patients during an acute exacerbation of COPD, it is unlikely to be as important in stable patients with CWD, although the absence of flow during expiration may increase carbon dioxide rebreathing.[30]

As in previous studies, we chose to use relatively high backup rates.[14][29] This was based on our observation during pilot studies that patients when asleep would often default to a very low ventilator backup rate, even when this significantly compromised nocturnal oxygenation. Controlled ventilation improved oxygenation, and did not adversely affect patient comfort when compared to their usual ventilator (data not reported). Despite this, patients in both groups spent a significant period of the night with saturations less than 90% (pressure  $73\pm 32$  vs. volume  $107\pm 40$  minutes). Inspection of the raw data suggests that this was predominantly related to leak. It is not known whether mild nocturnal hypoxia is harmful, and when supplemental oxygen should be added with NIV. By using controlled ventilation, we also tried to minimise the effect of patient-ventilator interaction. It was not possible from the data to establish the frequency of ineffective efforts but we think it unlikely that there were many, both from direct observation of the patients receiving NIV during the day and because of our early experience that when the back up rate was set low patients made very little respiratory effort.[31]

Compared to some studies we, like others, used relatively high inflation pressures.[32][33][14] Using this strategy we showed good control of CO<sub>2</sub> levels overnight, and our patients tolerated the high pressures well. We did see a lot of leak and it is possible that we might have seen comparable CO<sub>2</sub> control but with less leak had we used lower inflation pressures. The level of nocturnal leak with both modes of ventilation was similar to that observed in other studies, but contrasts however in that this did *not* impact on sleep quality or daytime function.[14][34] We have shown greater levels of leak during pressure ventilation, but this did not translate into an increase in arousals, worsening of quality of life, health status or daytime function. The low arousal index in this study compared to others may reflect that our patients were well-acclimatised ventilator users.[34] The recent study by Windisch et al. demonstrated similar levels of leak and also identified a trend to greater leak during pressure ventilation.[14] This may reflect differences in expiratory triggering but could only be proven by a direct comparison of support and controlled ventilation. Whilst inspiratory time during pressure mode was longer, indicating some degree of 'hang up', we have shown that the same expired minute volume is maintained in either mode, albeit with a greater degree of leak during pressure ventilation. Having identified excess leak in the pressure group, in retrospect it would have been informative to have included a measure of nasal symptoms.

Whilst there was no overall significant difference between the two modes, some individuals did show improvements with one mode compared to the other (Figure 2). This is consistent with other studies which have shown a deterioration in a subgroup of patients with CWD switched from volume to pressure targeted ventilation [29] or improved symptoms and gas exchange in a select group of patients who had

deteriorated with volume ventilation but who were then switched to pressure ventilation.[28] It was not possible to identify which patients would perform better with which mode from baseline characteristics, and this may just represent spontaneous variation. However in keeping with the work of others, this observation supports the concept of using the alternate mode if a patient is not succeeding with one mode of ventilation.[28][29] Our study was powered to detect a clinically significant change in  $P_aO_2$ . The reason for this was that correction of hypoxia has been shown to improve survival and we argued that even if there were other benefits from one mode, but  $P_aO_2$  worsened, this would not be desirable. It may be that there are subtle benefits with one mode, which were not detected because the study lacked sufficient power, but any such differences are likely to be small and do not appear to impact on patients' daytime function and health status.

In conclusion we have shown no advantage to pressure or volume ventilation for patients with chest wall deformity. There is therefore no indication to change the mode of ventilation for existing users. For new users the choice will be determined by other factors, including cost and the experience and expertise of the Unit in which NIV is initiated.

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### Figure Legends

Figure 1 - Study protocol. Measures were performed at the end of each treatment period (4 and 10 weeks).

Figure 2 – Individual changes in morning arterial blood gas tensions after each mode of ventilation; A:  $P_aO_2$ , B:  $P_aCO_2$ . Dark line identifies group mean.

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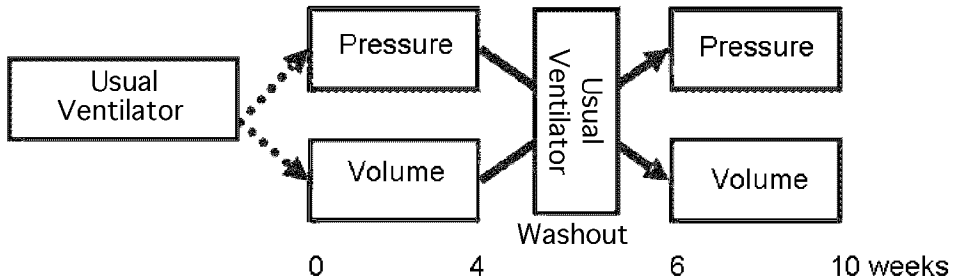


Figure 1

