Ventilation management in Victorian intensive care unit patients without acute respiratory distress syndrome

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Controlled mechanical ventilation (CMV) is an important aspect of the management of the critically ill patient. Despite the frequency of its use, the optimal approach to CMV in patients without acute respiratory distress syndrome (ARDS) is currently unknown.[1-7] Nonetheless, high tidal volume (V_T) and high airway pressures may cause ventilator-induced lung injury in non-ARDS patients, independent of the underlying pathology.[4,8-10] This notion is supported by prospective evidence showing that a low V_T per predicted body weight (V_T-PBW) approach (defined as between 6.0 and 8.0 mL/kg, depending on the study) reduces the incidence of ventilator-induced lung injury even in patients without ARDS.[11-13] Such practice, however, can lead to elevated arterial partial pressure of carbon dioxide ($Paco_2$),[14] the significance of which is unclear.[15,16] Current practice in Australia with regard to CMV and $Paco_2$ control in patients without ARDS is not known. We therefore performed a multicentre, prospective, observational study of current practices of CMV and $Paco_2$ control in intensive care units (ICUs) in Victoria, Australia. We hypothesised that in modern Australian ICUs, in patients without ARDS, high tidal volumes (V_T-PBW > 8.0 mL/kg) would be uncommon (< 10%), and appropriate adjustments would be made to V_T for females to avoid such overdistending V_T. Secondly, we hypothesised that hypercapnia would be tolerated in such patients, except where hypercapnia may be potentially physiologically contraindicated.

Methods

Centre participation and ethical considerations

Patients were recruited from seven ICUs in Victoria, Australia. We obtained prospective ethics approval for the principal site via the Austin Health Human Research Ethics Committee (LNR/15/Austin/286), with individual sites obtaining local governance approval.

ABSTRACT

Background: The setting of tidal volume (V_T) during controlled mechanical ventilation (CMV) in critically ill patients without acute respiratory distress syndrome (ARDS) is likely important but currently unknown. We aimed to describe current CMV settings in intensive care units (ICUs) across Victoria.

Methods: We performed a multicentre, prospective, observational study. We collected clinical, ventilatory and arterial blood gas data twice daily for 7 days. We performed subgroup analysis by sex and assessment of arterial partial pressure of carbon dioxide ($Paco_2$) management where hypercapnia was potentially physiologically contraindicated.

Results: We recorded 453 observational sets in 123 patients across seven ICUs. The most commonly selected initial V_T was 500 mL (33%), and this proportion did not differ according to sex (32% male, 34% female). Moreover, 38% of patients were exposed to initial V_T per predicted body weight (V_T-PBW) > 8.0 mL/kg. V_T-PBW in this range were more likely to occur in females, those with a lower height, lower ideal body weight or in those for whom hypercapnia was potentially physiologically contraindicated. As a consequence, females were more frequently exposed to a lower $Paco_2$ and higher pH.

Conclusions: In adults without ARDS undergoing CMV in Australian ICUs, the initial V_T was a stereotypical 500 mL in one-third of participants, irrespective of sex. Moreover, around 40% of patients were exposed to an initial V_T-PBW > 8.0 mL/kg. Finally, women were more likely to be exposed to a high V_T and hyperventilation.

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Patient eligibility and data collection

A sample size of over 120 patients was selected on the basis that 10 to 30 patients per institution, across several ICUs, would be representative of current practice within Victoria and, therefore, Australia. We screened all mechanically ventilated adults (age, ≥ 18 years) for eligibility. We included patients who were ventilated in a CMV mode who had been intubated within the preceding 24 hours. We excluded patients receiving extracorporeal life support and in whom death was expected in less than 48 hours. We collected demographic and clinical data, including height, weight, vital signs, current ventilator settings, and recent arterial blood gas results. Data were collected at two time points (8–10 am and 4–6 pm) daily for a maximum of 7 consecutive days. Data collection ceased once the patient was no longer being ventilated in a CMV mode, upon ICU discharge or death. Outcome data were not sought due to the observational nature of the study. Treating clinicians were blinded to the purpose of the study.

Grouping by risk associated with hypercapnia

We identified patients in whom hypercapnia may be physiologically contraindicated — those who had post-cardiac surgery; intracranial neurosurgery; acute intracranial pathology, including fulminant hepatic failure, known pulmonary hypertension or right heart dysfunction; diabetic ketoacidosis; or significant metabolic acidosis, defined as pH < 7.20. Patients were accordingly categorised into two groups: hypercapnia potentially physiologically acceptable (HPA) and hypercapnia potentially physiologically contraindicated (HPC).

Outcome measures and subgroup analyses

The primary outcome was the initial CMV strategy, including the ventilator settings, the resultant vital signs and biochemical analysis. We assessed for changes in CMV strategy between Day 1 and Days 2–4 as a secondary outcome. We planned a priori defined subgroup analyses to explore differences between those exposed to V_T-PBW ≤ 8.0 mL/kg and > 8.0 mL/kg, and differences in CMV settings with respect to sex and hypercapnia group.

Data handling and statistical analysis

Discrete variables were presented as number and percentage, whereas parametric continuous variables were described as mean, standard deviation (SD), and non-parametric continuous variables were presented using their median and interquartile range (IQR). Data collection was uniform throughout all sites. Data were recorded each day at two time points: morning or afternoon, which was abbreviated as Day 1 morning = D1, am; Day 1 afternoon = D1, pm etc. Data for Days 5–7 were removed from subsequent analysis due to the limited data at such time points. Calculations were performed for predicted body weight (men, ideal body weight [IBW] [kg] = 50 + [2.3 kg × height (inches) – 60]; women, IBW [kg] = 45.5 + [2.3 kg × height (inches) – 60])[17] and body mass index (BMI). Height was calculated from measured demi-span when necessary.[18,19] V_T per kilogram weight was calculated for absolute body weight (V_T-ABW) and predicted body weights (V_T-PBW). To assess for changes in ventilatory and biochemical data over time, the time

Table 1. Baseline characteristics

Variable	*n* = 123
Age (years), median (IQR)	58 (42–69)
Male	79 (64%)
Height (cm), median (IQR)	171 (165–178)
Actual body weight (kg), median (IQR)	83 (69–94)
Ideal body weight (kg), median (IQR)	66 (57–73)
Body mass index (kg/m^2), median (IQR)	28 (25–32)
APACHE II, median (IQR)	23 (15–36)
Hospital type	
Tertiary/teaching	71%
Admission type	
Unplanned	57%
Parent team	
Medical	47%
Diagnostic category	
General surgery	9%
Airway/thoracic surgery	5%
Cardiac surgery	21%
Neurosurgery	5%
Other surgery	6%
Sepsis (including CAP)	8%
Respiratory	7%
Cardiac	1%
Neurology	6%
Acute liver failure	3%
Medical other	12%
Pre-morbid respiratory disease	7%
Respiratory complication	4%

APACHE = Acute Physiology and Chronic Health Evaluation.
CAP = community-acquired pneumonia. IQR = interquartile range.

Table 2. Initial ventilatory and biochemical parameters, whole cohort and by sex

Variables	Whole cohort	Male *n* = 79	Female *n* = 44	*P*
Ventilatory mode				0.047
VCV	7%	4%	12%	
SIMV-VC	70%	77%	59%	
SIMV-PC	15%	16%	14%	
PCV	7%	3%	14%	
V_T 500 mL	33%	32%	34%	0.80
V_T-PBW				0.05
< 8.0 mL/kg	62%	70%	48%	
8.1–9.0 mL/kg	24%	17%	39%	
9.1–10.0 mL/kg	10%	12%	6%	
> 10.0 mL/kg	3%	2%	6%	
V_T (mL), median (IQR)	500 (450–550)	510 (500–580)	450 (420–500)	< 0.0001
V_T-PBW (mL/kg), median (IQR)	7.6 (6.9–8.8)	7.4 (6.8–8.5)	8.1 (7.0–8.9)	0.10
V_T-PBW (mL/kg), mean (SD)	7.8 ± 1.3	7.6 ± 1.2	8.1 ± 1.2	0.10
MV (L/min), median (IQR)	7.2 (6.2–9.2)	7.9 (6.7–9.9)	6.7 (5.6–7.6)	0.0018
RR (breaths/min), median (IQR)	14 (12–16)	15 (12–18)	14 (12–16)	0.07
PIP (cmH_20), median (IQR)	21 (18–25)	20 (18–25)	22 (18–25)	0.63
PEEP (cmH_20), median (IQR)	5 (5–8)	5 (5–8)	5 (5–5)	0.21
Fio_2, median (IQR)	0.35 (0.3–0.4)	0.4 (0.3–0.5)	0.3 (0.3–0.4)	0.30
Pao_2 (mmHg), median (IQR)	94 (79–124)	94 (79–122)	95 (78–127)	0.75
$Paco_2$ (mmHg), median (IQR)	40 (36–45)	42 (38–46)	37 (34–44)	0.0440
pH, median (IQR)	7.38 (7.33–7.42)	7.37 (7.31–7.41)	7.39 (7.35–7.44)	0.0364
Bicarbonate (mmol/L), median (IQR)	24 (21–26)	24 (21–26)	23 (21–26)	0.82

Fio_2 = fraction of inspired oxygen. IQR = interquartile range. MV = minute ventilation. $Paco_2$ = partial pressure of arterial carbon dioxide. Pao_2 = partial pressure of arterial oxygen. PCV = pressure control ventilation. PEEP = positive end-expiratory pressure. PIP = peak inspiratory pressure. RR = respiratory rate. SD = standard deviation. SIMV-PC = synchronised intermittent mandatory ventilation-pressure control. SIMV-VC = synchronised intermittent mandatory ventilation-volume control. VCV = volume controlled ventilation. V_T = tidal volume. V_T-PBW = tidal volume per kg predicted body weight.

points were divided into two discrete time point groups: Day 1 (time points 1 and 2) and Days 2–4 (time points 3–8). A single averaged mean value was calculated for each time point group by combining the mean value for each patient, within each time point group. Differences between V_T-PBW ≤ 8.0 mL/kg and > 8.0 mL/kg; hypercapnia potentially physiologically acceptable and HPC; male and female groups; and time point groups Day 1 and Days 2–4 were assessed using a two-sample Student *t* test assuming equal variance or χ^2 analysis depending on variable type (continuous or categorical). Statistical analysis was performed using Stata 14 (StataCorp, College Station, TX, USA); statistical significance was taken as a two-sided $P < 0.05$.

Results

Patient demographics

We recorded 453 CMV episodes across seven ICUs (three academic, three metropolitan and one regional) in Victoria, Australia. We studied 123 patients, of which 73 (59%) remained in CMV after Day 1, two-thirds were male and one-fifth had undergone cardiac surgery. Almost all patients were ventilated via an oral endotracheal tube, just over half were admitted after an operation, and just under half were elective ICU admissions. Additional demographic details are found in Table 1.

Figure 1. Percentage of initial absolute tidal volume overall and by sex

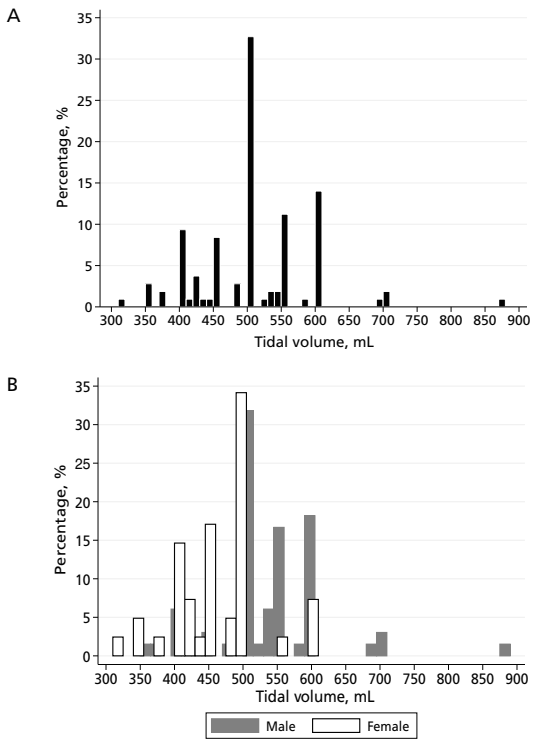

Figure 2. Percentage of initial absolute tidal volume by predicted body weight overall and by sex

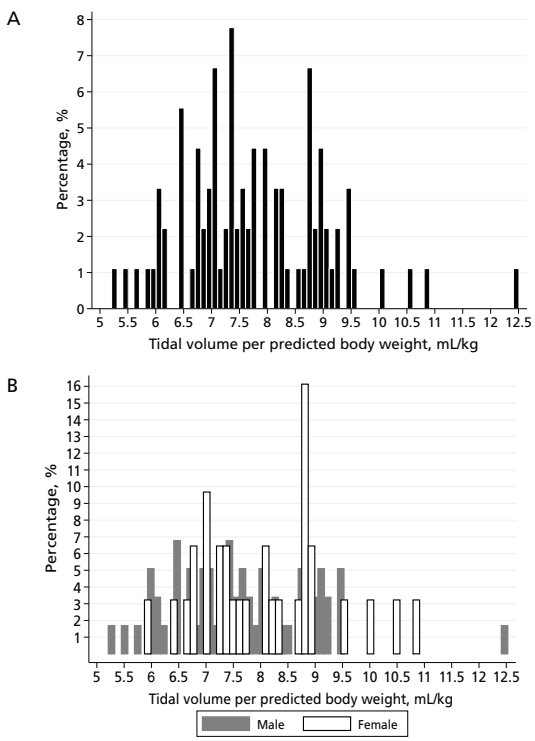

Table 3. Baseline characteristics by initial V_T-PBW group

Variable	V_T-PBW < 8.0mL/kg *n* = 56	V_T-PBW > 8.0mL/kg *n* = 34	*P*
Age (years)	62 (46–71)	62 (56–71)	0.29
Male	73%	53%	0.05
Height (cm)	175 (168–180)	165 (160–173)	< 0.0001
Actual body weight (kg)	85 (71–95)	79 (70–90)	0.24
Ideal body weight (kg)	69 (63–75)	58 (54–69)	< 0.0001
Body mass index (kg/m^2)	28 (25–31)	29 (25–32)	0.71
APACHE II	20 (16–28)	22 (15–35)	0.16
Hospital type			
Tertiary/ teaching	66%	74%	0.46
Admission type			
Unplanned	48%	47%	0.92
Parent specialty			
Medical	52%	33%	0.07
HPC	44%	77%	0.004

APACHE = Acute Physiology and Chronic Health Evaluation. CAP = community acquired pneumonia. HPC = hypercapnia potentially physiologically contraindicated. V_T-PBW = tidal volume per kg predicted body weight.

Initial ventilatory data

The most common CMV mode was synchronised intermittent mandatory ventilation in volume control (SIMV-VC) in over two-thirds of patients. One-third of patients' initial V_T was 500 mL and the median V_T-PBW was < 8.0 mL/kg. However, around 40% of patients were exposed to an initial V_T-PBW > 8.0 mL/kg, one-quarter of patients were exposed to V_T-PBW 8.1–9.0 mL/kg, while one in ten were exposed to 9.1–10 mL/kg. Additional initial ventilatory and biochemical data are presented in Table 2, Figure 1, and Figure 2.

Changes in ventilatory and biochemical data by time point group

There was no change in V_T or V_T-PBW nor in minute ventilation, peak inspiratory pressure or $PaCO_2$ between time point groups (online Appendix, Section 1, available at cicm.org.au/Resources/Publications/Journal). There was a decrease in positive end-expiratory pressure (P = 0.0360) and an increase in pH (P = 0.0002) and arterial bicarbonate (P = 0.0002) in the Days 2–4 time point group (online Appendix, Section 1).

Table 4. Initial ventilatory and biochemical data by V_T-PBW group

Variables	V_T-PBW < 8mL/kg *n* = 56	V_T-PBW > 8mL/kg *n* = 34	*P*
Ventilatory mode			0.37
VCV	2%	9%	
SIMV–VC	94%	71%	
SIMV–PC	2%	18%	
PCV	2%	3%	
V_T 500 mL	29%	29%	0.93
V_T (mL), median (IQR)	500 (418–537)	535 (500–600)	0.0002
V_T-PBW (mL/kg), median (IQR)	7.0 (6.5–7.5)	8.9 (8.7–9.2)	< 0.0001
MV (L/min), median (IQR)	7.34 (6.2–9.4)	6.9 (6.3–9)	0.88
RR (breaths/min), median (IQR)	15 (12–18)	14 (12–16)	0.19
PIP (cmH_20), median (IQR)	20 (18–25)	22 (20–25)	0.19
PEEP (cmH_20), median (IQR)	5 (5–8)	5 (5–6)	0.86
Fio_2, median (IQR)	0.33 (0.3–0.4)	0.38 (0.3–0.5)	0.44
Pao_2 (mmHg), median (IQR)	94 (79–125)	96 (77–123)	0.84
$Paco_2$ (mmHg), median (IQR)	40 (37–45)	40 (35–43)	0.11
pH, median (IQR)	7.38 (7.34–7.42)	7.38 (7.31–7.41)	0.28
Bicarbonate (mmol/L), median (IQR)	24 (23–26)	21 (19–24)	0.00161

Fio_2 = fraction of inspired oxygen. IQR = interquartile range. MV = minute ventilation. $Paco_2$ = partial pressure of arterial carbon dioxide. Pao_2 = partial pressure of arterial oxygen. PCV = pressure control ventilation. PEEP = positive end-expiratory pressure. PIP = peak inspiratory pressure. RR = respiratory rate. SIMV-PC = synchronised intermittent mandatory ventilation-pressure control. SIMV-VC = synchronised intermittent mandatory ventilation-volume control. VCV = volume controlled ventilation. V_T = tidal volume. V_T-PBW = tidal volume per kg predicted body weight.

Subgroup analyses by V_T-PBW group

A greater proportion of patients in the V_T-PBW ≥ 8.0 mL/kg group were female (*P* = 0.05), shorter (*P* < 0.0001), had a smaller IBW (*P* < 0.0001) and were in the HPC group (*P* = 0.004). No other baseline values approached statistical significance (Table 3), and there were no differences in ventilatory and biochemical parameters, except for a lower bicarbonate in the V_T-PBW > 8.0 mL/kg group (*P* = 0.00161) (Table 4).

Associations between V_T-PBW and independent variables

Height and admission with a neurological diagnosis (*n* = 4) were the only two independent variables associated with V_T-PBW in univariate analysis (*P* < 0.0001 and *P* = 0.042, respectively), while there was a possible weak unadjusted association with a potential physiological contraindication to hypercapnia *P* = 0.06 (online Appendix, Section 2). On multivariate analysis, the association with a potential physiological contraindication to hypercapnia reached significance (*P* = 0.019), while both height and admission for a neurological condition retained significance with *P* = 0.011 and *P* = 0.041, respectively (Table 5).

Subgroup analyses by sex

The median V_T was higher in males (*P* < 0.0001). Although there was no difference observed when comparing the median V_T-PBW (*P* = 0.10). A greater percentage of women were exposed to V_T > 8.0 mL/Kg (*P* = 0.05). Moreover, women were ventilated to a lower $Paco_2$ (*P* = 0.044) and higher pH (*P* = 0.036) (Table 2).

Subgroup analyses by hypercapnia group

Just over half the patients (55%) were within the HPC group. A greater proportion of such patients were admitted following cardiac, neurological, airway or thoracic, or other non-specific surgeries, or were admitted under a neurological specialty. The fraction of inspired oxygen (Fio_2) and arterial partial pressure of oxygen (Pao_2) were higher, and the pH and arterial bicarbonate lower, in the HPC group. However, there was no difference in initial $Paco_2$ level between hypercapnia groups. Further details of baseline characteristics and ventilatory and biochemical data are presented in the online Appendix, Section 3 and Section 4, respectively.

Discussion

Key findings

In this multicentre, prospective audit of CMV in Australian ICUs, one-third of initial V_T values were 500 mL and this proportion did not differ with sex. Nearly 40% of patients were exposed to initial V_T-PBW > 8.0 mL/kg, which was more likely in females, shorter patients, those with a lower IBW or in the HPC group. Moreover, women were more frequently exposed to lower $Paco_2$ and higher pH than

Table 5. Multivariate associations between selected variables and tidalvolume per predicted body weight using linear regression analysis

Variable	β-coefficient	Standard error	95% CI	*P*
Sex	–0.008	0.32	–0.64 to 0.62	0.98
Height	–0.044	0.017	–0.08 to –0.01	0.011
HPC	0.63	0.27	0.10 to 1.2	0.019
Neurology	–1.30	0.63	–2.5 to –0.06	0.041

CI = confidence interval. HPC = hypercapnia potentially physiologically contraindicated.

men. Finally, we found no significant difference in initial $Paco_2$ management for patients for whom hypercapnia was potentially physiologically contraindicated.

Relationship to previous studies

A recent 2015 retrospective audit of current practice over 14 years (2000–2013) in a single Australian tertiary hospital described similar median V_T-PBW and absolute V_T 8.2 mL/kg and 506 mL, respectively.[20] In keeping with our data, the authors described female sex and increasing BMI as risk factors for exposure to higher V_T-PBW. However, this was a retrospective study spanning over 10 years, thus open to the major confounder of secular trends and single centre features. A 2017 prospective, multicentre audit of current practice of mandatory ventilation in 16 ICUs in the United Kingdom described a similar mean V_T-PBW 7.2 mL/kg.[21] However, this study was performed over a single 24-hour period, excluded patients in whom hypercapnia was potentially physiologically contraindicated, involved fewer than 90 patients and its relevance to non-UK centres was unknown. In 2010, Determann and colleagues[11] performed a randomised controlled trial comparing lower V_T (V_T-PBW 6.0 mL/kg) with routine practice (10.0 mL/kg) in 150 critically ill patients without acute lung injury (ALI). The initial mean V_T-PBW pre-randomisation was 8.2 mL/kg and 8.4 mL/kg in the conventional and lower tidal volume groups, respectively, a value similar to our V_T-PBW 7.6mL/kg. In 2007, Yilmaz and colleagues[12] performed a before-and-after quality improvement observational study in 375 patients. There were 212 patients in the before period, whose median V_T-PBW was 10.6 mL/kg (IQR, 9.2–12.1 mL/kg). There were 50 patients in the before period of a 2005 multicentre before-and-after practice change observational study by Wolthius and colleagues,[13] where the V_T-PBW in patients without ALI or ARDS was 9.7 mL/kg (SD, 1.9 mL/kg). The proportion of patients with V_T-PBW > 8mL/kg was also higher, at between 78% and 88%, and V_T-PBW > 10 mL/kg was seen in 33% and 41% of patients, depending on the site. A 2004 multicentre cohort study of 332 patients without ALI by Gajic and colleagues[22] found that women were exposed to higher V_T-PBW (11.4 mL/kg) compared with men (10.4 mL/kg). In a 2004 single-centre, 11-year retrospective study of mechanical ventilation in patients without ALI by Wongsurakiat et al,[23] there was no difference between sexes in those receiving low (V_T-ABW < 10 mL/kg) or traditional (V_T-ABW > 10 mL/kg) V_T. However, this study reported V_T-ABW, not V_T-PBW. Our findings are broadly aligned with the above studies and suggest that, in Australian ICUs, there is a predilection for V_T 500 mL that may limit the application of potentially physiologically protective and individualised ventilatory settings in non-ARDS patients.

Implications for clinicians

Our findings imply that almost 40% of Victorian (and likely Australian) patients are exposed to potentially hazardous V_T and that one-third of patients receive stereotypical V_T 500 mL. They also imply that women are more likely to be exposed to potentially injurious V_T, greater degrees of hypocapnia and a more alkalotic pH. Finally, the lack of difference in initial carbon dioxide management between hypercapnia groups implies that fluctuations in $Paco_2$ are tolerated in both sets of patients despite the stated perceived risk of hypercapnia. Moreover, the observed increased risk of exposure to V_T-PBW > 8.0 mL/kg in the HPC group implies that increasing V_T (instead of increasing respiratory rate) is the preferred route to maintenance of normocapnia in such patients.

Strengths and limitations

To our knowledge, this is the first multicentre, prospective, observational study of current CMV practice in Australian ICU patients. The data we have provided are in keeping with larger studies and provides construct-validity. Moreover, clinicians were blinded to the purpose of the study. By including a range of metropolitan, rural and tertiary referral ICUs, we believe our results to be generalisable, with both external-validity and face-validity. Finally, the study findings provide evidence of very limited V_T adjustment in non-ARDS patients and deliver the background information necessary for the design of interventional studies. This was a prospective, observational study with the inherent limitations of such design. Moreover, twice-daily measurement of ventilatory settings may not have captured all adjustments, and around 40% of patients were no longer undergoing

CMV by Day 2. However, given that there were few changes in ventilatory settings between time point groups, the potential for missing changes in ventilatory settings appears small. We did not consider individual practice nor relevant hospital guidelines. Nevertheless, due to the large number of clinicians of varied backgrounds (> 150 intensive care physicians, > 300 nursing staff and physiotherapists) across multiple sites, this would have been logistically challenging. In addition, the signal is clear that adjustments to achieve low V_T ventilation are uncommon in these patients.

Conclusion

We performed a multicentre, prospective, observational study of current controlled mechanical ventilation practice in ICU patients without ARDS. The initial V_T was a stereotypical 500 mL in one-third of patients and this did not differ with sex. Almost 40% of patients were exposed to initial V_T-PBW > 8.0 mL/kg, which was more likely to occur in patients who were female (exposing them to lower $Paco_2$ and higher pH values), were short, had a lower IBW, or in those who were considered at risk of harm from hypercapnia. These findings support the view that IBW-adjusted ventilation parameters should be prescribed in non-ARDS patients receiving controlled mechanical ventilation in order to minimise the observed tendency of applying V_T 500 mL to most patients. They also provide the necessary background information for the design of interventional studies.

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Competing interests

None declared.

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Section 1 Averaged ventilatory and biochemical data by time-point group

Variables	Day 1 n = 83	Day 2-4 n = 73	p-value
VT, ml	500 (450-550)	500 (485-562)	0.43
VT-PBW, ml/kg	7.6 (6.8-8.8)	7.6 (6.9-8.7)	0.92
MV, L/min	7.0 (6.2-9.0)	7.8 (6.6-9.7)	0.10
RR, Breaths/min	14 (12-16)	14 (12-17)	0.15
PIP, cmH_20	20 (18-24)	22 (18-25)	0.78
PEEP, cmH_20	5 (5-7)	5 (5-9)	0.0360
FiO_2	0.35 (0.3-0.5)	0.3 (0.25-0.4)	0.0217
PaO_2, mmHg	102 (83-137)	81 (74-97)	0.06
$PaCO_2$, mmHg	40 (36-45)	39 (36-43)	0.91
pH	7.37 (7.32-7.41)	7.41 (7.38-7.44)	0.0002
Bicarbonate, mmol/L	23 (20-26)	26 (23-28)	0.0002

Section 1 Legend

VT = tidal volume, VT-PBW = tidal volume per kilogram predicted body weight, MV = minute ventilation, RR = respiratory rate, PIP = peak inspiratory pressure, PEEP = positive end-expiratory pressure, FiO_2 = fraction of inspired oxygen, PaO_2 = partial pressure of arterial oxygen, $PaCO_2$ = partial pressure of arterial carbon dioxide

Section 2

Univariate associations between selected variables and tidal volume per predicted body weight using linear regression analysis

Variable	β co-efficient	Standard error	95% CI	p-value
Sex	-0.46	0.28	-1.0 to 0.94	0.10
Height	-0.05	0.14	-0.08 to -0.02	<0.0001
Age	0.008	0.01	-0.1 to 0.28	0.43
APACHE II	0.007	0.008	-0.009 to 0.02	0.39
Hospital type	0.04	0.29	-0.53 to 0.62	0.88
Admission type	-0.16	0.27	-0.70 to 0.37	0.55
Admitting team	-0.14	0.27	-0.68 to 0.40	0.60
Hypercapnia contraindication	0.53	0.28	-0.03 to 1.08	0.06
Neurology	-1.32	0.64	-2.6 to -0.05	0.042

Section 2 Legend

95% CI = 95% confidence interval

Section 3

Baseline characteristics by hypercapnia group

Variable	HPA n = 53	HPC n = 64	p-value
Age (years)	63 (45 - 76)	62 (53 - 69)	0.83
Male (%)	64	64	0.99
Height (cm)	170 (164 - 179)	172 (165 - 177)	0.88
Actual Body Weight (kg)	80 (65 - 90)	85 (66 - 98)	0.33
Ideal Body Weight (kg)	63 (57 - 74)	66 (57 - 72)	0.93
Body Mass Index (kg/m^2)	26 (25 - 31)	29 (24 - 34)	0.36
APACHE II	20 (13 - 33)	24 (17 - 39)	0.25
Hospital type (%)			
Tertiary/Teaching	72	77	0.55
Admission type (%)			
Unplanned	70	52	0.045
Parent specialty (%)			
Medical	57	39	0.06

Section 3 Legend

HPA = Hypercapnia potentially physiologically acceptable, Hypercapnia potentially physiologically contraindicated = HPC, CAP = community acquired pneumonia

Section 4

Initial ventilatory and biochemical data by hypercapnia group

Variables	HPA, n = 53	HPC, n = 64	p-value
Ventilatory Mode			0.54
VCV (%)	4	11	
SIMV – VC (%)	75	63	
SIMV – PC (%)	13	18	
PCV (%)	6	9	
VT 500ml (%)	41	30	0.26
VT-PBW (%)			0.024
< 8ml/kg	81	51	
8.1 - 9ml/kg	11	30	
9.1-10ml/kg	8	13	
>10ml/kg	0	3	
VT, ml	500 (450-500)	500 (450-600)	0.09
VT-PBW, ml/kg	7.3 (6.9-7.9)	8 (6.9-8.9)	0.06
MV, L/min	7.1 (6.2-9.1)	7.0 (6.3-8.9)	0.79
RR, Breaths/min	14 (12-17)	15 (12-17)	0.62
PIP, cmH_20	19 (15-25)	22 (19-23)	0.10
PEEP, cmH_20	5 (5-7)	5 (5-6)	0.90
FiO_2	0.3 (0.25-0.4)	0.35 (0.3-0.5)	0.0419
PaO_2, mmHg	93 (76-112)	99 (80-143)	0.0145
$PaCO_2$, mmHg	40 (36-43)	41 (36-45)	0.69
pH	7.4 (7.37-7.44)	7.37 (7.31-7.41)	0.0086
Bicarbonate, mmol/L	24 (23-27)	23 (18-26)	0.0171

Section 4 Legend

HPA = Hypercapnia potentially physiologically acceptable, Hypercapnia potentially physiologically contraindicated = HPC, VT = tidal volume, VT-PBW = tidal volume per kilogram predicted body weight, MV = minute ventilation, RR = respiratory rate, PIP = peak inspiratory pressure, PEEP = positive end-expiratory pressure, FiO_2 = fraction of inspired oxygen, SpO_2 = pulse oximetry oxygen saturation, SaO_2 = arterial oxygen saturation, PaO_2 = partial pressure of arterial oxygen, $PaCO_2$ = partial pressure of arterial carbon dioxide