Oxygen (O₂) is a life-saving drug and is used ubiquitously in hospitals and intensive care units (ICU) worldwide. International consensus opinion on mechanical ventilation (MV) proposed using an inspired O₂ concentration (FiO₂) necessary to achieve at least 90% SaO₂ (arterial O₂ saturation) as an acceptable target for most applications of ventilatory support. Nevertheless, besides few specific clinical conditions, there is little or no evidence to guide ICU clinicians on titration of O₂ therapy. Furthermore, there is uncertainty about optimal arterial O₂ saturation (SpO₂) and tension (PaO₂) targets for O₂ therapy.

In a retrospective database study, hyperoxia was frequently present in Dutch ICU patients but usually did not lead to adjustment of ventilator settings. A recent study reported common use of liberal O₂ supplementation in ventilated patients with acute lung injury (ALI) and showed a correlation between exposure to excessive FiO₂ and worsening of oxygenation index in a dose response manner. In a post hoc analysis, high FiO₂ was associated with higher mortality even after controlling for PaO₂.

Current oxygenation practice in ventilated patients—an observational cohort study

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SUMMARY

Oxygen therapy is a mainstay of critical care medicine, yet its optimal therapeutic use has not been systematically evaluated. A detailed understanding of current practice in oxygen therapy in intensive care is required to enable future interventional studies. We aimed to describe current oxygenation practice in patients requiring ≥48 hours of mechanical ventilation (MV) at an academic tertiary referral centre.

We collected longitudinal arterial blood gas and hourly oxygenation data from intensive care unit charts in a consecutive cohort of 40 trauma, 41 medical and 20 surgical patients for their first seven MV days, analysed data for 14,063 MV hours, and derived time-weighted averages (TWA) of variables for each 24-hour interval on MV for all patients.

The TWA-FiO₂ was 0.42 (95% CI 0.41 to 0.44) and TWA-SpO₂ was 97.1% (95% CI 96.8 to 97.4) for the first seven MV days. TWA-PaO₂ was >80 mmHg on 80% of MV days. TWA-FiO₂ of ≥0.35 was used to achieve TWA-SpO₂ >95% on 61% of MV days. Of 58 MV days with TWA-FiO₂ ≥0.60, TWA-SpO₂ ≥96% occurred on 28 (48%) days. Mean SpO₂ and PaO₂ in patients with severe acute lung injury (ALI) scores were higher than recommended targets. Wide variability in the mean SpO₂ and PaO₂ was observed in patients with comparable ALI scores.

Inspired oxygen therapy in these MV patients was ‘liberal’, with PaO₂ and SpO₂ values generally above 80 mmHg and 96% respectively. An interventional study comparing current practice to more conservative targets (PaO₂=60 to 65 mmHg and/or SpO₂=90 to 92%) appears possible.

Key Words: intensive care, mechanical ventilation, oxygen inhalation therapy, time-weighted average (TWA), acute lung injury (ALI)
FiO₂. There is no strong evidence that targeting higher levels of SpO₂ or PaO₂ within the acceptable range is more advantageous. On the other hand, limits of hypoxia tolerance are not well defined.

Our hypothesis for this study was that in routine care during MV, patients spend long periods of time with more than necessary oxygenation levels (SpO₂, SaO₂, PaO₂ and FiO₂). At present, the longitudinal data on actual oxygenation practice outside of clinical trial setting is scarce; in particular, the data on mean oxygenation levels over a longer period of ventilation is non-existent. Ascertaining the current practice and pattern of O₂ therapy in detail may help design an interventional study. Accordingly, we investigated our current practice concerning oxygenation (SpO₂, SaO₂ and PaO₂) and use of FiO₂ in patients requiring MV for ≥48 hours in an academic tertiary care ICU in Melbourne, Australia. In addition to the main aim of describing longitudinal practice of O₂ therapy, our secondary objective was to determine if oxygenation practice differs significantly among patients with different ALI scores.

METHODS

We conducted an observational cohort study of 101 patients admitted between May 2010 and June 2011 in a mixed medical and surgical 45-bed ICU at a university-affiliated tertiary care hospital in Melbourne, Australia. The hospital ethics committee approved this study (approval number 29/11) and waived the requirement for informed consent. Eligible patients requiring ≥48 hours of MV were identified from the prospective ICU database. We excluded patients if they were either considered at risk for imminent death by the treating medical team, diagnosed with conditions where higher or lower O₂ levels are potentially contraindicated such as severe chronic obstructive pulmonary disease or carbon monoxide poisoning, or required extracorporeal membrane oxygenation or hyperbaric O₂ therapy, or transferred on MV from another ICU.

We recorded patient-related variables (demographics, admission diagnosis, Charlson’s comorbidity score, illness severity scores, worst lactate, pH range), process-of-care-related variables (FiO₂, positive end-expiratory pressure [PEEP], co-oximeter measured SaO₂, PaO₂, SpO₂, hours spent in prespecified FiO₂ and SpO₂ ranges, and time spent at PaO₂ >100 mmHg and PaO₂ >200 mmHg), and outcome-related variables (change (Δ) in PaO₂/FiO₂ from day 0 to day 3 or day 6, and in-hospital mortality) for all patients. We longitudinally collected hourly data for key oxygenation-related variables during the first seven days of invasive MV. We recorded all arterial blood gases (ABG) and derived a 24-hour time-weighted mean PaO₂ for the first four days and the seventh day of MV. In addition, the 24-hour time-weighted mean SaO₂ was derived for the first three days. Since the upper limits of the target range for SpO₂ and PaO₂ in major clinical trials of patients with ALI/acute respiratory distress syndrome were 95% and 80 mmHg respectively, oxygenation above these limits was considered as ‘liberal’.

Time-weighted averages (TWA) of the variables-of-interest were derived for each 24-hour interval of MV for all patients. The TWA was calculated as the sum-product of values of variable-of-interest and their duration intervals divided by sum of all intervals i.e., TWA(X) = Σ X t / Σ t; where t is the duration of the nth interval, X is the variable-of-interest level during the nth interval, and sum total of such intervals (Σ t) is equal to the time period for which TWA is calculated. The time-interval for variables recorded from ICU observation charts was one hour as the bedside nurse recorded clinical data every hour, whereas time-interval for variables recorded from ABG was calculated as the time-difference before the next ABG. We did not include days where less than 12 hours of data was available (e.g. if patient was extubated or died). We classified patients a priori into three groups based on the severity of their ALI scores on day 0. Oxygenation-related parameters were then compared among these groups. Sequential Organ Failure Assessment scores reported in the study exclude the Glasgow coma scale component. ALI scores were calculated as an average of scores across 24-hour TWA PaO₂/FiO₂ (≥300=0, 225–299=1, 175–224=2, 100–174=3, <100=4), chest X-ray (1 point per quadrant with infiltrate) and 24-hour TWA PEEP in cmH₂O (≤5=0, 6–8=1, 9–11=2, 12–14=3, ≥15=4) for that day. ALI scores <1, 1 to 2.5 and >2.5 identified mild, moderate and severe respiratory failure respectively. The number of quadrants showing infiltrates on chest X-rays were recorded after agreement between two investigators.

Statistical analysis

We aimed to study a convenience sample of at least 100 patients, as such a sample was anticipated to provide a sufficient representation of the unit practice. For patients who were readmitted to the ICU and required MV ≥48 hours, only the
index admission was considered. All analysis was performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA). Variables were assessed for normality and log-transformed if appropriate. Baseline comparisons were performed using chi-square tests for equal proportions or Fisher’s exact tests where numbers were small and reported as n (%). Continuous normally distributed variables were compared using student t-tests or analysis of variance and reported as mean (standard deviation), while non-normally distributed data were compared using Wilcoxon rank-sum tests or Kruskal-Wallis tests and reported as median (interquartile range). Changes over time were determined using repeat measures mixed linear modelling with each patient treated as a random effect. A two-sided $P$ value of 0.05 was considered statistically significant.

RESULTS

We screened 154 adult patients. We excluded 53 patients in accordance with pre-specified criteria (26—imminent death, 13—transfer from other ICU, eight—extracorporeal membrane oxygenation, four—severe chronic obstructive pulmonary disease, two—ICU record unavailable) and enrolled a consecutive cohort of 40 multi-trauma, 41 medical and 20 surgical patients. All patients were analysed in final analysis.

Data on SpO$_2$ and FiO$_2$ were collected and analysed for a total of 14,063 hours and 14,133 hours respectively. The TWA-FiO$_2$ was 0.42 (95% confidence interval [CI] 0.41 to 0.44) and TWA-SpO$_2$ was 97.1% (95% CI 96.8 to 97.4) for the initial seven days of MV (Table 1). During these days, patients spent most of their time above 96% SpO$_2$.

Table 1

<table>
<thead>
<tr>
<th>Patient characteristics and key results</th>
<th>Descriptive statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>101</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>56.7 (20.5)</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>30 (30%)</td>
</tr>
<tr>
<td>Diagnosis type</td>
<td></td>
</tr>
<tr>
<td>Trauma, n (%)</td>
<td>40 (40%)</td>
</tr>
<tr>
<td>Medical, n (%)</td>
<td>41 (41%)</td>
</tr>
<tr>
<td>Surgical, n (%)</td>
<td>20 (20%)</td>
</tr>
<tr>
<td>Admission type</td>
<td></td>
</tr>
<tr>
<td>Elective, n (%)</td>
<td>6 (6%)</td>
</tr>
<tr>
<td>Emergency, n (%)</td>
<td>95 (94%)</td>
</tr>
<tr>
<td>Admission APACHE II score, mean (SD)</td>
<td>19.3 (7.6)</td>
</tr>
<tr>
<td>Day 0 SOFA score, mean (SD)</td>
<td>6.5 (3.4)</td>
</tr>
<tr>
<td>Hospital length-of-stay, days, median [IQR]</td>
<td>20 [10.1–37.8]</td>
</tr>
<tr>
<td>Total FiO$_2$ hours studied per patient, mean (SD)</td>
<td>143 (36.5)</td>
</tr>
<tr>
<td>Hours on FiO$_2$ 0.81–1.00 [median, IQR]</td>
<td>3 [1–5]</td>
</tr>
<tr>
<td>Hours on FiO$_2$ 0.61–0.80 [median, IQR]</td>
<td>2 [1–7]</td>
</tr>
<tr>
<td>Hours on FiO$_2$ 0.41–0.60 [median, IQR]</td>
<td>25 [10–64]</td>
</tr>
<tr>
<td>Hours on FiO$_2$ 0.21–0.40* [median, IQR]</td>
<td>91 [57–132]</td>
</tr>
<tr>
<td>Total SpO$_2$ hours studied per patient, mean (SD)</td>
<td>142 (36.4)</td>
</tr>
<tr>
<td>Hours on SpO$_2$ 88–91% [median, IQR]</td>
<td>1 [0–4]</td>
</tr>
<tr>
<td>Hours on SpO$_2$ 92–95% [median, IQR]</td>
<td>24 [10–52]</td>
</tr>
<tr>
<td>Hours on SpO$_2$ 96–100% [median, IQR]</td>
<td>108 [77–140]</td>
</tr>
<tr>
<td>7 days TWA SpO$_2$ mean (CI)</td>
<td>97.1 (96.8–97.4)%</td>
</tr>
<tr>
<td>7 days TWA FiO$_2$ mean (CI)</td>
<td>0.42 (0.41–0.44)</td>
</tr>
</tbody>
</table>

APACHE=Acute Physiological and Chronic Health Evaluation*, SD=standard deviation, SOFA=Sequential Organ Failure Assessment† excluding Glasgow coma component, IQR=interquartile range, TWA=Time-weighted average, CI=confidence interval. * Hours on FiO$_2$ $<$0.30 (median, IQR) per patient were 0 (0–9); only 13% of hours on FiO$_2$ 0.21–0.40 were spent with FiO$_2$ $<$0.30.
The lower limits of the 95% CIs for 24-hour TWA-SpO₂ on each of the first seven days of MV were >96.2% (Table 2). The ranges of 24-hour TWA-PaO₂ and SpO₂ for the entire study cohort were 64 to 299 mmHg and 88 to 100% respectively. The 24-hour TWA-PaO₂ was >80 mmHg on 80% of MV days (Figure 2).

A significant variation in the achieved TWA-SpO₂ was observed particularly when FiO₂ requirements were >0.35 (Figure 3). TWA-FiO₂ of ≥0.35 was used to achieve TWA-SpO₂ >95% on the majority (61%) of MV days. Of 612 MV days, a TWA-SpO₂ of 90 to 96% was achieved on 128 (21%) days with TWA-FiO₂ of 0.25 to 0.60; and a TWA-SpO₂ >96% was achieved on 120 (20%) days with TWA-FiO₂ of 0.45 to 0.95. Of 58 MV days with TWA-FiO₂ ≥0.60, a TWA-SpO₂ ≥96% occurred on 28 (48%) days. Of eight MV days with TWA-FiO₂ >0.80, a TWA-SpO₂ >96% occurred on three (38%) days.

There was a wide variation in clinical practice with respect to SpO₂ achieved at comparable ALI scores (Figure 4), and particularly with PaO₂/FiO₂.
A trend to accept lower SpO\textsubscript{2} with worsening ALI scores was noticed, although even on days with severe ALI scores (>2.5), the TWA-SpO\textsubscript{2} varied widely from 89 to 99%. Compared to patients in the high ALI score group, those in the lower ALI score groups had higher mean SpO\textsubscript{2} and PaO\textsubscript{2}, and spent more time at supra-normal O\textsubscript{2} levels (number of hours at PaO\textsubscript{2} >100 mmHg, \(P=0.01\); and number of hours at PaO\textsubscript{2} >200 mmHg, \(P<0.0001\)) during the first 72 hours of MV. The PaO\textsubscript{2}/FiO\textsubscript{2} on day 3 and day 6, when compared to day 0, were significantly worse in the lower ALI score group compared to the higher ALI score groups (Table 3). There were no significant differences in the average tidal volumes (\(P>0.5\)) in the three ALI subgroups during the initial three MV days, but TWA-PEEP values, as expected, were higher (\(P<0.0001\)) in the high ALI score group. Patients with lower ALI scores spent more time in higher SpO\textsubscript{2} ranges compared to other subgroups (\(P<0.0001\)).

There were no differences amongst the trauma, medical and surgical patients with regard to the

![Figure 2: Scatter plot for 24-hour weight-average PaO\textsubscript{2} achieved vs ALI score on that day.](image)

![Figure 3: Scatter plot for 24-hour weight-average SpO\textsubscript{2} achieved vs 24-hour weight-average FiO\textsubscript{2} utilised, depicting data for 612 ventilated days. We speculate a tolerance line (bold line) that connects the lowest accepted 'SpO\textsubscript{2} at FiO\textsubscript{2} of 0.25' and 'SpO\textsubscript{2} at FiO\textsubscript{2} of 1' in the study.](image)
mean SaO₂ (P=0.9), PaO₂ (P=0.4), SpO₂ (P=0.1), FiO₂ (P=0.6), ALI score (P=0.2) or the time spent in various SpO₂ and FiO₂ ranges. The frequency of ABG tests was assessed in the lowest and the highest quartile of patients based on 72-hour TWA-SaO₂ or TWA-PaO₂. During the initial 72 hours in the lowest quartile of patients (TWA-SaO₂ <96%, or TWA-PaO₂ <94 mmHg), an ABG analysis was performed every 2.8 hours compared to 3.1 hours for the highest quartile of patients (TWA-SaO₂ >97.4%, or TWA-PaO₂ >126 mmHg).

Forty-nine patients did not survive to hospital discharge. Patients who died were older, had non-trauma related admission, had higher Acute Physiology and Chronic Health Evaluation II scores and had more pre-existing comorbidities. Patients who died spent more time in lower SpO₂ ranges although the differences were non-significant.

![Figure 4: Scatter plot for 24-hour weight-average SpO₂ vs ALI score on that day.](image)

![Figure 5: Scatter plot for 24-hour weight-average SpO₂ achieved vs 24-hour weight-average PaO₂/FiO₂ ratio.](image)
when adjusted for baseline imbalances using multivariate logistic regression. There were no significant differences in the level of FiO₂ exposure between survivors and non-survivors.

**DISCUSSION**

**Key findings**

We conducted an observational cohort study to describe current oxygenation practice in patients who needed MV for at least 48 hours. We found that the blood oxygenation levels achieved in this cohort were ‘liberal’. Patients were, on average, ventilated for several days with supra-normal PaO₂ values. There was a wide variability in the observed mean SpO₂ particularly when FiO₂ requirements were more than 0.35. Large variations in the mean SpO₂ and PaO₂ were noticed among patients who had days with comparable ALI scores. Finally, compared to patients with higher ALI scores on day 0 of MV, patients with lower ALI scores spent more time with supra-normal PaO₂ during the initial 72 hours of MV; and in the lower ALI score patients, mean PaO₂/FiO₂ decreased significantly from day 0 to day 6 compared to patients with higher ALI score.

**Relationship to previous studies**

This is the first report of longitudinal measurements of the TWA oxygenation levels (SpO₂, FiO₂) achieved each day during the first seven days of MV at a tertiary ICU. A study of worst blood gas within the first 24 hours of ICU admission in

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>ALI score &lt;1</th>
<th>ALI score 1–2.5</th>
<th>ALI score &gt;2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0 ALI score, mean (SD)</td>
<td>0.3 (0.04)</td>
<td>1.5 (0.06)</td>
<td>2.9 (0.08)</td>
</tr>
<tr>
<td>Day 0 24-h TWA PEEP median [IQR]*</td>
<td>5 [5–5.4]</td>
<td>7.8 [6.8–9.6]</td>
<td>10.8 [10–12.8]</td>
</tr>
<tr>
<td>Day 1 worst lactate, mmol/l, median [IQR]</td>
<td>1.5 [1.1–2.4]</td>
<td>1.7 [1.2–2.4]</td>
<td>2.8 [1.6–4.8]</td>
</tr>
<tr>
<td>Day 2 worst lactate, mmol/l, median [IQR]†</td>
<td>1.1 [1–1.7]</td>
<td>1.3 [1–1.2]</td>
<td>2.2 [1.4–2.5]</td>
</tr>
<tr>
<td>No. of ABG in first 72 h, mean (SD)</td>
<td>23 (1)</td>
<td>26 (1)</td>
<td>25 (2)</td>
</tr>
<tr>
<td>Mean SOFA score for first 72 h, mean (SD)*</td>
<td>4.8 (0.4)</td>
<td>7.5 (0.5)</td>
<td>8.3 (0.8)</td>
</tr>
<tr>
<td>TWA-SpO₂ for first 72 h, %, mean (SD)*</td>
<td>98.3 (0.2)</td>
<td>97.1 (0.2)</td>
<td>95.9 (0.6)</td>
</tr>
<tr>
<td>TWA-PaO₂ for first 72 h, mmHg, mean (SD)*</td>
<td>126 (4)</td>
<td>104 (3)</td>
<td>96 (5)</td>
</tr>
<tr>
<td>TWA-FiO₂ for first 72 h, mean (SD)*</td>
<td>0.39 (0.01)</td>
<td>0.46 (0.02)</td>
<td>0.53 (0.03)</td>
</tr>
<tr>
<td>Mean tidal volume for first 72 h, ml/kg PBW ‡</td>
<td>8.3 (1.1)</td>
<td>8.6 (1.4)</td>
<td>8.6 (2.3)</td>
</tr>
<tr>
<td>No. of h on PaO₂ &gt;200 mmHg in first 72 h, mean (SD)§</td>
<td>32.7 (2.6)</td>
<td>23.5 (2.4)</td>
<td>20.3 (3.3)</td>
</tr>
<tr>
<td>No. of h on PaO₂ &gt;200 mmHg in first 72 h, mean (SD)*</td>
<td>6.8 [4.2–10.6]</td>
<td>2.9 [1.4–4.8]</td>
<td>0 [0–1.8]</td>
</tr>
<tr>
<td>(Day 3 – Day 0) Δ PaO₂/FiO₂, median [IQR]*</td>
<td>-82 [-153–34]</td>
<td>-12 [-73–38]</td>
<td>17 [-15–70]</td>
</tr>
<tr>
<td>TWA-FiO₂ for first 7 days, mean (SD)*</td>
<td>0.38 (0.01)</td>
<td>0.44 (0.01)</td>
<td>0.50 (0.03)</td>
</tr>
<tr>
<td>TWA-SpO₂ for first 7 days, %, mean (SD)*</td>
<td>97.8 (0.2)</td>
<td>97 (0.2)</td>
<td>95.7 (0.5)</td>
</tr>
<tr>
<td>(Day 6 – Day 0) Δ PaO₂/FiO₂, median [IQR]§</td>
<td>-86 [-152–6]</td>
<td>-23 [-56–49]</td>
<td>20 [-13–79]</td>
</tr>
<tr>
<td>Total SpO₂ h per patient, mean (SD)</td>
<td>138 (6)</td>
<td>144 (6)</td>
<td>148 (9)</td>
</tr>
<tr>
<td>H on SpO₂ 88–91%, median [IQR]*</td>
<td>0 [0–1]</td>
<td>1 [0–4]</td>
<td>9 [2–16]</td>
</tr>
</tbody>
</table>

Significant difference between three groups. * P <0.0001, † P=0.01, ‡ P <0.05. § Predicted body weight (as used for ARDSnet protocol): for males = 2.3 (height in inches - 60) + 50 kg; and for females = 2.3 (height in inches - 60) + 45.5 kg. ALI=acute lung injury, SD=standard deviation, BMI=body mass index, IQR=interquartile range, h=hours, TWA=time-weighted average, APACHE=Acute Physiological and Chronic Health Evaluation, ABG=arterial blood gas, SOFA=Sequential Organ Failure Assessment excluding Glasgow coma component, PBW=predicted body weight.
patients on MV, reported a mean PaO₂ of 99 mmHg at a mean FiO₂ of 0.50. Another study examined data from the worst blood gas within the first 24 hours of ICU admission, and reported a mean PaO₂ of 152 mmHg at a mean FiO₂ of 0.62 in ventilated patients. In our study during the initial 24 hours of MV, the mean TWA-PaO₂ of 144 mmHg and the mean TWA-FiO₂ of 0.52 is similar to the above reports. The FiO₂ data were also similar to those reported in other large epidemiological studies of MV. These results suggest that clinicians often deliver liberal amounts of O₂ in critically ill patients and obtain higher oxygenation targets, despite the absence of supportive data.

Oxygenation targets in major randomised controlled trials (RCT) including the ARDSnet study of lower tidal volumes and lung open ventilation study required a SpO₂ of 88 to 95% or PaO₂ of 55 to 80 mmHg. The mean PaO₂ achieved in these patients with severe ALI on the first day were 76 to 88 mmHg at a mean FiO₂ of 0.50 to 0.58. Even in these rigorous clinical trial settings, the mean levels of oxygenation achieved were either close to or exceeded the assigned upper limits. In our study, patients with high ALI scores on day 0 had mean SpO₂, PaO₂, and FiO₂ levels of 96%, 111 mmHg and 0.64, respectively, all higher than recommended targets. A similar disparity between recommendations and clinical practice has been reported in other situations.

When Australian intensivists were asked “after how long would a stable SpO₂ of 90% in a ventilated 50-year old-patient with ARDS cause concern?”—53% replied never, 16% said >48 hours and 11% said <1 hour. When Canadian intensivists were asked about a patient with SaO₂ of 85 to 90% at FiO₂ of 0.50 to 0.60, 52% of the respondents replied that they would not change FiO₂. However, what clinicians say and what they do appear somewhat different. In our study, TWA-SpO₂ ≥96% was achieved on nearly half (48%) of the 58 MV days during which patients received TWA-FiO₂ ≥0.60. As reported, there were many ventilation days when SpO₂ of 90 to 96% occurred despite mild–moderate levels of FiO₂, and many days when moderate–high levels of FiO₂ were used to achieve SpO₂ above 96%. These observations may imply some arbitrariness in O₂ titration.

Trends in PaO₂/FiO₂ have been reported to predict clinical outcomes in some conditions. In our study, we assessed change in PaO₂/FiO₂ from day 0 to day 3 and day 6 in all three ALI subgroups. We found that PaO₂/FiO₂ improved in the higher ALI score group and deteriorated in the lower ALI score group. Patients in the lower ALI score group were also exposed to liberal levels of FiO₂ in relation to their PaO₂ and SaO₂ levels. This finding is consistent with a recent study that showed both exposure to higher FiO₂ and longer duration of exposure were associated with worsening oxygenation index at 48 hours. It may also be a reflection of practice where clinicians use more lung-protective ventilation and take active measures to avoid fluid overload in severe ALI patients. The use of lung-protective ventilation has been demonstrated in a previous RCT to induce lesser systemic and intrapulmonary inflammatory response than standard of care ventilation. Although the mean PEEP levels were greater in the higher ALI score group, the tidal volumes (as ml/kg predicted body weight) were similar in the three groups.

Various preclinical and clinical studies over the past few decades have shown that protracted supra-normal O₂ levels in blood and tissues may be injurious. Although the rise in arterial O₂ content is trivial when SaO₂ is raised from 90 to 97%, the increase in toxic oxidants due to higher tissue O₂ levels may overwhelm anti-oxidative reserves and lead to oxidative injury, particularly in the presence of inflammation. On the other hand, a limited duration (<24 hours) of sub-toxic regimens of normobaric hyperoxia has been shown to exert moderate beneficial effects on the systemic and pulmonary inflammatory response in the peritonitis-induced septic shock animal models. Recently, titrated O₂ therapy (SpO₂ 88 to 92%) during prehospital management was shown to reduce risk of death by 78% in chronic obstructive pulmonary disease patients. Contrary to the results from a previous landmark RCT, one RCT reported high FiO₂ as a predictor of surgical site infection on multivariate regression analysis. A multicentre RCT in patients undergoing laparotomy showed that patients who received 80% O₂ compared to 30% O₂ perioperatively had a 1.5% absolute increase in 30-day mortality (P=0.13) and a statistically significant increase in long-term mortality (hazard ratio 1.3, 95% CI 1.03 to 1.64, P=0.03). Such data, combined with lack of quality data for other clinical situations in ICU, make it uncertain if patients on MV are optimally managed with conservative or liberal oxygenation targets.

Significance of study findings

Our study supports the view that clinicians usually target relatively high PaO₂ and SpO₂ values. This provides an opportunity to study whether a more conservative approach to O₂ therapy is possible and
perhaps, beneficial. It also defines the characteristics of a possible control group, its mortality rates and the $O_2$ related parameters that could be used for such a group in RCTs. In response to these findings, we are currently designing a phase 2 multicentre trial to assess the feasibility, safety and physiological efficacy of a ‘conservative’ approach to $O_2$ therapy in mechanically ventilated patients. Given the magnitude of variability in practice and the achieved TWA-$SpO_2$ of 97% (CI 96.8 to 97.4) over the initial seven days of MV, a case can be made for the ‘liberal’ or control arm to target a $SpO_2$ of at least 96% in order to achieve a reasonable degree of separation between the mean oxygenation levels of the two groups.

**Strength and limitations**

The strength of this study is that we have comprehensively described the longitudinal pattern of $O_2$ use and the achieved oxygenation levels by investigating hourly data for the first seven days of MV at a tertiary academic centre. The 24-hour weighted averages for oxygenation-related variables in our study are described for the first time. The main limitation is that this is a single centre study. The data for initial 24 hours of MV in this study is consistent with other multicentre reports. Our sample size was sufficient to derive a point estimate for oxygenation-related variables with sufficiently narrow confidence intervals. Since we enrolled only those patients who required at least 48 hours of MV, our study may have a selection bias towards a sicker cohort of patients. Further, there could be a number of other unmeasured confounding factors that might have influenced the choice of $SpO_2$ or $PaO_2$ targets in the real-time clinical situation. As mixed venous or central venous blood gases were checked infrequently, we did not examine venous oxygenation or other measures of tissue oxygenation in this study. Therefore, we cannot assess whether clinicians targeted higher levels of $SpO_2$ or $SaO_2$ based on a lower level of venous or tissue oxygenation. However, seeking to improve tissue oxygenation by changing $SpO_2$ values by a few percentage points may not be an efficient strategy.

**CONCLUSIONS**

The mean oxygenation levels achieved in ventilated patients were ‘liberal’ and quite variable, resulting in potentially higher than necessary $SpO_2$, $PaO_2$ and $FiO_2$ values. Further research is needed to confirm validity of these findings at other centres, and clarify whether trials are possible where a more conservative approach to $O_2$ therapy is compared with such ‘liberal’ $O_2$ therapy.

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**REFERENCES**

13. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network.