INTRODUCTION

One-lung ventilation (OLV) facilitates surgical access to the diseased site during thoracic surgery and serves to isolate the healthy lung. The positive pressure ventilation, however, causes differential alveolar expansion and an invariable alveolar collapse, depending on the delivered tidal volume (TV). A conservative ventilation strategy increases the alveolar atelectasis, while a larger TV relates to lung injury.[1,2] To limit the complications, interest is shifted to pressure-controlled ventilation (PCV).[3,4] Other adjuvant measures including recruitment manoeuvre and the positive end-expiratory pressure (PEEP) re-aerate the alveoli and keep them open. Both, however, require a monitoring tool to avoid the risk of associated barotrauma.[2,5] A higher arterial oxygen partial pressure (PaO$_2$) attained during the two-lung ventilation (TLV) correlates to better PaO$_2$ levels and allows for better oxygenation during thoracic surgery.
during the OLV. Thus, the ventilation strategy should target a higher PaO₂ during TLV. Although intraoperative complications have decreased through various approaches, identifying an ideal ventilation strategy for thoracic surgery remains a matter of research.

Lung ultrasound has been a valuable bedside non-invasive tool to diagnose pulmonary pathologies. It has been recently shown to identify and personalise the optimal threshold pressure for achieving alveolar re-aeration during the lung recruitment manoeuvre.[1,2]

We hypothesised that lung ultrasound-guided titration of inspiratory pressure (IP) in PCV mode (UG-PCV), targeted to achieve alveolar aeration at the dependent lung base, would attain better intraoperative PaO₂ during the thoracic surgery. We explored the effect of ‘UG-PCV’ ventilatory strategy on the blood gas and ventilatory parameters, during thoracic surgery of unilateral pulmonary disease, compared with volume-targeted PCV (VT-PCV).

METHODS

After institutional ethical approval and written informed consent, all consecutive American Society of Anesthesiologists physical status I–III patients of either gender, aged 18–60 years, undergoing elective thoracic surgery under general anaesthesia (GA) and requiring at least 1 h of OLV, were included in this prospective, randomised, parallel-group, double-blinded trial (Clinical Trials Registry-India No.: CTRI/2018/06/014618), conducted over 13 months (August 2018–2019), in accordance with ethical guidelines of the declaration of Helsinki. Those with cardiac/hepatic/renal dysfunction, bilateral pulmonary disease, airway abnormalities prohibiting insertion of the double-lumen endotracheal tube (DLT), body mass index ≥30 kg/m², or refusal for consent were excluded. The enroled patients were randomised in a 1:1 allocation ratio to two groups, using a computer-generated random sequence and concealed via serially numbered sealed-opaque-envelope technique. An investigator undergoing patient randomisation, anaesthetist assigned for the procedure, an investigator (≥5-year experience) performing the ultrasonography, and the outcome assessor remained blinded to other aspects, respectively.

All patients were shifted to the operation theatre, and a multipara monitor, radial arterial cannulation, invasive blood pressure monitoring and intravenous (IV) line were placed. The baseline parameters were recorded. After preoxygenation (3 min), GA was induced with fentanyl (2 µg/kg IV), propofol (2 mg/kg IV) and vecuronium (0.10 mg/kg IV). The trachea was intubated with a left-sided DLT size: 35–39 Fr (male); 33–37 Fr (female) (Smiths Medical India Private Limited, Mumbai, India), unless contraindicated. The tube position was confirmed through fibreoptic bronchoscopy and ventilation was initiated as per group allocation.

Group A: Received TLV on VT-PCV mode, at an IP that provided a TV 9 mL/kg of predicted body weight (PBW), fractional inspiratory oxygen (FiO₂) 100%, PEEP 5 cmH₂O and respiratory rate (RR) 12 breaths/min, adjusted further to maintain an end-tidal carbon dioxide tension (EtCO₂) 35–40 mmHg.

Group B received TLV on UG-PCV mode, at an initial IP 5 cmH₂O, FiO₂ 100%, PEEP 5 cmH₂O and RR 12 breaths/min. In the supine position, a convex ultrasound probe (2–5 MHz, GE Parallel Design Inc., Phoenix, US) was positioned at the dependent portion of the healthy lung, perpendicular to the skin, parallel to ribs and just anterior to the posterior axillary line at lung bases, and the zone of atelectasis was identified. The IP was then increased by 2 cmH₂O every 15 s until the atelectasis disappeared on ultrasound and alveolar aeration was achieved (progression from lung collapse to B lines to normal lung image). The IP was fixed at this level, and RR was adjusted to maintain an EtCO₂ 35–40 mmHg. The patients were turned to the lateral decubitus position (surgical side up). The DLT position was reconfirmed by auscultation, all monitoring lines were reassessed, and the patient position was secured.

At 30 min after the anaesthesia induction, the TLV was switched to OLV. In Group A, under VT-PCV mode, the IP was titrated to a TV 5 mL/kg PBW, keeping other parameters unchanged. In Group B, on UG-PCV mode, IP was reduced to 5 cmH₂O, and the convex ultrasound probe was positioned again at the base of the dependent lung, perpendicular to the skin, parallel to ribs and just posterior to the posterior axillary line. A similar methodology was followed (as for TLV) to achieve the alveolar aeration. For both groups, the other parameters included inspiratory time 33%, end-inspiratory pause time 10%, flow rate 1.5 L/min, peak airway pressure (Ppeak) limit 35 cmH₂O and...
plateau airway pressure ($P_{\text{plat}}$) limit 25 cmH$_2$O, during both TLV/OLV.

It followed surgical incision. Anaesthesia was maintained with fentanyl (0.05 µg/kg/min IV), propofol 100 µg/kg/min and vecuronium (0.03 mg/kg every 30 min). We defined light sedation as mean arterial pressure (MAP) >20% of pre-induction levels, heart rate (HR) >90 beats/min, somatic stimulation or autonomic response. It was treated by fentanyl bolus (0.5 µg/kg) followed by a 50% increase in the infusion rate of fentanyl and propofol. For hypotension (MAP <20% of pre-induction levels) and bradycardia (HR <40 beats/min), the rate of fentanyl and propofol infusion was decreased by 50%. For persistent symptoms, phenylephrine (for hypotension) and atropine (for bradycardia) was administered as a rescue measure. Patients were extubated at the end of surgery and shifted to the post-anaesthesia care unit.

The primary outcome included PaO$_2$ in the arterial blood. The secondary outcome included other arterial blood gas (ABG) parameters (partial pressure of carbon dioxide [PaCO$_2$], alveolar-arterial oxygen difference [P(A-a)O$_2$], bicarbonate and pH) and ventilatory parameters [TV, $P_{\text{peak}}$, $P_{\text{plat}}$ and mean airway pressure ($P_{\text{mean}}$)]. The outcome parameters were measured at 4-timepoints: At baseline just before anaesthesia induction (T1) (only ABG), at 30 min immediately before conversion from TLV to OLV (T2), 30 min after initiating OLV (T3) and at the end of surgery just before termination of OLV (T4). Surgical manipulation was not allowed while measuring the ventilatory parameters. Any intraoperative complication related to mechanical ventilation (pneumothorax, bradycardia, hypotension, etc.) was also noted.

Assuming a maximum 40 mmHg difference in the observed PaO$_2$ among the groups, with a standard deviation of 44 mmHg and 42 mmHg in group A and B, respectively (estimated from pilot observations), at the intraoperative time points T2–T4, with 80% power, and 95% confidence interval, we required 19 patients/group. Taking 5% dropouts, we included 20 patients/group. The sample size was calculated by OpenEpi Collection of Epidemiologic Calculator 3.01 (Andrew G. Dean, Kevin M. Sullivan, Atlanta, GA, US). The statistical analysis was performed with Statistical package for Social Sciences (SPSS) 23.0 (IBM Corp. Armonk, NY, US). We analysed the quantitative data by Mann-Whitney U test. The qualitative data were analysed by Chi-square test. A $P < 0.05$ was considered significant.

**RESULTS**

Over a period of 13 months, we included 40 eligible patients (20 in each group), with no dropouts [Figure 1]. The baseline parameters were comparable among the groups. The patients were intubated using a DLT of size ranging from 35–39 Fr. The surgical procedure lasted for about 4½ h and included both left (40% patients) and right thoracotomies (60% patients) [Table 1].

We observed an increase in PaO$_2$ levels at 30 min after the initiation of TLV, with a moderate decrease

| Parameters | Group A ($n=20$) | Group B ($n=20$) |
|------------|-----------------|-----------------|
| Age (years) | 33.2±13.3 | 33.0±15.4 |
| Sex (male) | 14 (70%) | 14 (70%) |
| BMI (kg/m$^2$) | 22.1±2.3 | 22.0±2.5 |
| Predicted body weight (kg) | 57.3±11.6 | 60.3±6.7 |
| ASA grade | I/II/III | 8/11/1 | 6/12/2 |
| Diagnosis | | | |
| Empyema | 6 | 7 |
| Post-traumatic | 5 | 6 |
| Hydatic cyst | 2 | 3 |
| Bronchogenic cyst | 1 | 0 |
| Gun-shot injury | 1 | 1 |
| Pott’s spine | 2 | 0 |
| Malignancy | 3 | 2 |
| Bronchoesophageal fistula | 0 | 1 |
| Arteriovenous malformation | 0 | 1 |
| FEV1 (%) | 48.4±6.8 | 48.2±6.9 |
| FVC (%) | 60.8±4.6 | 61.0±4.9 |
| FEV1/FVC (%) | 79.2±6.1 | 78.5±5.9 |
| PEF (%) | 35.5±3.5 | 36.3±5.1 |
| FEV 25-75 (%) | 24.0±2.7 | 24.3±3.0 |
| PaO$_2$ (mmHg) | 72.0±6.1 | 72.0±4.3 |
| PaCO$_2$ (mmHg) | 36.3±3.8 | 36.8±2.9 |
| P(A-a)O$_2$ (mmHg) | 32.3±7.4 | 31.6±5.9 |
| pH | 7.40±0.07 | 7.39±0.06 |
| HCO$_3$ (mEq/L) | 21.9±2.7 | 22.1±1.9 |
| Thoracotomy | | | |
| Left/Right | 8/12 | 8/12 |
| Duration of surgery (min) | 272.2±53.5 | 265.5±60.0 |
| DLT size | 35/37/39 Fr | 9/5/6 |

Data are presented as mean±standard deviation or number. BMI indicates body mass index; ASA=American society of Anesthesiologists; FEV1=forced expiratory volume in 1 s; FEV 25-75=forced expiratory volume in mid-50% of expiration; FVC=forced vital capacity; PEF=pulse expiratory flow; PFT=pulmonary function test; PaO$_2$=partial pressure of oxygen; PaCO$_2$=partial pressure of carbon dioxide; P(A-a)O$_2$=alveolar arterial oxygen difference; pH=power of hydrogen; HCO$_3$=bicarbonate; DLT=double lumen endotracheal tube. A $P < 0.05$ considered statistically significant.
during the OLV, in both the groups. The PaO$_2$ levels were significantly higher in group B at the time points T2–T4 compared to group A. The P(A-a) O$_2$ values increased from baseline until 30 min after the initiation of OLV, and a slight decrease was observed at the end of surgery in all the patients. On intergroup comparison, the P(A-a) O$_2$ values obtained during OLV were significantly higher in group A than in group B. In Group A, the PaCO$_2$ levels increased consistently till the end of surgery. In Group B, the PaCO$_2$ values remained static at all the 4 timepoints. The PaCO$_2$ values were comparable between the groups for up to 30 min on TIV but were higher in Group A at both timepoints during the OLV (T3-T4). The pH values also followed a similar pattern, though on the reverse side. The patients in group A had acidosis at both time points T3 and T4 during OLV, while pH of group B patients remained stable throughout the surgery. The bicarbonate levels remained uniform and comparable at all time points in both groups [Table 2].

The airway pressures and TV were higher in group B than group A during OLV. These parameters were lower for OLV as compared to the TIV, in both the groups. P$_{mean}$ was not significantly different at any time point in the two groups [Table 3]. None of the patients developed any complication throughout the intraoperative period.

**DISCUSSION**

This study demonstrated that the UG-PCV mode offered higher arterial oxygenation, better preservation of carbon-dioxide levels, and a more physiological acid-base status during the thoracic surgery. Though delivered TV and airway pressures were marginally higher with this technique, P$_{mean}$ remained equivalent in both the groups, with no intraoperative complications.

The GA induction is associated with alveolar atelectasis and bronchial collapse, especially in dependent lungs. The open thoracotomy procedure, diseased lung, lateral decubitus position and the intraoperative OLV further increase the atelectasis and thereby ventilation-perfusion mismatch, even in the healthy lung.[8] Brat et al. found a positive correlation between the lung ultrasound score and the PaO$_2$ in critically ill neonates.[9] We observed a higher PaO$_2$ in adult patients by using UG-PCV mode.
capillary uptake of alveolar gases and individualised ventilatory targets for each patient. After initiating the OLV, PaO₂ levels decreased in both groups. It was an expected outcome, considering the vascular shunting through the non-ventilated lungs, and decreased TV during the OLV. A generalised trend of improved PaO₂ levels was observed at the end of surgery. It could be related to established hypoxic pulmonary vasoconstriction, leading to perfusion shift to the dependent lungs. Ishikawa et al. also observed that initiation of OLV leads to a drop in PaO₂, and while the further continuation of OLV leads to a subsequent rise in PaO₂.\(^{[10]}\)

The ventilation/perfusion ratio is lowest at the lung bases. Petersson et al. showed that PaCO₂ has an inverse correlation to the ventilation/perfusion ratio.\(^{[11]}\) The alveolar atelectasis further augments the problem. Gazmuri et al. observed that an increase in TV has a reciprocal effect on the PaCO₂.\(^{[12]}\) We observed that the UG-PCV offered better preservation of PaCO₂, while the VT-PCV was associated with increased PaCO₂, especially during the OLV. It also explains the effect of lung aeration and lower ventilation-perfusion mismatch in group B. A comparatively lesser \(P (A-a) O_2\) in group B, further indicates a better gaseous exchange.\(^{[11]}\) An increased \(P (A-a) O_2\) during OLV could be related to increased ventilation/perfusion mismatch. Subsequent improvement signifies a better perfused dependent lung by hypoxic pulmonary vasoconstriction.

The static intraoperative bicarbonate levels indicate a stable metabolic status in all the patients. The pH, on the other hand, varied significantly, with progressive acidosis in group A until T3 time point. As bicarbonate levels remained stable, this is attributed to carbon-dioxide retention in these patients. Reduced minute ventilation precipitates as acidosis. If minute ventilation is kept constant, an increase in RR is per se insufficient to compensate for decreased TV, in preventing hypercapnia and the respiratory acidosis.\(^{[13]}\) The EtCO₂ is normally 2–5 mmHg lower than PaCO₂ in a healthy individual. In our study, the delivered TV was slightly lower in group A, although we adjusted the RR to maintain the EtCO₂ in between 35–40 mmHg in both the groups. The EtCO₂ often differs from PaCO₂ by a larger factor in ventilated patients with lung disease, due to increased dead space ventilation.\(^{[14]}\) Though we ventilated the non-surgical lung during the OLV, an increased dead space at lung bases (due to atelectasis) could attribute

Table 2: Comparison of arterial blood gas parameters among the groups

| Parameters                  | Time point | Group A (n=20) | Group B (n=20) | \(P\)  |
|-----------------------------|------------|----------------|----------------|-------|
| \(\text{PaO}_2\) (mmHg)     | T1         | 72.0±6.1       | 72.0±4.3       | 0.998 |
|                             | T2         | 353.3±38.1     | 374.5±25.9     | 0.046 |
|                             | T3         | 272.6±37.9     | 321.7±35.2     | <0.001|
|                             | T4         | 295.3±40.1     | 357.0±24.7     | <0.001|
| \(\text{PaCO}_2\) (mmHg)   | T1         | 36.3±3.8       | 36.8±2.9       | 0.615 |
|                             | T2         | 37.3±3.8       | 37.3±2.6       | 0.946 |
|                             | T3         | 44.2±2.9       | 36.9±2.4       | <0.001|
|                             | T4         | 44.8±2.4       | 36.6±1.7       | <0.001|
| \(P(A-a)O_2\) (mmHg)       | T1         | 32.3±7.4       | 31.6±5.9       | 0.737 |
|                             | T2         | 325.0±37.9     | 303.6±27.0     | 0.047 |
|                             | T3         | 393.6±38.3     | 354.3±36.8     | 0.002 |
|                             | T4         | 370.7±40.0     | 319.5±24.8     | <0.001|
| \(\text{pH}\)              | T1         | 7.40±0.06      | 7.39±0.06      | 0.825 |
|                             | T2         | 7.35±0.07      | 7.36±0.06      | 0.601 |
|                             | T3         | 7.28±0.05      | 7.36±0.05      | <0.001|
|                             | T4         | 7.31±0.05      | 7.40±0.03      | <0.001|
| \(\text{HCO}_3^-\) (mEq/L) | T1         | 21.9±2.7       | 22.1±1.9       | 0.857 |
|                             | T2         | 20.2±2.4       | 20.7±1.9       | 0.463 |
|                             | T3         | 20.4±1.9       | 20.6±1.9       | 0.830 |
|                             | T4         | 21.9±2.2       | 21.9±1.7       | 0.905 |

Data is presented as mean±standard deviation. \(T1=\)donates baseline just before anaesthesia induction; \(T2=30\) min immediately before conversion from two-lung ventilation to one-lung ventilation (OLV); \(T3=30\) min after initiating OLV; \(T4=\)end of surgery just before terminating OLV; PaO₂=Partial pressure of oxygen; PaCO₂=Partial pressure of carbon dioxide; \(P(A-a)O_2=\)Alveolar arterial oxygen difference; pH=Power of hydrogen; HCO₃⁻=Bicarbonate. \(P<0.05\) considered statistically significant.

Table 3: Comparison of ventilatory parameters among the groups

| Parameters | Time point | Group A (n=20) | Group B (n=20) | \(P\)  |
|------------|------------|----------------|----------------|-------|
| \(P_{peak}\) (cmH₂O) | T2         | 16.2±1.1       | 16.3±1.3       | 0.703 |
|            | T3         | 11.7±0.8       | 12.6±1.3       | 0.020 |
|            | T4         | 11.6±0.9       | 12.7±1.2       | 0.004 |
| \(P_{mean}\) (cmH₂O)  | T2         | 7.9±0.6        | 8.2±0.6        | 0.135 |
|            | T3         | 7.1±0.5        | 7.2±0.5        | 0.757 |
|            | T4         | 7.1±0.5        | 7.2±0.4        | 0.503 |
| \(P_{plat}\) (cmH₂O)  | T2         | 15.7±1.2       | 15.9±1.3       | 0.614 |
|            | T3         | 11.2±0.7       | 12.3±1.1       | 0.001 |
|            | T4         | 11.1±0.8       | 12.1±1.2       | 0.003 |
| TV (mL)    | T2         | 514.2±99.6     | 562.3±73.5     | 0.091 |
|            | T3         | 288.4±57.7     | 322.1±42.6     | 0.042 |
|            | T4         | 287.8±59.2     | 321.2±39.1     | 0.042 |

Data are presented as mean±standard deviation. \(P_{peak}=\)Peak airway pressure; \(P_{mean}=\)Mean airway pressure; \(P_{plat}=\)Plateau pressure; TV=Tidal volume. Time point \(T2=\)At 30 min immediately before conversion from two-lung ventilation to OLV; \(T3=30\) min after initiating OLV; \(T4=\)End of surgery just before terminating OLV. A \(P<0.05\) considered statistically significant.

A rise in \(P_{mean}\) causes alveolar recruitment and hence improved oxygenation, though it also carries a risk of decreased venous return.\(^{[21]}\) We did not observe any difference in \(P_{mean}\) in the two groups though \(P_{peak}\) and \(P_{plat}\) were higher with UG-PCV. We inferred that ultrasound-guided aeration of the atelectatic areas led to improved ventilation/perfusion ratio, better
to above results in group A, even at an EtCO$_2$ range of 35–40 mmHg.

Targeting a TV during thoracic surgery is difficult at times, considering variable patient demographics, the extent of lung pathology and invasiveness of the surgical intervention. While underventilation leads to atelectasis, overinflation causes lung injury. Though higher TV may be tolerated for a short period, the risk of lung injury increases with the surgery duration. Tusman et al. showed that lung ultrasound helps in detection of atelectatic zones and guides their resolution with alveolar recruitment manoeuvre. We used real-time ultrasound to target an IP just enough to abolish the atelectasis in dependent lung areas. The consequent delivered TV was slightly higher in these patients, though the intergroup difference was mildly significant during OLV, and reflected in corresponding $P_{\text{peak}}$ and $P_{\text{plat}}$ values. Blank et al. showed that delivered TV is inversely proportional to respiratory complications, though low TV by itself does not prevent the complications. The application of PEEP to low TV strategy also by itself does not prevent the atelectasis. The ultrasound-guided technique individualised the alveolar ventilation for each patient, offering an optimal TV.

The oxygenation index (OI) is an independent predictor of mortality in ventilated patients. Both groups had a similar mean OI (1.6) at T2, while group A (1.9, 1.8) had higher OI than group B (1.6, 1.5) at T3 and T4. Thus, the ultrasound-guided strategy may offer a better outcome; could be tested in future trials.

This study had several limitations. We excluded the patients with bilateral pulmonary disease. Depiction by lung ultrasound may be inaccurate in such patients if the scan is performed at the diseased site. However, if applied to the healthy lung portion, it may still help in targeting the TV. We could not quantify the effect of hypoxic pulmonary vasoconstriction, due to ongoing surgical procedure which may affect the results. Although the achieved PaO$_2$ levels may not be important at this range, it serves as an approach for targeting the ventilation of patients at risk of hypoxemia. We could not investigate the patients for any postoperative lung injury due to logistic and financial constraints. However, none of the patients developed any post-anesthesia untoward event. Use of 100% FiO$_2$ and a 9 mL/kg TV could be another issue. We used a 100% FiO$_2$ to avoid intraoperative hypoxic events. A "lower FiO$_2$" would have mandated change in intraoperative FiO$_2$ during any such event, and thus may have made PaO$_2$ comparison difficult to interpret. Previous trials have used a TV of 8–12 mL/kg for TLV and 5–8 mL/kg for OLV, in thoracic surgery. Considering unilateral pulmonary disease, we chose a TV of 9 mL/kg for TLV and 5 mL/kg for OLV (group A).

In conclusion, ultrasound-guided PCV resulted in better arterial oxygenation than volume-targeted PCV during thoracic surgery.

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**Conflicts of interest**

There are no conflicts of interest.

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