Positive end-expiratory pressure and risk of postoperative pulmonary complications in patients living at high altitudes and undergoing surgery at low altitudes: a single-centre, retrospective observational study in China

Kaixi Shang, Zongjing Xia, Xiaoli Ye, Zhuoning Li, Chongcong Gong

ABSTRACT

Objectives To examine whether a high positive end-expiratory pressure (PEEP ≥5 cmH₂O) has a protective effect on the risk of postoperative pulmonary complications (PPCs) in a cohort of patients living at high altitudes and undergoing general anaesthesia.

Design Retrospective, observational study.

Setting A tertiary hospital in China.

Participants Adult Tibetan patients living at high altitudes (≥3000 m) and who went to the low-altitude plain to undergo non-cardiothoracic surgery under general anaesthesia, from January 2018 to April 2020.

Measurements This study included 1905 patients who were divided according to the application of an intraoperative PEEP: low PEEP (<5 cmH₂O, including 0 cmH₂O) or high PEEP (≥5 cmH₂O). The primary outcome was a composite of PPCs within the first 7 postoperative days. The secondary outcomes included reintubation and unplanned intensive care unit (ICU) admission within the first 7 postoperative days and total hospital stays (day).

Results The study included 1032 patients in the low PEEP group and 873 in the high PEEP group. There were no differences in the incidence of PPCs between the high and low PEEP groups (relative risk (RR) 0.913; 95% CI 0.716 to 1.165; p=0.465). After propensity score matching, 643 patients remained in each group, and the incidence of PPCs in the low PEEP group (18.0%) was higher than in the high PEEP group (13.7%; RR 0.720; 95% CI 0.533 to 0.974; p=0.033). There were no differences in the incidence of reintubation, unplanned ICU admission or hospital stays. The risk factors of PPCs derived from multiple regression showed that the application of >5 cmH₂O PEEP during intraoperative mechanical ventilation was associated with a significantly lower risk of PPCs in patients from a high altitude (OR=0.725, 95% CI 0.530 to 0.992; p=0.044).

Conclusions The application of PEEP ≥5 cmH₂O during intraoperative mechanical ventilation in patients living at high altitudes and undergoing surgery at low altitudes may be associated with a lower risk of PPCs. Prospective longitudinal studies are needed to further investigate perioperative lung protection ventilation strategies for patients from high altitudes.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ All patients in this large cohort came from high-altitude areas and both propensity score matching and logistic regression were used to mitigate the confounding factors.

⇒ We classified the altitude where the patients came from as high altitude (<3500 m), very high altitude (3500–4500 m) and extremely high altitude (>4500 m) to determine the possible influence of different altitude levels on postoperative pulmonary complications.

⇒ The number of patients who came from extremely high altitude (>4500 m) was small, which may increase the potential for residual confounding.

⇒ Another limitation of this study was there was no control group of patients living at lower altitudes, so it cannot address whether differences in postoperative pulmonary complications between different levels of positive end-expiratory pressure apply to lowlanders.

INTRODUCTION

At high altitudes (≥2500 m), the human body needs to cope with the decreased partial pressure of oxygen (PaO₂) along with decreased barometric pressure (altitude of Lhasa: 3000–3500 m; PaO₂: 14.55 kPa). Previous studies reported changes in the respiratory and circulatory systems through genetic, endocrine and neurological regulation in highlanders, known as the high-altitude adaptation (HAA). The classic physiological responses include hyperventilation, polycythaemia and hypoxic pulmonary vasoconstriction. Conversely, when high-altitude dwellers return to lower altitudes or sea levels...
levels, the hypoxic compensation state cannot be immediately reversed but is progressive. This multifaceted process that involves the loss of HAA over time is called high-altitude de-adaptation (HADA) and is considered a type of hypoxia–reoxygenation injury.3 After returning to sea level or low altitude, the impact of hypoxia–reoxygenation on ventilation can cause a series of symptoms such as cough, chest tightening, shortness of breath and even pulmonary atelectasis when the PaO₂ increases with the lower altitude.4 This hypoxia–reoxygenation injury is a time-dependent process. A cluster-randomised controlled trial reported that hypoxia recovery processes took a long time after descending to the plain (≥100 days), probably due to reoxygenation after hypoxia."7

Following the economic development and the convenience of transportation, more and more Tibetan highlanders have been flying to Chengdu Plain (altitude: 500 m; PaO₂: 21.15 kPa) for treatments or surgeries each year. Consequently, many patients have to endure their perioperative period in the HADA process since most of them are admitted to the hospital within 1 month or even 1 week after descending to the plain. The chronic stress of hypoxia at high altitude combined with the acute surgery stress can affect their respiratory, cardiovascular and autonomic nervous systems during HADA,5 7 increasing postoperative complications.

In particular, the unrecovered respiratory function might theoretically increase the postoperative pulmonary complications (PPCs) after general anaesthesia. PPCs are the leading cause of postoperative morbidity, mortality and prolonged hospital stay.8-10 The incidence of PPCs following thoracic surgery has been reported to be as high as 30%–50%,11 12 while the prevalence of PPCs following non-cardiothoracic surgery ranges between 1% and 23% and varies depending on patient-related and surgical factors.8 13 A multicentre study based on a non-thoracic surgery perioperative network survey in the USA showed that the rate of PPCs in patients undergoing abdominal, orthopaedic and neurosurgery operations was as high as 33.4%, highlighting the urgency to reduce PPCs among high-altitude populations.14

Lung protective ventilation strategies (PVS) effectively minimise ventilator-induced lung injury in an intensive care unit (ICU) and in surgical settings to reduce PPCs.15 16 The key components of intraoperative PVS mainly involve low tidal volume (VT), positive end-expiratory pressure (PEEP) and recruitment manoeuvres (RMs).16 17 The protective role of low VT is widely accepted, but the precise setting of PEEP remains unclear.18 19 In addition, it remains unclear whether the incidence of PPCs in HADA patients increases due to factors such as atelectasis, closure of small airways, reduced lung volume and increased airway resistance after prolonged general anaesthesia. It has not been reported whether the use of PEEP during mechanical ventilation affects the occurrence of PPCs in HADA patients. Consequently, the setting of PEEP needs to be further investigated.

Therefore, this study aimed to investigate whether the use of PEEP during general anaesthesia was associated with decreased PPCs in HADA patients. The results could help improve the perioperative safety of highlanders and reduce postoperative complications.

METHODS
Study design
This single-centre retrospective study adhered to the applicable 2007 Strengthening the Reporting of Observational Studies in Epidemiology guidelines.20

Patient inclusion
Adult Tibetan patients treated in West China Hospital Sichuan University Tibet Chengdu Branch Hospital between January 2018 and April 2020 were included in this study. The inclusion criteria were Tibetan highlanders (1) living at high altitudes for more than three generations (altitude ≥3000 m), (2) who underwent non-cardiothoracic surgery under general anaesthesia with endotracheal intubation, (3) ≥18 years of age, (4) who had American Society of Anesthesiologists (ASA, I: no organic, physiological, biochemical or psychiatric disturbance; II: a patient with mild systemic disease that results in no functional limitation; III: a patient with severe systemic disease that results in functional impairment; IV: severe systemic disease that is a constant threat to life; V: moribund condition in a patient who is not expected to survive with or without the operation; VI: declared brain dead patient whose organs are being harvested for transplantation) physical status I–III, and (5) who had surgical duration ≥1 hour.

The exclusion criteria were those who had (1) single lung ventilation during surgery, (2) prone position or side-lying position during surgery, (3) received lung surgery at any previous time, (4) underwent general anaesthesia or preoperative ventilation support within 30 days before surgery, (5) thoracic or intrathoracic diseases, including thoracic deformity, mediastinal tumours or thoracic tumours, or (6) missing important data, such as living history information, vital signals and parametric ventilation data (figure 1).

Anaesthesia and intraoperative care
In the operating room, all patients were monitored continuously using an ECG, pulse oximetry, non-invasive blood pressure, pulse oxygen saturation (SpO₂), body temperature, bispectral index (BIS) electrode, end-tidal partial pressure of carbon dioxide (PETCO₂) and end-tidal gas concentration of volatile anaesthetics. Invasive arterial pressure or central venous pressure was monitored when clinically needed. Anaesthesia was induced intravenously with midazolam (0.03–0.05 mg/kg), sufentanil (0.3–0.6 μg/kg), propofol (1.3–2.6 mg/kg), muscle relaxants (0.3–0.4 mg/kg cisatracurium or 0.5–1.0 mg/kg rocuronium) by the attending anaesthesiologist. Anaesthesia was maintained by sevoflurane and BIS level.
The primary outcome was the incidence of a composite group (PEEP < 5 cmH\(_2\)O, including PEEP = 0 cmH\(_2\)O).


12 (FiO\(_2\)), respiratory rate and PEEP was left to the discretion ratio was 1:2. The choice of fraction of inspired oxygen of predicted body weight, and the inspirator mode was volume-controlled ventilation, VT at 8 mL/kg of predicted body weight, and the inspiratory–expiratory ratio was 1:2. The choice of fraction of inspired oxygen (FiO\(_2\)), respiratory rate and PEEP was left to the discretion of the attending anaesthesiologist. The intraoperative restrictive fluid therapy was standardised using crystalloid fluid throughout the surgery at 4–6 mL/kg/hour, while colloid solution was administrated when regarded as clinically necessary. Patients were extubated soon after surgery as appropriate, and then routine reversal of neuromuscular blockade (neostigmine of 0.02–0.05 µg/kg/min) until the end of surgery.

All patients were subjected to single-lumen endotracheal tubes after anaesthesia induction. The ventilation mode was volume-controlled ventilation, VT at 8 mL/kg of predicted body weight, and the inspiratory–expiratory ratio was 1:2. The choice of fraction of inspired oxygen (FiO\(_2\)), respiratory rate and PEEP was left to the discretion of the attending anaesthesiologist. The intraoperative restrictive fluid therapy was standardised using crystalloid fluid throughout the surgery at 4–6 mL/kg/hour, while colloid solution was administrated when regarded as clinically necessary. Patients were extubated soon after surgery as appropriate, and then routine reversal of neuromuscular blockade (neostigmine of 0.02–0.05 µg/kg/min) until the end of surgery.

The intraoperative information was obtained from the electronic surgical anaesthesia system (Suzhou Madstone Medical Technology, Co): types of surgery, duration of anaesthesia, intraoperative ventilation parameters, PEEP values, peak airway pressure (P\(_{\text{peak}}\)), VT, P\(_{\text{ETCO}}\)\(_2\) estimated blood loss, urine output and intravascular fluid balance including transfusion of blood products. The types of surgery included orthopaedics, laparotomy, laparoscopic surgery and others (mainly maxillofacial surgery and urological surgery in the lithotomy position). Postoperative information, including postoperative vital signs, PPCs, hospital stay and unplanned ICU admission, was collected. Moreover, according to the medical record information, the patients were evaluated using the Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) to assess the risk of PPCs. The ARISCAT score was evaluated according to age, preoperative SpO\(_2\), respiratory infection in the last month, anaemia, duration of surgery and emergency procedure; a score < 26 was regarded as low risk, 26–44 as moderate risk and ≥ 44 as high risk (online supplemental table S2).

**Statistical analysis**

All statistical analyses were performed using IBM SPSS Statistics V.22.0. All tests were two-tailed, with significance defined as p ≤ 0.05. Continuous and ordinal variables were expressed as mean±SD or median and IQR (25%–75%), and categorical variables as n (%) The Shapiro-Wilk test was first used to test the normal distribution of data, after which Student’s t-test was used for comparison of normally distributed variables, and the Mann-Whitney U test was used for variables with a non-normal distribution. The comparison of categorical variables was conducted with the \(X^2\) test or Fisher’s exact test.

The final statistical analysis plan included propensity score matching (PSM) to adjust for differences between high PEEP and low PEEP groups. The PSM model contained age, BMI, ASA physical status, altitude, ARISCAT score and surgery types. High PEEP group patients were propensity score-matched 1:1 to the low PEEP group using the matching algorithm. Residual covariable imbalance after matching was assessed by

**Figure 1** Flow diagram of the study population. ASA, American Society of Anesthesiologists; PEEP, positive end-expiratory pressure; P\(_{\text{plat}}\), plateau pressure; VT, tidal volume.

was maintained at 40–60. Intraoperative analgesia was provided with remifentanil (0.1–0.2 µg/kg/min) until the end of surgery.

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computing standardised differences, where variables with an absolute standardised difference <10% were considered a strong match. Patients who had the closest PSM in sum were matched in the two groups. Matching was done without replacement and within a tolerance limit of 0.00075. The X² method was used to compare the paired groups.

Furthermore, we analysed the association of intraoperative PEEP with the risk of PPCs in the matched cohort. First, the preoperative and intraoperative factors were used as covariables to perform single-factor analysis first. Then, the variables of PEEP, age and single-factor analysis that were meaningful (p<0.10) were included in the multivariable logistic regression model analysis, adjusted for age, ASA classification, ARISCAT score for prediction of PPCs, pre-existing pulmonary disease, major preoperative comorbidity and types of surgery.

**Patient and public involvement**

There was no patient or public involvement in the study.

**RESULTS**

**Patient inclusion**

A total of 3708 patients from the Tibetan Plateau who underwent non-cardiothoracic surgery between January 2018 and April 2020 met the inclusion criteria. After excluding cases based on the exclusion criteria, a final set of 1905 patients was included, 1032 of whom were in the high PEEP group and 873 in the low PEEP group (figure 1).

**Unmatched cohort**

The demographic information and preoperative and intraoperative characteristics are shown in tables 1 and 2. There were significant differences in weight, height and living altitude, but no differences in age, sex, ASA class, ARISCAT score, smoking status and major preoperative comorbidity between the two groups. There was a difference in the proportion of laparoscopic surgery between the two groups. In terms of intraoperative parameters, the value of PEEP in the high PEEP group was 5.7±0.8 cmH₂O and in the low PEEP group was 2.1±0.7 cmH₂O (p<0.001) (online supplemental figure S1). The median PIP (peak inspiratory pressure) in the high PEEP group was 16.7±2.9; p<0.001). There were no differences in the venti-

**Matched cohort**

PSM addressed the differences between the baseline characteristics of the low and high PEEP groups. Of the 873 cases in the high PEEP group, 643 (75.7%) were matched to the low PEEP group, resulting in a matched cohort population of 1286 patients (table 1). In the matched cohort, the average value of PEEP in the high PEEP group was 5.68±0.9 cmH₂O vs 2.47±0.8 cmH₂O in the low PEEP group (p<0.001) (online supplemental figure S1). The median PIP (peak inspiratory pressure) in the high PEEP group was also higher than in the low PEEP group (17.9±3.0 vs 16.9±3.0; p<0.001) (table 2). There were no differences in the other variables between the two matched groups.

In the matched cohort, the incidence of PPCs within the 7 postoperative days was 18% in the low PEEP group and 13.7% in the high PEEP group (RR 0.720; 95% CI 0.533 to 0.974; p=0.033) (table 3). The incidence of pulmonary infection within the first 7 postoperative days was higher in the low PEEP group (11.4%) than in the high PEEP group (7.8%) (RR 0.658; 95% CI 0.451 to 0.961; p=0.029). Atelectasis occurred in the low PEEP group and was higher than in the high PEEP group (3.7% vs 1.7%; RR 0.449; 95% CI 0.218 to 0.924; p=0.026). There were no significant differences in the individual components of the other PPCs (respiratory failure, pleural effusion, pneumothorax, bronchospasm and aspiration pneumonia). The secondary outcomes, including postoperative reintubation, unplanned ICU admission and hospital stay, were not significantly different between the two groups in the matched cohort.

**Sensitivity analyses**

For the matched cohort of HADA patients, there was a significant protective effect of high PEEP (OR 0.725, 95% CI 0.530 to 0.992; p=0.044) in reducing PPCs (figure 2). We evaluated the effect of PEEP on PPCs in patients at different altitudes in the matched cohort. There were no differences in the incidence of PPCs in patients at high altitude (>3500m) (13.9% vs 12.1%, p=0.525) nor at extremely high altitude (>4500m) (46.3% vs 44.8%, p=0.900) (figure 3). The incidence of PPCs in the low PEEP group was higher than in the high PEEP group (18.2% vs 12.3%, p=0.033) in patients at very high altitudes (3500–4500m) (figure 3). The living history at an extremely high altitude (>4500m) was associated with the risk of PPCs for HADA patients (OR 6.204, 95% CI 3.514 to 10.955; p<0.001) (figure 2).
In order to verify the sensitivity of the results, we examined a subgroup analysis of the included factors. After PSM, the effect of PEEP in HADA patients undergoing abdominal surgery revealed a significant protective effect of high PEEP (24.7% vs 10.3%, RR 0.351, 95% CI 0.153 to 0.805; p=0.011) compared with low PEEP in reducing PPCs. Furthermore, the effect of high PEEP in HADA patients with a history of living at high altitudes (3500–4500 m) resulted as a significant protective factor (18.2% vs 12.3%, RR 0.631, 95% CI 0.412 to 0.966; p=0.033), so as age >65 years, ASA classification III, moderate to high risk and COPD (chronic obstructive pulmonary disease) history (figure 3).

DISCUSSION
This cohort study investigated the association between PEEP and PPCs after general anaesthesia in patients living at high altitudes. The PSM data showed that the application of high PEEP (≥5 cmH₂O) during intraoperative mechanical ventilation was associated with a significantly lower risk of PPCs in perioperative period with HADA.
Mechanical ventilation during general anaesthesia can deform the lung parenchyma and cause lung injuries such as volutrauma, barotrauma and biaxial trauma, which can precipitate the development of PPCs. The common physiological basis of PVS is preventing excessive expansion of the alveoli and reducing the repeated opening and closing of the alveoli, thus minimising lung injuries caused by mechanical ventilation. Although low VT can improve lung compliance and reduce inflammatory mediators, ventilation with only low VT might reduce the end-expiratory lung volume (EELV) after anaesthesia induction and increase the areas of atelectasis. The loss of EELV contributes to preventing part of the collapsed alveoli from opening, further leading to atelectasis. The loss of EELV contributes to preventing part of the collapsed alveoli from opening, further leading to atelectasis. The loss of EELV contributes to preventing part of the collapsed alveoli from opening, further leading to atelectasis. The loss of EELV contributes to preventing part of the collapsed alveoli from opening, further leading to atelectasis. Nonetheless, some other studies argued that PEEP did not show benefits for PPCs. For example, a large trial of high versus low PEEP during general anaesthesia for open abdominal surgery showed no differences in the development of PPCs with either high or low levels of PEEP (≤2 vs 12 cmH\textsubscript{2}O). Another large trial that included obese patients undergoing surgery under general anaesthesia with a higher level of PEEP (12 cmH\textsubscript{2}O) and alveolar RMs revealed no differences in reducing PPCs compared with a lower level of PEEP (4 cmH\textsubscript{2}O) either.

Nevertheless, all of the above studies on lung PVS during general anaesthesia have focused on populations in the plains. At present, there are about 85 million people around the world living at altitudes ≥2500 m, and they at some point will need specialised surgical interventions. Faced with such a large population base, it is necessary to investigate enhanced recovery after surgery (ERAS) and perioperative safety of the highlanders in combination with the special physiological changes. To the best of our knowledge, there are no studies on perioperative lung PVS in patients living at high altitudes. The results of our study showed that PEEP was associated with a lower risk of PPCs, and it may reduce the incidence of PPCs in patients from high altitudes. It could be because the occurrence and progression of HADA involve damage from hypoxia and reoxygenation leading to respiratory, haematological and cardiovascular system abnormalities that are observed.
Table 3  Outcomes within the first 7 days after surgery of unmatched patients and matched patients after propensity scoring

<table>
<thead>
<tr>
<th></th>
<th>Unmatched patients</th>
<th>Matched patients</th>
<th>Relative risk (95% CI)</th>
<th>P value</th>
<th>Relative risk (95% CI)</th>
<th>P value</th>
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<tbody>
<tr>
<td></td>
<td>Low PEEP (n=1032)</td>
<td>High PEEP (n=873)</td>
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<td>Low PEEP (n=643)</td>
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<td>Primary outcomes</td>
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<tr>
<td>All PPCs</td>
<td>176 (17.1%)</td>
<td>138 (15.8%)</td>
<td>0.913 (0.716 to 1.165)</td>
<td>0.465</td>
<td>116 (18.0%)</td>
<td>0.720 (0.533 to 0.974)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>45 (4.4%)</td>
<td>39 (4.5%)</td>
<td>1.026 (0.661 to 1.590)</td>
<td>0.910</td>
<td>23 (3.8%)</td>
<td>1.273 (0.728 to 2.226)</td>
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<tr>
<td>Pulmonary infection</td>
<td>99 (9.6%)</td>
<td>83 (9.5%)</td>
<td>0.990 (0.729 to 1.346)</td>
<td>0.950</td>
<td>73 (11.4%)</td>
<td>0.658 (0.451 to 0.961)</td>
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<tr>
<td>Pleural effusion</td>
<td>7 (0.7%)</td>
<td>5 (0.6%)</td>
<td>0.843 (0.267 to 2.667)</td>
<td>0.711</td>
<td>3 (0.5%)</td>
<td>1.335 (0.298 to 5.991)</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>37 (3.6%)</td>
<td>20 (2.3%)</td>
<td>0.631 (0.363 to 1.095)</td>
<td>0.099</td>
<td>24 (3.7%)</td>
<td>0.449 (0.218 to 0.924)</td>
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<tr>
<td>Bronchospasm</td>
<td>4 (0.4%)</td>
<td>0</td>
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<td>Aspiration pneumonitis</td>
<td>0</td>
<td>0</td>
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<td>Secondary outcomes</td>
<td></td>
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<tr>
<td>Reintubation</td>
<td>19 (1.8%)</td>
<td>11 (1.3%)</td>
<td>0.680 (0.322 to 1.438)</td>
<td>0.310</td>
<td>16 (2.5%)</td>
<td>0.494 (0.210 to 1.162)</td>
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<tr>
<td>Unplanned ICU admission</td>
<td>35 (3.4%)</td>
<td>24 (2.7%)</td>
<td>0.805 (0.475 to 1.365)</td>
<td>0.420</td>
<td>24 (3.7%)</td>
<td>0.658 (0.346 to 1.251)</td>
</tr>
<tr>
<td>Hospital stays (days)</td>
<td>12 (10–15)</td>
<td>12 (10–14)</td>
<td>0.180</td>
<td></td>
<td>12 (10–15)</td>
<td>0.058</td>
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*Fisher’s exact test.
ICU, intensive care unit; PEEP, positive end-expiratory pressure; PPCs, postoperative pulmonary complications.

In our study, we found that a history of living at an extremely high altitude (>4500 m) is a possible risk factor for PPCs in patients from high altitudes. At present, most scholars take 2500 m as the altitude threshold point for highlanders when they return to lower altitudes. In highlanders, when they return to lower altitudes, the PaO2 increases, and the PaCO2 decreases, which can activate many signalling pathways in neurons, endothelial cells, and stress-related homeostatic dysregulation, which can acti-...
altitude classification, we classified the altitude where the patients came from as high altitude, very high altitude and extremely high altitude to determine the possible influence of different altitudes on PPCs. Although many studies on HADA have been previously reported, almost all of them were related to short-term exposure to high altitude, while there are no studies on perioperative patients with HADA. Improvements in the transportation system and economy in Tibet have resulted in more people coming to the plains for medical treatment, usually lasting for several months. These patients who descend from a high-altitude to a low-altitude region for surgical treatment have received little attention thus far. Our study focused on the most common perioperative and postoperative complications to find effective ways to reduce PPCs and promote perioperative safety and ERAS.

Also, there are some limitations to this study. First, although this may be a geographical limitation, the number of patients who came from extremely high altitude (>4500m) was small, which may cause the potential for residual confounding. Second, 761 patients were excluded because of missing data, and 619 patients were unmatched by PSM and excluded, which could introduce biases. Third, the incidence of pulmonary hypertension was not examined since it was not systematically screened during the study period. Fourth, our study included patients undergoing non-cardiothoracic surgery and general anaesthesia rather than a fixed type of surgery. The number of patients who came from high altitudes was so few that choosing a single surgical type would further reduce the number of participants. Nonetheless, the bias was minimised by removing cardiothoracic surgery. Finally, there was no control group of patients living at lower altitudes, and the study is only applicable to high-altitude populations in the clinical setting of our centre, which cannot answer the question of whether the difference in PPCs between different PEEP levels applies to lowlanders.

The results suggest that a higher PEEP setting is beneficial to prevent PPC in patients from high altitudes undergoing mechanical ventilation. This finding, of course, needs to be viewed in light of the inherent limitations of the study design, as mentioned above. As there is no control group of patients living at lower altitudes, the study can also not answer whether the difference in PPC between different PEEP levels is a characteristic intrinsic to highlanders or whether it also applies to lowlanders. Therefore, a prospective trial including, for example, four groups of patients from either high or low altitudes and with fixed levels of PEEP would be desirable to

**Figure 2** Risk factors for postoperative pulmonary complications derived from multiple regression for the matched group after propensity score matching. ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; HAPC, high-altitude polycythaemia; PEEP, positive end-expiratory pressure.
corroborate the hypothesis drawn from the present retrospective study.

CONCLUSION

Our study suggests that the application of PEEP $\geq$ 5 cmH$_2$O during intraoperative mechanical ventilation in patients living at high altitudes and undergoing surgery at low altitudes may be associated with a lower risk of PPCs. In addition, a history of living at an extremely high altitude (>4500 m) might be a possible risk factor for PPCs in patients from high altitudes. However, in the clinical environment of our centre, this difference did not change the treatment and outcome of the patients. Therefore, prospective longitudinal studies are needed to further investigate perioperative lung protection ventilation strategies for patients from high altitudes.

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Competing interests None declared.

Figure 3 Subgroup analyses of the primary outcome for the matched group after propensity score matching. ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; PEEP, positive end-expiratory pressure; PPCs, postoperative pulmonary complications.
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