

Review Article

Meta-analysis of risk factors associated with postoperative hypoxemia in the postanesthesia care unit

Ni Xiong¹, Yueqin Nong², Yaping Yi³

¹Department of Anesthesiology, The 923rd Hospital of The Joint Logistics Support Force of The People's Liberation Army of China, No. 52 Zhizhi Road, Qingxiu District, Nanning 530021, Guangxi, China; ²Department of Diagnostic Radiology, The 923rd Hospital of The Joint Logistics Support Force of The People's Liberation Army of China, No. 52 Zhizhi Road, Qingxiu District, Nanning 530021, Guangxi, China; ³Department of Disinfection Supply, The 923rd Hospital of The Joint Logistics Support Force of The People's Liberation Army of China, No. 52 Zhizhi Road, Qingxiu District, Nanning 530021, Guangxi, China

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Abstract: Objective: To identify the risk factors associated with postoperative hypoxemia in the postanesthesia care unit (PACU), providing evidence-based recommendations for its prevention. Methods: Observational studies examining the risk factors for postoperative hypoxemia in PACU patients were systematically searched in PubMed, Embase, Cochrane Library, and Web of Science databases from their inception to June 2024. Two independent reviewers screened the literature, extracted data, and assessed the quality of the studies. Meta-analysis was performed using RevMan 5.3 software, employing fixed or random effects models to calculate odds ratios (OR), relative risks (RR), and 95% confidence intervals (CI). Results: A total of 11 studies were included, comprising 8 cohort studies, 2 case-control studies, and 1 cross-sectional study, with a total of 24,147 subjects, of whom 5,587 experienced hypoxemia. The meta-analysis identified the following significant risk factors for postoperative hypoxemia in the PACU: Advanced age (OR=1.19, 95% CI: 1.11-1.29, $P<0.001$); Elevated body mass index (BMI) (OR=1.64, 95% CI: 1.36-1.97, $P<0.001$); Low preoperative oxygen saturation (OR=3.16, 95% CI: 2.56-3.91, $P<0.001$); Smoking status (OR=1.67, 95% CI: 1.15-2.43, $P<0.05$); Surgery duration >120 minutes (OR=1.43, 95% CI: 1.22-1.69, $P<0.001$); Opioid analgesic use (OR=1.51, 95% CI: 1.31-1.74, $P<0.001$). Conclusion: These findings highlight the need for targeted preventive strategies in patients at high risk for postoperative hypoxemia in the PACU.

Keywords: Postoperative, postanesthesia care unit, hypoxemia, risk factor, meta-analysis

Introduction

During surgical procedures, patients often require anesthetic intervention to mitigate the surgical stress response and ensure a smooth execution of the operation. Postoperatively, anesthetic agents are primarily metabolized and eliminated through the urinary and gastrointestinal tracts, minimizing potential cerebral toxicity. As a critical component of the perioperative anesthesia continuum, the postanesthesia care unit (PACU) plays a pivotal role in facilitating the transition of patients from anesthesia to full consciousness. However, various complications can arise during this period, with hypoxemia being one of the most prevalent.

Hypoxemia is defined as an insufficient oxygen level in the blood, characterized by arterial oxy-

gen tension below the normal lower limit for the patient's age group, accompanied by reduced oxygen saturation [1]. Studies have shown that 19.12% of patients experience hypoxemia during transport from the operating room to the PACU, and 69.8% develop hypoxemia within 30 minutes of PACU admission. Additionally, between 35% and 55% of adult patients experience at least one episode of hypoxemia during their stay in the PACU [2]. Prolonged or severe hypoxemia can lead to arrhythmias, abnormal blood pressure fluctuations, delayed postoperative wound healing, and even cardiac arrest or death [3, 4]. Therefore, early identification of hypoxemia risk factors in PACU patients is crucial for developing targeted intervention strategies and ensuring a smooth recovery from anesthesia.

Risk factors for postoperative hypoxemia

Previous studies have identified anesthetic, surgical, and patient-related factors associated with the occurrence of hypoxemia in the PACU [5]. However, inconsistencies in study populations, sample selection, research variables, and other methodological differences have resulted in conflicting findings, hindering the establishment of a unified understanding and standardized management protocols. Consequently, a systematic review and comprehensive meta-analysis of the existing literature are needed to investigate thoroughly the risk factors for postoperative hypoxemia in PACU patients. This review is to help clinicians to formulate individualized prevention strategies and optimize perioperative management to reduce postoperative hypoxemia in the PACU.

Materials and methods

Eligibility criteria

Inclusion criteria: (1) Observational study designs, including cohort studies, case-control studies, and cross-sectional studies; (2) Study participants were surgical patients transferred from the operating room to the PACU; (3) Hypoxemia was the exposure variable, with clearly defined diagnostic criteria; (4) The outcome measure was factors influencing postoperative hypoxemia in PACU patients.

Exclusion criteria: (1) Studies with incomplete or insufficient data; (2) Inability to access full-text articles or extract necessary data; (3) Duplicate publications; (4) Studies predominantly consisting of reviews, case reports, experience summaries, expert opinions, or animal studies.

Information sources

This review has been registered on PROSPERO (registration number: CRD42024587694). A comprehensive search was conducted for observational studies investigating the factors influencing postoperative hypoxemia in PACU patients using PubMed, Embase, Cochrane Library, and Web of Science databases from their inception to June 2024. Relevant references will also be collected for supplementary analysis.

Search strategy

The search terms included “postanesthesia care unit”, “PACU”, “hypoxia”, and “risk factors”.

The strategy combined controlled vocabulary and free-text terms, tailored to each database. For instance, the PubMed search strategy was: (((postanesthesia care unit [Title/Abstract]) OR (PACU [Title/Abstract])) AND (((((((hypoxia [MeSH Terms]) OR (deficiencies, oxygen [Title/Abstract]) OR (oxygen deficiency [Title/Abstract]) OR (anoxemia [Title/Abstract]) OR (hypoxemia [Title/Abstract]) OR (anoxia [Title/Abstract]))) AND (((((((risk factors [MeSH Terms]) OR (factor, risk [Title/Abstract]) OR (populations at risk [Title/Abstract]) OR (risk scores [Title/Abstract]) OR (correlates, health [Title/Abstract]) OR (factors, social risk [Title/Abstract])))).

Selection process

Two authors independently screened the literature by initially reviewing article titles and abstracts to exclude studies that do not meet the inclusion criteria. They then performed a full-text review of the selected articles. Any discrepancies in the selection process were resolved through discussion or consultation with a third reviewer if necessary.

Data collection process

Two authors independently used a standardized data extraction form to collect relevant information, including the title, first author, publication year, country/region, study design, sample size, and identified risk factors. After data extraction, they cross-checked the collected data, and any discrepancies were resolved through consultation with a third reviewer if necessary.

Data items

The primary outcome variables were the independent variables for the binary logistic regression model for postoperative hypoxemia in PACU patients. From these, calculable odds ratios (OR) or relative risks (RR) and 95% confidence intervals (CI) were extracted.

Study risk of bias assessment

The two authors independently evaluated the quality of cohort and case-control studies using the Newcastle-Ottawa Scale (NOS). The NOS assesses studies based on three domains: selection (4 items), comparability (1 item), and

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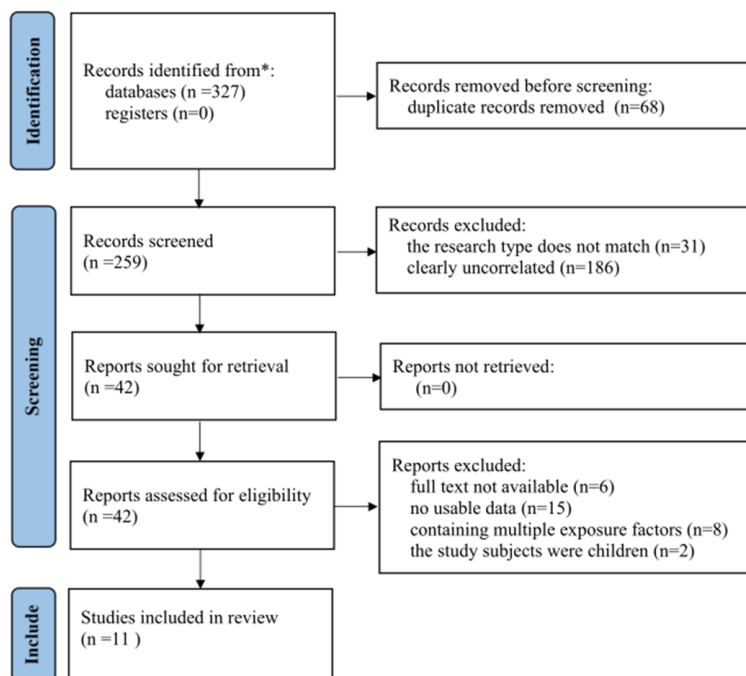


Figure 1. Process of literature screening.

exposure/outcome (3 items), for a total of 8 items. The scoring system uses a semi-quantitative star system, where each item, except for comparability (up to 2 stars), can receive 1 star. Each star corresponds to 1 point, with a maximum score of 9 points. A total score of ≥ 6 points indicates high-quality article. The quality of cross-sectional studies was assessed using the Agency for Healthcare Research and Quality (AHRQ) tool, which consists of 11 items. A score of ≥ 8 out of 11 points was considered indicative of high-quality article.

Statistical analysis

Statistical analyses were performed using RevMan 5.3 software. Binary variables were expressed as log odds ratios (Log OR) with 95% CI. Heterogeneity among the included studies was assessed using the I^2 statistic. If $I^2 \leq 50\%$ or $P \geq 0.05$, homogeneity was considered present, and a fixed-effects model was used for analysis. If $I^2 > 50\%$ or $P < 0.05$, significant heterogeneity was indicated. Sensitivity analysis and subgroup analysis were performed to identify sources of heterogeneity. If heterogeneity could not be resolved, a random-effects model was applied. A significance level of $P < 0.05$ was considered statistically significant. Publication bias was assessed using a funnel plot, with

asymmetry suggesting potential bias.

Results

Study selection

The comprehensive search yielded 327 relevant articles. After removing 68 duplicates, 259 unique articles remained. A further 217 articles were excluded based on titles and abstracts. Following a full-text review, an additional 31 articles were excluded, leaving 11 studies that met the inclusion criteria. The selection process is illustrated in **Figure 1**.

Study characteristics

The 11 studies included were, published between 2011 and 2023. Ethiopia had the highest

number of publications (three studies). The predominant study design was cohort analysis, with a combined sample size of 24,147 participants, including 5,587 cases of hypoxemia. Most studies investigated up to seven risk factors, while a few focused on a single factor. The fundamental characteristics of the included studies are presented in **Table 1**.

Risk of bias in studies

Among the 11 included studies, 6 were prospective cohort studies and 4 were retrospective studies (including 2 case-control studies). All studies had Newcastle-Ottawa Scale (NOS) scores of ≥ 6 , indicating appropriate selection of study subjects and well-defined groups. However, only half of the studies adjusted for the crude odds ratio in regression analysis, as detailed in **Table 2**. One study (Quintero-Cifuentes IF) received an Agency for Healthcare Research and Quality (AHRQ) score of 10, indicating high quality.

Analysis of factors related to postoperative hypoxemia in PACU patients

Age: 8 included studies examined age-related factors. Significant heterogeneity was observed ($I^2=89\%$, $P < 0.001$), and sensitivity analysis

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Table 1. Fundamental characteristics of included literature

Included study	Nation	Research type	Hypoxemia (n)	Total sample size (n)	Research factor
Liu SS 2011 [6]	America	Case-control study	348	701	②
Aust H 2012 [7]	Germany	Cohort study	163	959	① ② ⑧
Labaste F 2016 [8]	France	Cohort study	67	505	②
Kaushal A 2018 [9]	India	Cohort study	61	452	① ② ③
Quintero-Cifuentes IF 2018 [10]	Colombia	Cross-sectional study	60	365	①
Taye MG 2021 [11]	Ethiopia	Cohort study	194	424	② ③ ⑤
Andualem AA 2022 [12]	Ethiopia	Cohort study	225	298	①
Lin F 2022 [13]	China	Case-control study	116	756	① ②
Bang YJ 2023 [14]	Korea	Cohort study	842	12109	① ② ③ ④ ⑤ ⑥ ⑦
Berhanu M 2023 [15]	Ethiopia	Cohort study	149	352	① ⑥ ⑦
Haller K 2023 [16]	Germany	Cohort study	3362	6724	④ ⑧

①: Age; ②: Body Mass Index; ③: Smoking; ④: Gender; ⑤: Hypertension; ⑥: American Sociological Association grade \geq III; ⑦: Surgery duration over; ⑧: Administration of opioid analgesics.

Table 2. Bias risk assessment for cohort study/case-control study

Included study	Selection	Comparability	Exposure	Score
Liu SS 2011 [6]	☆☆☆	☆	☆☆	6
Aust H 2012 [7]	☆☆☆☆	☆	☆☆	7
Labaste F 2016 [8]	☆☆☆☆	☆	☆☆	7
Kaushal A 2018 [9]	☆☆☆☆	☆	☆☆	7
Taye MG 2021 [11]	☆☆☆☆	☆☆	☆☆	8
Andualem AA 2022 [12]	☆☆☆☆	☆☆	☆☆	8
Lin F 2022 [13]	☆☆☆	☆☆	☆☆	7
Bang YJ 2023 [14]	☆☆☆	☆☆	☆☆	7
Berhanu M 2023 [15]	☆☆☆☆	☆☆	☆☆	8
Haller K 2023 [16]	☆☆☆	☆	☆☆	6

☆ symbolizes 1 point.

revealed stable I^2 values even when individual studies were excluded. No source of heterogeneity was identified, necessitating the use of a random-effects model for analysis. Advanced age was identified as a significant risk factor for postoperative hypoxemia in PACU patients [OR=1.19 (95% CI: 1.11-1.29), $P<0.001$], as depicted in **Figure 2**.

Body mass index (BMI): 8 studies investigated BMI. Substantial heterogeneity was observed ($I^2=87\%$, $P<0.001$), with stable I^2 values across sensitivity analyses. The consistent P values indicated robust results. A random-effects model was used, revealing that elevated BMI was a risk factor for postoperative hypoxemia in PACU patients [OR=1.64 (95% CI: 1.36-1.97), $P<0.001$], as shown in **Figure 3**.

Preoperative oxygen saturation: 6 studies examined preoperative oxygen saturation. No significant heterogeneity was found ($I^2=0\%$, $P=0.83$), so a fixed-effects model was applied. The results showed that lower preoperative oxygen saturation was a risk factor for postoperative hypoxemia in PACU patients [OR=3.16 (95% CI: 2.56-3.91), $P<0.001$], as depicted in **Figure 4**.

Smoking status: 3 included studies analyzed smoking status as a risk factor. Substantial heterogeneity was present ($I^2=73\%$, $P=0.02$), with stable I^2 values observed during sensitivity analyses. The consistent changes in P values indicated a degree of result stability, with no identifiable source of heterogeneity. A random-effects model was used, demonstrating that smoking status was a risk factor for postoperative hypoxemia in PACU patients [OR=1.67 (95% CI: 1.15-2.43), $P=0.007$], as shown in **Figure 5**.

Other factors: Two studies investigated additional factors, including gender, hypertension, American Society of Anesthesiologists grade, surgery duration, and opioid analgesic use. The meta-analysis identified surgery duration >120 minutes [OR=1.43 (95% CI: 1.22-1.69), $P<0.001$] and opioid analgesic use [OR=1.51 (95% CI: 1.31-1.74), $P<0.001$] as risk factors for postoperative hypoxemia, as shown in **Table 3**.

Risk factors for postoperative hypoxemia

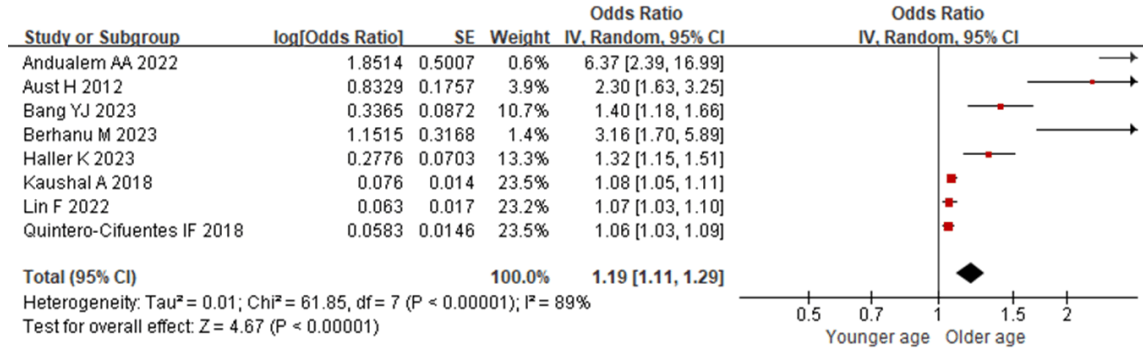


Figure 2. Relationship between age and postoperative hypoxemia in PACU patients. PACU: postanesthesia care unit.

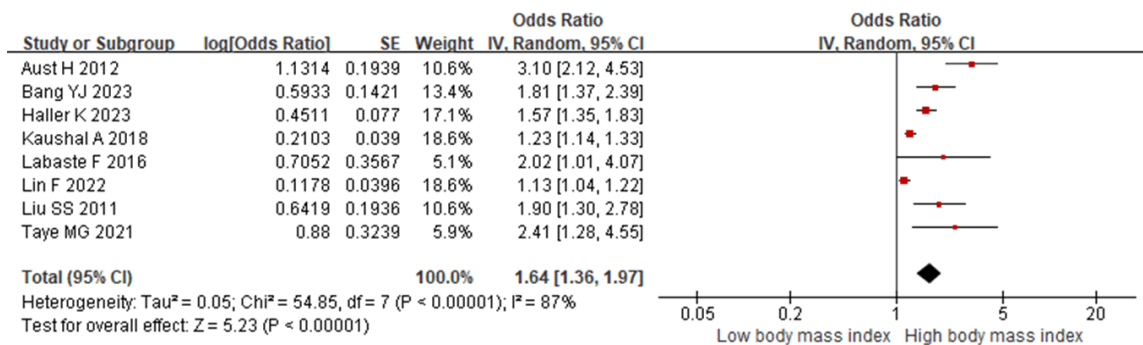


Figure 3. Relationship between body mass index and postoperative hypoxemia in PACU patients. PACU: postanesthesia care unit.

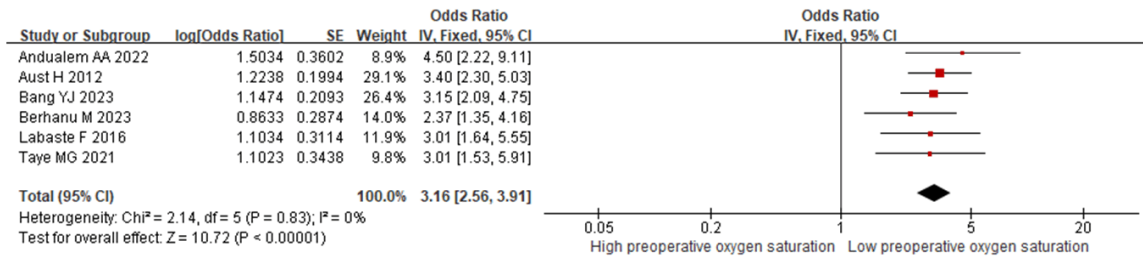


Figure 4. Relationship between preoperative oxygen saturation and postoperative hypoxemia in PACU patients. PACU: postanesthesia care unit.

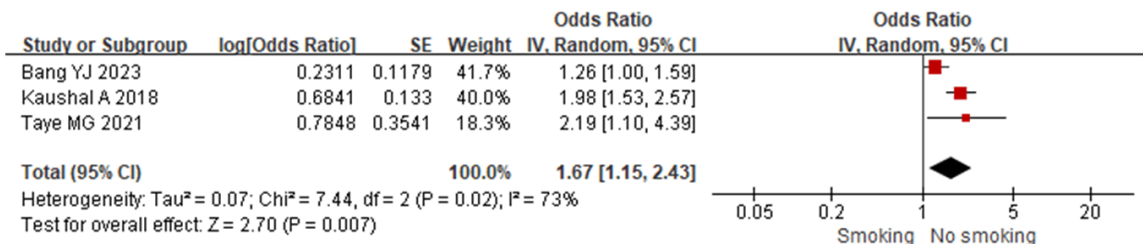


Figure 5. Relationship between smoking and postoperative hypoxemia in PACU patients. PACU: postanesthesia care unit.

Risk factors for postoperative hypoxemia

Table 3. Meta-analysis of risk factors for postoperative hypoxemia in PACU patients

Included study	Research factor	Heterogeneity test		Fixed effect model		Random effects model	
		<i>I</i> ²	<i>P</i>	OR	<i>P</i>	OR	<i>P</i>
Bang YJ 2023 [14], Haller K 2023 [16]	Male	92%	<0.001	-	-	0.98 (0.65-1.47)	0.92
Taye MG 2021 [11], Bang YJ 2023 [14]	Hypertension	89%	0.003	-	-	1.98 (0.78-5.03)	0.15
Bang YJ 2023 [14], Berhanu M 2023 [15]	ASA grade ≥III	93%	<0.001	-	-	4.32 (0.63-29.72)	0.14
Bang YJ 2023 [14], Berhanu M 2023 [15]	Surgery duration over 120 minutes	46%	0.18	1.43 (1.22-1.69)	<0.001	-	-
Aust H 2012 [7], Haller K 2023 [16]	Opioid analgesic	0%	0.35	1.51 (1.31-1.74)	<0.001	-	-

ASA: American Society of Anesthesiologists; PACU: postanesthesia care unit.

Risk factors for postoperative hypoxemia

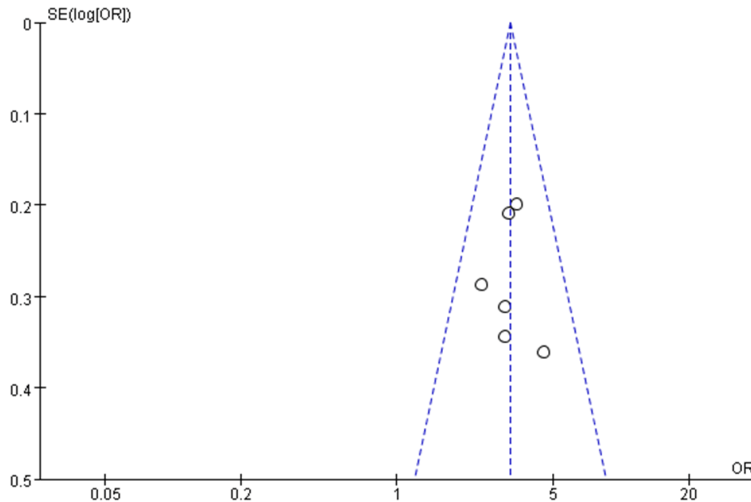


Figure 6. Funnel plot.

Publication bias

A funnel plot illustrating the correlation between preoperative oxygen saturation and postoperative hypoxemia in the PACU is presented in **Figure 6**. Although all studies fell within the 95% CI, notable asymmetry suggests possible publication bias.

Discussion

Low oxygen saturation in the PACU is a critical respiratory adverse event. Its pathogenesis may be linked to inadequate ventilation, airway obstruction, ventilation/perfusion mismatch, increased alveolar-arterial oxygen gradient, impaired oxygen diffusion, elevated pulmonary shunt, and decreased cardiac output [17, 18]. This meta-analysis aims to identify the risk factors for hypoxemia in the PACU and propose corresponding preventive measures. The findings are as follows.

This meta-analysis identified advanced age as an independent risk factor for postoperative hypoxemia in PACU patients. Previous studies [19] have shown that aging contributes to small vessel disease, resulting in decreased vascular reactivity and inadequate perfusion, ultimately leading to hypoxemia. Another study [20] suggested that with increasing age, imbalances in the renin-angiotensin system exacerbate inflammation and lung injury, reducing lung elasticity, increasing alveolar collapse, and ultimately causing hypoxemia. In summary, aging

is associated with a decline in physiological function, reduced surgical tolerance, and increased risk of cerebral hypoxia, all of which heighten the risk of hypoxemia. Consequently, clinicians should consider extending recovery and extubation times for elderly patients while closely monitoring their respiratory function, assessing acid-base balance, ensuring regular clearance of tracheal secretions, and conducting real-time monitoring of exhaled carbon dioxide to facilitate early intervention and reduce the risk of respiratory depression.

An elevated BMI is also an independent risk factor for postoperative hypoxemia in PACU patients. A study [21] reported that the incidence of perioperative hypoxemia is 16% in patients with a normal BMI, compared to 28% and 35% in patients with a BMI >30 kg/m² and >40 kg/m², respectively. Obesity is characterized by chronic inflammation, leading to the release and dysregulation of fatty acids, which destabilizes pulmonary vasculature and alters the expression of endothelial adhesion molecules, thereby increasing the susceptibility to acute lung injury [22]. As such, patients with elevated BMI should receive individualized guidance on appropriate dietary practices and weight management strategies tailored to their specific needs. Preoperative assessments should include evaluations of oral tolerance and surgical risk, followed by enhanced postoperative monitoring of vital signs and early initiation of nasal cannula oxygen therapy.

A lower preoperative oxygen saturation level is an independent risk factor for postoperative hypoxemia in PACU patients. Decreased oxygen saturation may result from insufficient oxygen supply or impaired oxygen delivery due to factors such as inadequate ventilation, respiratory failure, circulatory disorders, anemia, or impaired gas exchange in the lungs. These conditions can adversely affect oxygen supply and transport. The patient's preoperative health status is closely associated with the risk of postoperative hypoxemia. A low preoperative oxygen saturation level indicates that the

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patient may already have one or more of these issues before surgery, increasing the likelihood of deterioration postoperatively and leading to hypoxemia [23, 24]. Therefore, for patients with reduced preoperative oxygen saturation, comprehensive assessment of the respiratory system should be conducted, and respiratory and circulatory measurements should be closely monitored. An individualized preoperative preparation plan, including oxygen therapy, respiratory management, and preoperative breathing exercises, should be developed to optimize oxygenation and reduce the risk of hypoxemia.

Smoking is another independent risk factor for postoperative hypoxemia in PACU patients. Long-term smoking results in the accumulation of tar, nicotine, and other substances in lung tissue, impairing mucus clearance and increasing pulmonary vascular resistance. Smoking also damages the bronchi and alveoli, causing necrosis and shedding of epithelial cells, which reduces lung clearance capacity and increases sputum production and viscosity, thereby elevating the risk of hypoxemia [25, 26]. It is crucial to emphasize the harmful effects of smoking before surgery and provide smoking cessation counseling. Effective coughing techniques should be encouraged; if the patient's coughing ability is inadequate, techniques such as suctioning and chest percussion can be used to facilitate secretion clearance. Additionally, appropriate pulmonary protective measures should be implemented.

Surgery duration exceeding 120 minutes and the administration of opioid analgesics have also been identified as independent risk factors for postoperative hypoxemia in PACU patients. Prolonged surgical procedures can increase mechanical ventilation time, possibly causing mucosal ulceration, organ necrosis, and a higher risk of pulmonary infection, ultimately leading to hypoxemia [27]. Opioids, although highly effective for pain management during the perioperative period, have adverse effects such as respiratory depression. A study [28] demonstrated that excessive intraoperative opioid use is associated with a higher incidence of postoperative hypoxemia. Therefore, a comprehensive preoperative assessment should be conducted for each patient, followed by the development of a surgical plan aimed at preventing hypoxemia associated with pro-

longed surgery. Close monitoring of sedation levels and ventilation is essential, and strategies such as preoperative preventive analgesia, intraoperative protective measures, optimized anesthesia, and early postoperative pain management should be implemented. Nonsteroidal anti-inflammatory drugs, local wound infiltration, and nerve blocks may be used to minimize the adverse effects of inadequate analgesia.

This meta-analysis was limited by the small number of included studies, which were predominantly cohort and case-control studies. Limitations in study design, research subjects, and data extraction may have introduced selection bias. Some risk factors were evaluated in only a few studies, potentially leading to biased results. The heterogeneity among some included studies and the variation in sample sizes could affect the accuracy of the findings. The inconsistencies in the identified risk factors prevented a comprehensive analysis. Therefore, high-quality, large-sample randomized controlled trials are needed to further validate these findings.

In summary, advanced age, elevated body mass index, low preoperative oxygen saturation, smoking status, surgery duration over 120 minutes, and opioid analgesic use are all associated with an increased risk of postoperative hypoxemia in the PACU. It is essential to conduct thorough risk assessments and implement preventive measures for any high-risk patients.

Disclosure of conflict of interest

None.

Address correspondence to: Yaping Yi, Department of Disinfection Supply, The 923rd Hospital of The Joint Logistics Support Force of The People's Liberation Army of China, No. 52 Zhizhi Road, Qingxiu District, Nanning 530021, Guangxi, China. E-mail: 126013011@qq.com

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