

## Review Article

# Meta-analysis of the optimal ventilation strategies to improve perioperative oxygenation in obese patients

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**Abstract:** The objective of this meta-analysis is to determine the optimal strategy to improve perioperative oxygenation in obese patients. We searched the EBSCO, PubMed, Springer, Ovid, Wiley, CNKI, VIP, Wanfang, Google scholar, and Cochrane Library databases (updated to March, 2016) for studies in which the perioperative oxygenation in obese patients who received surgery and general anesthesia was assessed. The meta-analysis was conducted by RevMan 5.3 software. As a result, twenty-one studies with a total of 842 patients were included. During anesthesia induction, a head-up position could prolong the safe apnea duration compared with a supine position ( $P<0.0001$ ); when CPAP was used during spontaneous breathing,  $\text{PaO}_2$  increased to a higher level ( $P=0.005$ ). When IPPV with PEEP was applied during mechanical ventilation after spontaneous breathing disappeared, the safe apnea duration was longer ( $P=0.0009$ ) and  $\text{PaO}_2$  was higher ( $P<0.0001$ ). During anesthesia maintenance, the oxygen index (OI) was higher in the large tidal volume (TV) group than in the small tidal volume group when PEEP was applied ( $P=0.01$ ), but without PEEP, there was no difference in the OI ( $P=0.19$ ) between the large and small TV groups. After extubation,  $\text{PaO}_2$  was higher in the non-invasive positive pressure ventilation (NIPPV) group than in the nasal catheter group ( $P=0.004$ ). The results showed that the optimal ventilation strategies in obese patients for improving perioperative oxygenation include the head-up position plus CPAP for spontaneous breathing and IPPV with PEEP for mechanical ventilation during induction, large tidal volume ventilation with PEEP during anesthesia maintenance, and NIPPV applied for oxygen delivery after extubation.

**Keywords:** Oxygenation, obesity, general anesthesia, ventilation

## Introduction

The proportion of obese patients who receive surgery and general anesthesia is increasing, and some complications, including difficult airway or atelectasis, often accompany these patients perioperatively. Hypoxemia may occur in this case, prolonging the stay in the post-anesthesia care unit or delaying discharge from hospital [1]. Implementing a better ventilation strategy for obese patients during general anesthesia to improve perioperative oxygenation is of great concern. A meta-analysis has shown that volume-controlled ventilation combined with higher PEEP and single recruitment maneuver during an operation is optimal for obese patients [2], but the effects of the patient positions and ventilatory modes during induction, the tidal volume (TV) during anesthesia maintenance, and the mechanism for oxygen delivery after surgery on oxygenation in obese patients are unclear and even contradictory.

Thus, we identified the relevant randomized, controlled trials (RCTs) in this area, conducted a meta-analysis, and attempted to discover the optimal ventilation strategy for obese patients to improve perioperative oxygenation.

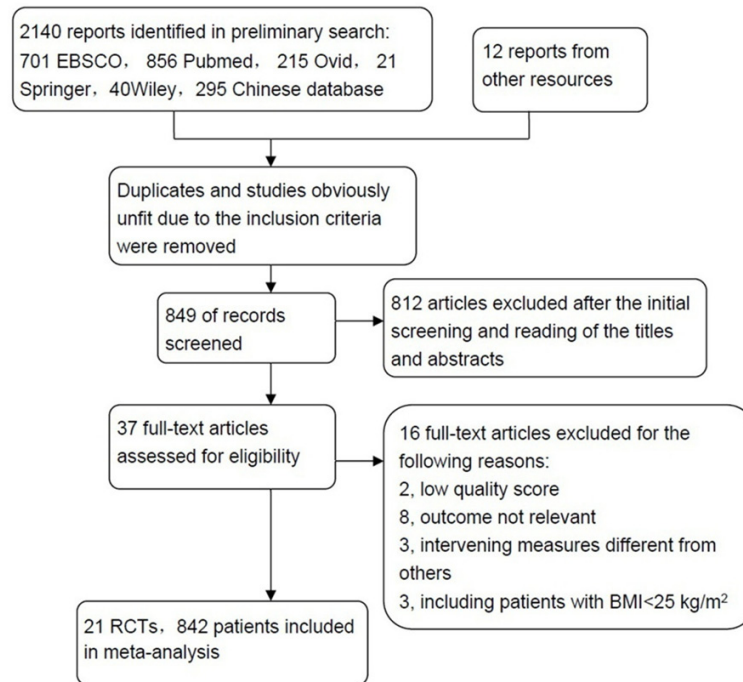
## Methods

We conducted our meta-analysis in accordance with the methods recommended by the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.

### Literature search

The databases (updated to March, 2016) of EBSCO, PubMed, Ovid, Springer, Wiley, CNKI, VIP, Wanfang, Cochrane Library and Google scholar were searched. The reference lists of the RCTs and previous meta-analysis articles were also checked to find any further potential eligible trials. To reduce publication bias, the abstracts in the database were searched without any language restriction.

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**Figure 1.** Flow chart summarizing the procedure of the study selection for the meta-analysis.

The key words for the search strategy included: obese or obesity, induction position, tidal volume, and oxygenation. The inclusion criteria were defined as follows: studies that included obese patients ( $\text{BMI} > 25 \text{ kg/m}^2$ ), elective surgery under general anesthesia, randomized controlled trials (RCTs), interventions including ventilation modes and patient positions during induction, tidal volume during anesthesia maintenance, and methods of oxygen delivery after surgery with perioperative oxygenation as the outcome. The exclusion criteria were defined as studies with subjects of  $\text{BMI} < 25 \text{ kg/m}^2$  and younger than 18 years old.

### Outcome parameters and data collection

The primary outcomes of this study were  $\text{PaO}_2$ , safe apnea duration, time of  $\text{SpO}_2$  recovery to 96-97%, and  $\text{PaO}_2/\text{FiO}_2$  (Oxygenation index, OI). Data were collected by two authors independently. When necessary, the original data were requested from the authors, or Plot-digitizer software was used to transform the data from a graph to numbers.

### Quality assessment

The risk of bias was checked by appraising the inclusion of phrases such as “adequate

sequence generation”, “allocation concealment”, “blinding”, “incomplete outcome data addressed”, “free of selective reporting” and “free of other bias” recommended by the Cochrane Collaboration.

### Statistical analysis

Meta-analysis was performed using Review Manager, version 5.3 for Windows (the Cochrane Collaboration, Oxford, UK). The effect size for continuous data was expressed as the mean difference (MD) with a 95% confidence interval (CI). Statistical heterogeneity was assessed by the Q statistic ( $P < 0.1$  was considered to indicate statistically significant heterogeneity) and  $I^2$  statistics ( $I^2 \geq 50\%$  was considered to indicate significant heterogeneity). The fixed-effect model was used when

$I^2 < 50\%$ , while the random-effect model was used when  $I^2 \geq 50\%$ . We made subgroup analysis if necessary or possible when heterogeneity among studies was statistically significant or  $I^2 \geq 50\%$ . Sensitivity analysis was performed to test the robustness of uncertainty in the meta-analysis. Publication bias was evaluated using the Egger test with Stata 12.0 software, and  $P > 0.05$  meant no statistical significance in the publication bias.

## Results

### Literature search results and characteristics of the eligible trials

We identified 2140 potential articles: 856 articles from MEDLINE, 215 articles from Ovid, 701 articles from EMBASE, 21 articles from Springer, 40 articles from Wiley, 295 articles from the Chinese database and 12 articles from other sources. After an initial screening and reading of the titles or abstracts, 37 relevant articles were left. Then, 2 articles with a low quality score, 3 articles including patients with  $\text{BMI} < 25 \text{ kg/m}^2$ , 8 articles in which outcomes were different from those in the other articles and 3 articles in which intervening measures were different from others were excluded after further detailed selection. Finally, 21 articles [3-23], with a total of 842

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**Table 1.** Characteristics of the trials

ID	Group (n)	BMI (kg/m <sup>2</sup> )	Detail strategies	Out-come	Remarks
1 Altermatt FR et al. 2005 [3]	Sitting (n=19) Supine (n=19)	43 (5) 46 (5)	5 minutes with 100% oxygen delivered by mask	ABD	Induction
2 Boyce JR et al. 2003 USA [4]	30° head-up (n=10) Supine (n=10)	56 (8) 59 (10)	5 minutes with 100% oxygen delivered by mask	ABD	Induction
3 Dixon BJ et al. 2005 [5]	30° head-up (n=21) Supine (n=21)	45 (6) 47 (7)	Unclear Unclear	BC	Induction
4 Tang LJ et al. 2008 [6]	15° head-up (n=20) Supine (n=20)	28 (2) 28 (2)	3 minutes with 100% oxygen delivered by mask (10 L/min)	ABC	Induction
5 Dan L et al. 2011 [7]	15° head-up (n=32) Supine (n=30)	29 (6) 28 (5)	4 minutes with 100% oxygen delivered by mask (10 L/min)	ABC	Induction
6 Zhang BF et al. 2012 [8]	15° head-up (n=25) Supine (n=25)	28 (2) 28 (1)	3 minutes with 100% oxygen delivered by mask (10 L/min)	AB	Induction
7 Ge YF et al. 2011 [9]	VCV+PEEP (n=10) VCV (n=10)	44 (2) 42 (2)	VCV+PEEP 8 cmH <sub>2</sub> O 5 min, TV 8 ml/kg, RR 8 bpm. VCV 5 min, TV 8 ml/kg, RR 8 bpm.	ABC	Induction
8 Shao DQ et al. 2013 [10]	VCV+PEEP (n=30) VCV (n=30)	33 (2) 33 (2)	VCV+PEEP 6 cmH <sub>2</sub> O 3 min, TV 10 ml/BWI, RR 12 bpm. VCV 3 min, TV 10 ml/BWI, RR 12 bpm	B	Induction
9 Gander S et al. 2005 [11]	CPAP+PCV+PEEP (n=12) PCV (n=15)	46 (7) 47 (6)	CPAP 10 cmH <sub>2</sub> O+PCV 14 cmH <sub>2</sub> O+PEEP 10 cmH <sub>2</sub> O PCV 14 cmH <sub>2</sub> O	BD	Induction
10 Coussa M et al. 2001 [12]	CPAP+VCV+PEEP (n=9) Control (n=9)	42 (6) 44 (7)	CPAP 10 cmH <sub>2</sub> O+PEEP 10 cmH <sub>2</sub> O+ VCV, TV 10 ml/kg, RR10 bpm. VCV, TV 10 ml/kg, RR10 bpm.	A	Induction
11 Harbut P et al. 2014 [13]	CPAP/PSV (n=22) Control (n=22)	>35 >35	CPAP/PSV (5+5 cmH <sub>2</sub> O) 2 min. 2 minutes with FiO <sub>2</sub> 80% by mask (15 L/min).	A	Induction
12 Delay JM et al. 2008 [14]	NPPV+PEEP(n=14) Control (n=14)	47(6) 52 (14)	PSV and PEEP were 8 and 6 cmH <sub>2</sub> O. 5 min with 100% oxygen delivered by mask (18 L/min).	AB	Induction
13 Edmark L et al. 2016 [15]	CPAP+PCV+PEEP (n=20) VCV (n=20)	41.9 (39.7-44.6) 38.1 (36.1-41.2)	CPAP 10 cmH <sub>2</sub> O+PCV+PEEP (<10 cmH <sub>2</sub> O) Manual control without CPAP	A	Induction
14 Shao DQ et al. 2015 [16]	CPAP+VCV+PEEP (n=15) VCV (n=15)	28 (2) 27 (2)	CPAP+VCV (VT 10 ml/kg, RR 12 bpm) +PEEP 6 cmH <sub>2</sub> O VCV (TV 10 ml/kg, RR 12 bpm)	AD	Induction
15 Shen YY et al. 2013 [17]	8 ml/ABW (n=20) 8 ml/IBW (n=20) 8 ml/CBW (n=20)	34.4 (2.8) 35.1 (4.4) 34.8 (3.4)	TV =8*ABW, PEEP=0 cmH <sub>2</sub> O TV =8*IBW, PEEP=0 cmH <sub>2</sub> O TV =8*CBW, PEEP=0 cmH <sub>2</sub> O	AD	Intraoperative: FiO <sub>2</sub> 100%, supine
16 Peng DH et al. 2010 [18]	6 ml/kg (n=10) 9 ml/kg (n=10) 12 ml/kg (n=10)	- - -	TV =6*ABW, PEEP=5 cmH <sub>2</sub> O TV =9*ABW, PEEP=5 cmH <sub>2</sub> O TV =12*ABW, PEEP=5 cmH <sub>2</sub> O	AD	Intraoperative: FiO <sub>2</sub> 100%, supine
17 Enekvist B et al. 2011 [19]	Normal TV (n=10) Increased TV (n=10)	30 (26-36) 27 (26-28)	TV was adjusted to achieve a P <sub>ET</sub> CO <sub>2</sub> at 4.5 kPa, PEEP=0 cmH <sub>2</sub> O TV was increased until P <sub>plateau</sub> was 0.04 cmH <sub>2</sub> O kg <sup>-1</sup> over the initial P <sub>plateau</sub> , PEEP=0 cmH <sub>2</sub> O	AD	Intraoperative: FiO <sub>2</sub> 35%, supine
18 Deng J et al. 2014 [20]	MBMI*H <sup>2</sup> *8 ml/kg (n=20) (male) 8 ml/kg (n=20) (male) MBMI*H <sup>2</sup> *8 ml/kg (n=20) (female) 8 ml/kg (n=20) (female)	27.42 (1.87) 27.44 (2.84) 26.5 (1.12) 26.91 (1.95)	TV =8*MBMI*H <sup>2</sup> , PEEP=5 cmH <sub>2</sub> O TV =8 ml*ABW, PEEP=5 cmH <sub>2</sub> O TV =8*MBMI*H <sup>2</sup> , PEEP=5 cmH <sub>2</sub> O TV =8 ml*ABW, PEEP=5 cmH <sub>2</sub> O	D	Intraoperative: FiO <sub>2</sub> 50%, supine
19 Chen GD et al. 2014 [21]	8 ml/ABW (n=32) 8 ml/IBW (n=32) 8 ml/CBW (n=32)	34.5 (2.9) 35.2 (4.5) 34.9 (3.5)	TV =8*ABW, PEEP=0 cmH <sub>2</sub> O TV =8*IBW, PEEP=0 cmH <sub>2</sub> O TV =8*CBW, PEEP=0 cmH <sub>2</sub> O	AD	Intraoperative: FiO <sub>2</sub> 100%, supine
20 Gaszynski T et al. 2007 [22]	CPAP (n=10) Control (n=9)	42.43 (3.3) 42.43 (3.3)	CPAP 9.4 cmH <sub>2</sub> O Nasal catheter 4 l/min O <sub>2</sub>	A	After extubation
21 Pessoa KC et al. 2010 [23]	BiPAP (n=10) Control (n=8)	48.5 (8.2) 46.3 (5.7)	NIV use BiPAP Nasal catheter 4 l/min O <sub>2</sub>	A	After extubation

A: PaO<sub>2</sub> (mmHg), B: safe apnea duration (s), C: time for SpO<sub>2</sub> to regain to 96-97% (s), D: PaO<sub>2</sub>/FiO<sub>2</sub>; Oxygenation Index (OI, mmHg), TV: tidal volume, ABW: actual body weight, IBW: ideal body weight, CBW: calibrated body weight, MBMI: mean BMI, H: height, NIV: noninvasive ventilation, CPAP: continuous positive airway pressure, NIPPV: noninvasive positive pressure ventilation, BiPAP: bi-level positive airway pressure.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Altermatt FR 2005	+	?	?	+	+	+	?
Boyce JR 2003	?	?	?	+	?	+	?
Chen GD 2014	?	?	?	?	+	+	?
Coussa M 2001	?	?	+	?	+	+	?
Dan L 2011	?	?	?	?	?	+	?
Delay JM 2008	?	+	+	+	+	+	+
Deng J (1) 2014	?	?	?	?	+	+	?
Deng J (2) 2014	?	?	?	?	+	+	?
Dixon BJ 2005	+	?	?	?	?	+	?
Edmark 2016	+	+	+	+	+	+	+
Enekvist B 2011	+	+	?	?	+	+	+
Gaszynski T 2007	?	?	?	?	?	+	+
Gender S 2005	?	?	+	?	+	+	?
Ge YF 2011	?	?	?	?	?	+	?
Harbut P 2014	?	?	?	?	+	+	?
Peng DH 2010	?	?	?	?	+	+	?
Pessoa KC 2010	+	+	+	+	+	+	+
Shao DQ 2013	?	?	?	?	?	+	?
Shao DQ 2015	?	?	?	?	+	+	?
Shen YY 2013	+	+	?	?	+	+	+
Tang LJ 2008	?	?	?	?	?	+	?
Zhang BF 2012	+	?	?	?	?	+	?

**Figure 2.** Risk of bias summary. Green indicates low risk of bias; red indicates high risk of bias; yellow indicates unclear risk of bias.

patients were included. The details of the eligibility process are presented in **Figure 1**. The trials in these 21 articles were conducted in different countries, and published from 2001 to 2016. The characteristics of these trials are presented in **Table 1**. The risk of bias summary is shown in **Figure 2**.

### Results of meta-analysis

**Patient positions and ventilation modes during induction:** Data on the induction positions were from 6 RCTs [3-8]; there was significant heterogeneity among the RCTs ( $I^2=84\%$ ,  $P<0.0001$ ), and the random-effect model showed that the sitting and head-up position could prolong the safe apnea duration ( $SpO_2$  dropping to 90-92%) ( $P<0.0001$ ), but could not increase  $PaO_2$  ( $P=0.10$ ) or shorten the latency for improving the  $SpO_2$  to 96-97% ( $P=0.50$ ) compared with the supine position (**Figure 3**). The subgroup analysis showed that the 15° head-up position could shorten the latency for improving the  $SpO_2$  to 96-97% compared with the supine position ( $P<0.0001$ ), but a 25-30° head-up position could not ( $P=0.38$ ) (**Table 2**).

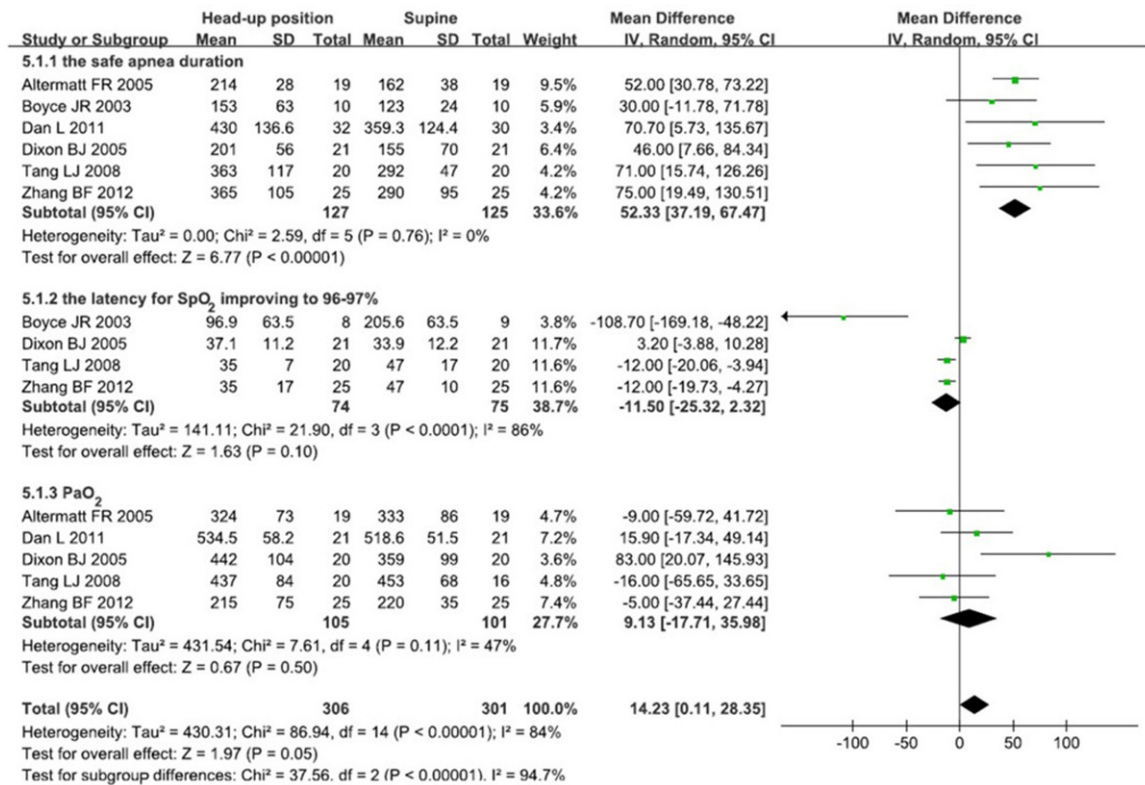
Data on ventilation modes during the induction were from 8 RCTs [9-16]. CPAP (5-10  $cmH_2O$ ) was used during spontaneous breathing in 5 of the 8 RCTs, and there was significant heterogeneity among them ( $I^2=73\%$ ,  $P=0.005$ ). The random-effect model showed that  $PaO_2$  increased to a higher level when CPAP was applied ( $P=0.005$ ) (**Figure 4**). The sensitivity analysis showed that the findings were robust when any suspicious study was omitted. Then, IPPV with or without PEEP (6-10  $cmH_2O$ ) was applied in all 8 RCTs after spontaneous breathing disappeared. There was significant heterogeneity among the RCTs ( $I^2=81\%$ ,  $P<0.0001$ ), and the random-effect model showed that the safe apnea duration was longer ( $P=0.0009$ ) and  $PaO_2$  was higher ( $P<0.0001$ ) when IPPV with PEEP was applied (**Figure 5**). The sensitivity analysis showed that neither PCV nor VCV had an effect on the outcome.

### Intraoperative ventilation strategies for obese patients

Five RCTs studied OI under different tidal volumes (TVs) [17-21]. According to classification criteria in these RCTs, a large TV was defined as  $\geq 8$  ml per actual body weight (ABW), and a



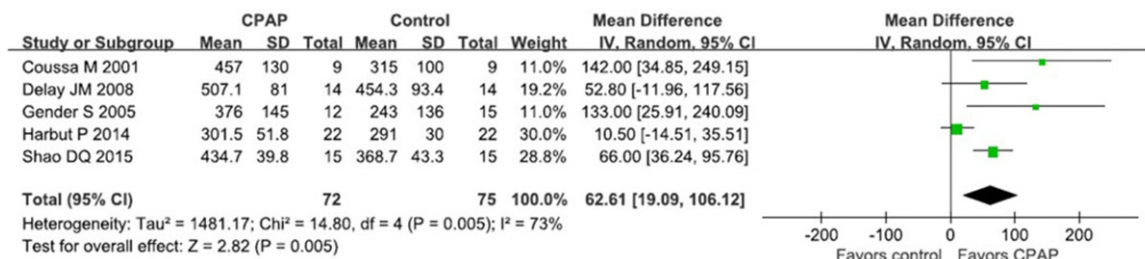
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**Figure 3.** Forest plot: effect of different induction positions on the safe apnea duration, the latency for improving the SpO<sub>2</sub> to 96-97% and PaO<sub>2</sub>.

**Table 2.** Subgroup analysis of the head-up position compared with supine for the latency for regaining SpO<sub>2</sub> to 96-97%

Intervening measures	Case number	RCTs	MD	95% CI	P	I <sup>2</sup>
15° head-up vs supine	90	2	-12	-17.58-6.42	P<0.0001	0%
25-30° head-up vs supine	59	2	-48.55	-157.91-60.80	0.38	92%



**Figure 4.** Forest plot: effect of different respiratory modes on PaO<sub>2</sub> during induction.

small TV was defined as 8 ml per ideal body weight (IBW) or 6 ml/ABW. There was significant heterogeneity among the RCTs ( $I^2=63\%$ ,  $P=0.02$ ); the subgroup analysis showed that when PEEP (5 cmH<sub>2</sub>O) was applied, the OI in the large TV group was higher than in the small TV group ( $P=0.01$ ), but when PEEP was not applied,

there was no difference between the large and small TV groups ( $P=0.19$ ) (Figure 6).

### Oxygen delivery after extubation

Data on PaO<sub>2</sub> were from 2 RCTs [22, 23], and the random-effect model ( $I^2=65\%$ ,  $P=0.09$ )

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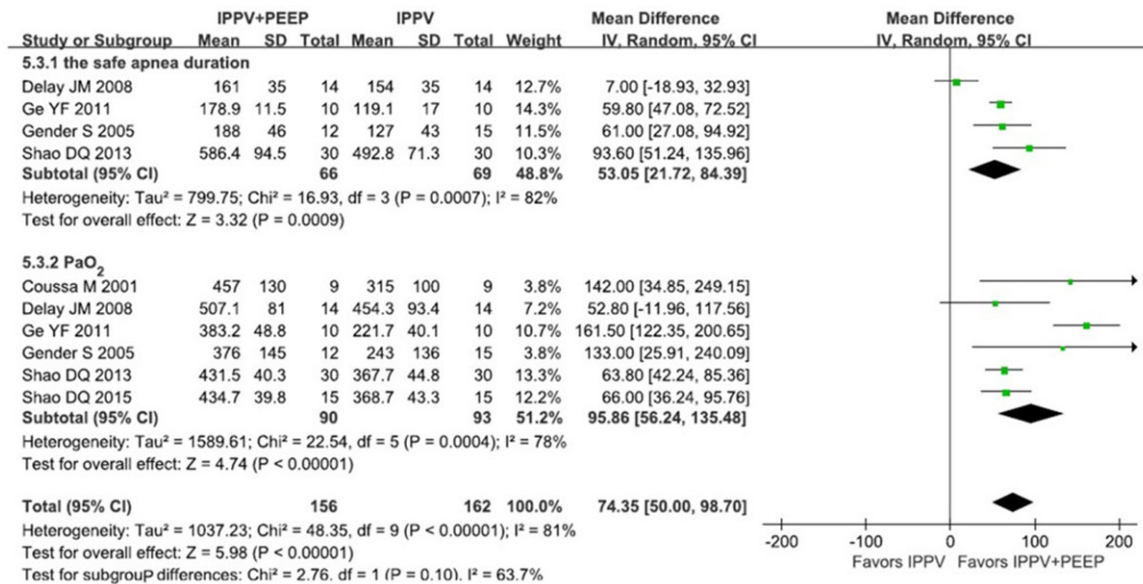


Figure 5. Forest plot: effect of different ventilation modes on the safe apnea duration and PaO<sub>2</sub> during induction.

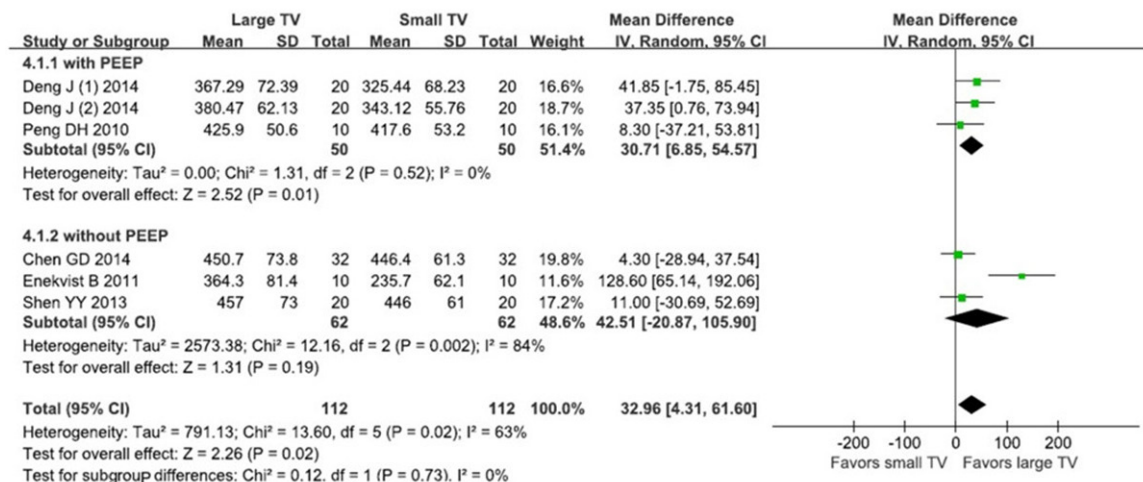


Figure 6. Forest plot: effect of different tidal volumes (TVs) on the Oxygenation index during surgery.

showed that PaO<sub>2</sub> was higher in the CPAP/ BiPAP group than in the nasal catheter group ( $P=0.004$ ) (Figure 7).

### Publication bias

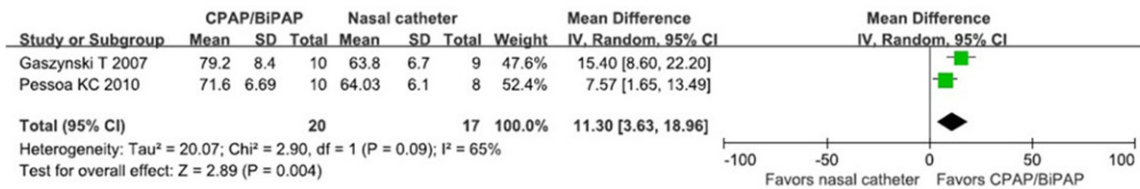
There were no publication biases in the RCTs corresponding to the primary outcome according to the Egger test ( $P>0.05$ ).

### Discussion

Respiratory complications often accompany obesity perioperatively. For obese patients receiving general anesthesia, the most common concern is the development of hypoxemia

at the three phases, including preoxygenation and induction, maintenance of anesthesia, and post-extubation. The possibility of a difficult face mask ventilation or intubation is very high in these patients; in addition, high oxygen consumption and low oxygen reservoir exist, making hypoxemia very likely to occur in the induction or after extubation. In these patients, a higher BMI suggests a faster decline of the SpO<sub>2</sub> [24]. Therefore, preoxygenation is very crucial during induction in obese patients. This meta-analysis showed that preoxygenation in a head-up position or with CPAP application was preferred during the induction. The main reason for this is that the diaphragm can be dis-

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**Figure 7.** Forest plot: effect of different oxygen delivery strategies on  $PaO_2$  after extubation.

placed cephalad in the supine position in obese patients, and the lung compliance and functional residual capacity are reduced. This change is small in the head-up or sitting position, but the  $15^\circ$  head-up position is superior to the  $25\text{--}30^\circ$  head-up position in improving oxygenation from this meta-analysis; however, the mechanism for this needs to be elucidated. In the induction of anesthesia, after muscular relaxants are administered, atelectasis often occurs in obese patients [15]. Our meta-analysis showed that IPPV with PEEP can prolong the safe apnea duration during mechanical ventilation in the induction, and PEEP can maintain the expanding of the alveoli. The optimal oxygen concentration for anesthesia induction in obese patients is controversial; Edmark L [25] showed that pure oxygen caused a higher incidence of atelectasis and shortened the time of desaturation, but Bluth T [26] recommend that an 80% or higher concentration of oxygen should be applied in the induction.

For non-obese patients, low TV combined with PEEP and an oxygen concentration less than 80% is recommended to reduce intra- or post-operative respiratory complications [27]. A multicenter study has shown that moderate to large TV is commonly used in clinical anesthesia, especially in obese and female patients [28]. However, our meta-analysis showed that large TV combined with PEEP could greatly increase OI in obese patients during anesthesia maintenance, while large TV alone could not. Large TV with PEEP may more effectively prevent alveoli from collapsing, and the functional residual capacity (FRC) can be kept in a relatively stable and high state [19]; however, large TV can cause higher airway pressure and lead to potential barotraumas [29].

Our meta-analysis showed that NIPPV application after extubation could improve oxygenation, but NIPPV is rarely used in obese patients after surgery, mainly because it can potentially increase the risk of gastric reflux and aspira-

tion. However, it has been proven to be safe and efficient in obese patients after bariatric surgery in another trial [30]. Therefore, to improve oxygenation after extubation in obese patients, NIPPV, rather than a nasal catheter, for oxygen delivery should be taken into account.

There was significant heterogeneity among the RCTs, and we made subgroup analysis when necessary and possible in our meta-analysis. The reasons for the heterogeneity may be, the level of head-up position, CPAP level, and PEEP level were not the same, and the methods for calculation of tidal volume in obese patients were some different in these RCTs; in addition, the sample size was not big enough in our meta-analysis, so more RCTs with large sample size will be needed in the near future.

This article has some limitations; the sample size was not very big, and the levels of obesity were different among the trials. The trials included in this meta-analysis lacked pulmonary complications or lung function. More high quality trials are needed in this research area.

### Conclusions

The results of our meta-analysis suggest that the optimal ventilation strategies to improve perioperative oxygenation in obese patients should be a head-up position plus CPAP for spontaneous breathing and IPPV with PEEP for mechanical ventilation during induction of general anesthesia, large tidal volume ventilation with PEEP during anesthesia maintenance, and NIPPV applied for oxygen delivery after extubation.

### Disclosure of conflict of interest

None.

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