

Research Article

Efficacy and Safety of Three Alveolar Recruitment Manoeuvres after Off-Pump Coronary Artery Bypass Grafting

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Abstract

The aim of study was to assess the efficacy and safety of three different modes of alveolar recruitment manoeuvre (RM) and to evaluate their influence on early postoperative period after off-pump coronary artery bypass grafting (OPCAB). We randomized 80 adult patients after OPCAB to four groups: CPAP-40 group was exposed to RM by changing the ventilator mode to continuous positive airway pressure of 40 cm H₂O for 40 seconds; in a Peak-40 group, RM was achieved by inflating the lungs at constant flow until a peak inspiratory pressure of 40 cm H₂O was reached and held for 40 seconds; the PEEP-15 group received RM by raising the positive end-expiratory pressure to 15 cm H₂O for five minutes; the control group received no RM. Arterial oxygenation and dynamic compliance increased in all groups receiving RM ($P < 0.017$). In the CPAP-40 group, mean arterial pressure decreased significantly during RM ($P = 0.01$). In the PEEP-15 group, the duration of respiratory support was shortened by 1 hr compared with the control group ($P = 0.012$). Alveolar RM using Peak-40 and PEEP-15 improved oxygenation after OPCAB without negative influence on haemodynamics. Application of a PEEP of 15 cm H₂O for five minutes reduced the time to tracheal extubation.

Keywords: Alveolar Recruitment; Mechanical Ventilation; Coronary Artery Bypass Grafting

Introduction

The formation of atelectases is a common complication of mechanical ventilation during general anaesthesia [1–3]. Chest radiograms display crest-shaped changes of increased density in dependent lung regions within minutes after induction of anaesthesia and neuromuscular blockade. These changes are concerted by a fall in functional residual capacity and a cranial displacement of the diaphragm [2,3]. Following cardiac surgery, collapse of pulmonary parenchyma can persist postoperatively and contribute to increased morbidity and additional health care costs [1]. Notably, the incidence of atelectases is particularly high after cardiosurgical interventions because the patients are exposed to multiple promoting factors. Attention also has been paid to the sternotomy per se and to lung compression by mediastinal structures. Moreover, the use of retractors during the surgery, manipulations in the pleural cavities and mechanical ventilation with high

inspiratory oxygen fractions might all add to the de-aeration of lung tissue [4,5].

Over the last years, different strategies have been used to re-expand collapsed lung areas, both intra- and postoperatively [6–8]. Several studies have shown that the application of an alveolar recruitment manoeuvre (RM) can improve respiratory function by re-opening atelectatic regions after cardiac surgery. It is widely accepted that RM reduces intrapulmonary shunt and ventilation-perfusion mismatch and subsequently improves arterial oxygenation [1,9]. However, some effects of the RM might be deleterious since it might affect the cardiovascular system adversely; besides this it might induce barotrauma, volumotrauma and biotrauma [5,10,11].

Currently, there is a wide variety of methods for recruitment manoeuvres in clinical practice, including different levels of continuous positive airway pressure

(CPAP), positive end-expiratory pressure (PEEP), increased tidal volume and peak or plateau pressures for different periods of time [5–8]. However, to date there is no general agreement on which mode of RM is most advantageous postoperatively for the individual patient [12]. Correspondingly, the significance of RM after coronary surgery is also still unsettled [13].

Thus, the aim of our study was to assess the efficacy and safety of three different modes of RM and to evaluate their influence on the postoperative ventilation time and early postoperative period after off-pump coronary artery bypass grafting (OPCAB).

Methods

The study design and the informed consent form were approved by the Ethical Committee of Northern State Medical University, Troitsky av. 51, 163001 Arkhangelsk, Russian Federation, on 1 February 2011 (No 2; Chairperson Professor A. Gudkov). Written informed consent was obtained from every patient.

The study was performed in a 900-bed university hospital (City Hospital #1 of Arkhangelsk, Russia). During the period from March 2011 to January 2012, 80 adult patients undergoing OPCAB were enrolled into a prospective randomized study. Exclusion criteria were age > 75 years, morbid obesity with body mass index (BMI) > 35 kg/m², history of acute myocardial infarction within the preceding month, pre-existing COPD at the stage of decompensation, lung surgery, pregnancy, signs of acute lung injury after the surgery and unstable haemodynamics defined as requirement for dobutamine/dopamine > 10 mcg/kg/min, or epinephrine/norepinephrine > 0.1 mcg/kg/min to maintain the mean arterial pressure (MAP) within 60–80 mm Hg.

All the patients received a standard anaesthesia using propofol (Diprivan, AstraZeneca, UK) 3 mg/kg/hr and fentanyl (Moscow Endocrine Factory, Russia) 2–4 mcg/kg/hr. Mechanical ventilation in the operating room was performed by means of a semi-closed anaesthetic circuit (Fabius GS, Dräger, Germany) with FiO₂ 0.5 to obtain SpO₂ values above 95%, tidal volume (VT) 8 mL/kg of predicted body weight (PBW), respiratory rate 12–14/min aiming at PaCO₂ of 35–45 mm Hg, PEEP was set to 5 cm H₂O and fresh gas flow of 1 L/min. Nobody received RM during the surgery.

At the end of surgery and transfer to the cardiosurgical ICU, all the patients were randomized by using the envelope method into the following groups:

1) The CPAP-40 group (n = 19) where RM was achieved by changing the ventilator mode to CPAP of 40 cm H₂O for 40 seconds.

2) The Peak-40 group (n = 20) where RM was performed by increasing inspiratory pressure in constant flow rate to achieve peak inspiratory pressure of 40 cm H₂O during 40 seconds.

3) The PEEP-15 group (n = 19) where alveolar RM was achieved by raising positive end-expiratory pressure to 15 cm H₂O for five minutes.

4) The Control group (n = 16) received no RM during conventional assist-control ventilation.

Six patients were excluded from the analysis: one because of protocol violation (inability to follow the protocol of ventilation for technical reasons), one due to deviation from the inclusion criteria (emphysematous changes in the lung diagnosed intraoperatively) and four due to problems with data sampling.

During RM, all groups were sedated with continuous infusion of propofol 1–2 mg/kg to suppress spontaneous breathing. All patients received epidural analgesia at the Th_{2–4} level with a continuous infusion of ropivacaine 0.2% (Naropin, AstraZeneca, UK) at rate 3–8 ml/hr aiming at a visual analogue scale (VAS) score <30 mm at rest. All the patients received respiratory support using pressure controlled ventilation (PCV) (Avea, Viasys, USA). Inspiratory pressure was adjusted to deliver a VT of 8 mL/kg predicted body weight, PEEP was set to 5 cm H₂O, FiO₂ to 0.5 or higher to obtain SpO₂ above 95%. Respiratory rate (RR) was adjusted to provide EtCO₂ of 30–35 mm Hg. Haemodynamic parameters were optimized according to the goal-directed therapy protocol [14].

After stabilization of haemodynamic and ventilation variables following transfer from the operation room, the RM was performed according to the group allocation, or the patients received ventilation without any RM (control group). The RM was discontinued if hypotension (MAP < 50 mm Hg) and/or bradycardia below 35 /min occurred during the procedure.

Within 10 min after RM, the ventilation mode was changed, if possible, to pressure support ventilation (PSV) with inspiratory pressure increasing gradually from 6 cm H₂O to a level sufficient for obtaining a spontaneous VT of 6 mL/kg PBW. The ventilatory parameters were assessed every 30 min and adjusted, if necessary, aiming at a stepwise decreasing pressure support of by 2–4 cm H₂O each time. In case of dyspnoea or reduction of VT, inspiratory pressure was increased to the previous level. After decrease of pressure support to 6 cm H₂O (8 cm H₂O in case of BMI > 30 kg/m²), the spontaneous breathing trial (SBT) was started.

The SBT was considered to be passed if the patient displayed no episodes of tachypnoea (RR > 30 /min),

had VT > 6 mL/kg PBW, PaO₂/FiO₂ > 250 mm Hg, f/VT < 105 breaths/min/mL and HR < 100/min during the last 30 minutes. After passing the SBT all the patients were immediately extubated. After the tracheal extubation, the patients received a supplementary oxygen flow of 4 L/min via a nasal catheter.

The measurements included ventilatory parameters (P_{peak} (peak inspiratory pressure), VT, RR, dynamic compliance), blood gases (ABL800Flex, Radiometer, Denmark), EtCO₂ and SpO₂ (Capnostream-20, Oridion, Israel), and haemodynamics including HR, MAP and CVP assessed by electrocardiogram and invasive monitoring of arterial and central venous pressure, respectively. All these parameters were registered before and at 10 min after RM, after SBT, as well as at 1, 6, and 12 hrs after extubation. After tracheal extubation, all the values were measured after three minutes without supplemental oxygen (FiO₂ 0.21). EtCO₂ at 1, 6 and 12 hrs after extubation was measured using EtCO₂ breath sampling lines for non-intubated patients (Smart CapnoLine® Plus, Oridion, Israel). In addition, we recorded the perioperative fluid balance and length of postoperative ICU stay. Chest radiographs were taken on postoperative day one. Atelectases were graded as 0: no atelectasis and 1: partial or total atelectasis. The treating staff in the ICU was blinded to the patient's randomization. The primary end-point of the study assessing the efficacy of RM was the decrease in duration of postoperative respiratory support. The secondary end-point was an increment in PaO₂/FiO₂ ratio by at least 10 mm Hg at 10 minutes after RM.

Statistical analysis

For data collection and analysis, we used SPSS software (version 16.0; SPSS Inc., IL, USA). All the variables were expressed as median (25th-75th interquartile interval).

Calculation of sample size was based on initial observations (5 cases in each group) and the hypothesis that RM would shorten the duration of postoperative respiratory support by 60 min compared with the control group. In order to find a statistically significant difference with α of 0.05 and β of 0.2, a sample size of 16 patients in each group proved to be sufficient.

The groups were compared using Kruskal-Wallis and post hoc Mann-Whitney tests with Bonferroni correction. The intragroup comparisons with baseline (before RM) were performed by Friedman and post hoc Wilcoxon tests with Bonferroni correction. Discrete data were compared using Fisher's exact test and expressed as patient number. For post hoc intragroup comparisons, p value < 0.01 was considered as statistically significant. In case of post hoc intergroup comparisons, p < 0.017 was regarded as statistically significant.

Results

We found no statistically significant intergroup differences with regard to sex, age, BMI, PBW, ejection fraction determined by echocardiography, EuroSCORE assessment, duration of surgery and postoperative fluid balance (Table 1).

Table 1. Key clinical characteristics of the patients

Parameter	Groups			
	CPAP-40 (n = 19)	PEEP-15 (n = 19)	Peak-40 (n = 20)	Control (n=16)
Gender, (male / female)	16/3	11/8	16/4	11/5
Age, yrs	57 (54-65)	60 (58-62)	62 (55-65)	61 (54-70)
Body mass index, kg / m ²	27 (24-31)	25 (23-31)	26 (24-28)	25 (24-29)
Predicted body weight, kg	69 (62-72)	62 (47-68)	66 (56-71)	66 (55-72)
Ejection fraction, %	59 (53-61)	61 (59-66)	59 (57-62)	60 (54-66)
EuroSCORE, points	2 (1-4)	3 (3-5)	2 (2-4)	3 (1-5)
Duration of surgery, min	185 (155-205)	185 (175-195)	178 (155-194)	188 (168-205)
Postoperative fluid balance, mL	1550 (1350-1900)	1725 (1400-2000)	1475 (1237-1725)	1425 (1175-1912)
Postoperative time to tracheal extubation, min	150 (107-190)	115 (83-148)*	120 (115-180)	175 (115-180)
Intensive care unit time, hrs	45 (24-63)	44 (24-50)	46 (24-48)	46 (24-48)
Atelectases	2	3	3	4

* — p < 0.017 between groups compared with the control, data represented as median (25th-75th interquartile interval)

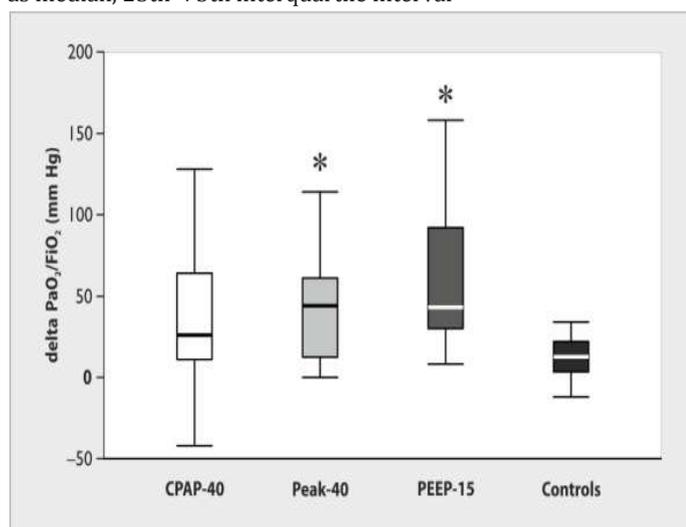
During the RM peak inspiratory pressure in groups CPAP-40 and Peak-40 was 40 cm H₂O; in PEEP-15 group it was 29 (28 -31) cm H₂O.

The efficacy of the recruitment manoeuvres

After RM, we observed an increase in PaO₂/FiO₂ in comparison with intragroup baseline by 17, 18 and 16% in the PEEP-15, Peak-40 and CPAP-40 groups, respectively (P < 0.01; Table 2). The difference between PaO₂/FiO₂ before and 10 min after RM (delta PaO₂/FiO₂) in the PEEP-15 and the Peak-40 groups was significantly higher as compared to delta PaO₂/FiO₂ in the Control group (P < 0.017, Figure 1). The increment in PaO₂/FiO₂ following RM persisted during the post-extubation period. In the Control group, we observed a transient increase in PaO₂/FiO₂ at 1 and 6 hrs after tracheal extubation (P < 0.013). In parallel with the increase in arterial oxygenation, dynamic respiratory compliance increased significantly in all the three groups of RM (P < 0.03). EtCO₂ and PaCO₂ registered 5 and 10 minutes after the RM did not differ significantly between or within the groups. However, in the RM groups, EtCO₂ increased after tracheal extubation compared with baseline (P < 0.01) and with the Control group (P < 0.017). Respiratory rate rose in all the groups after the discontinuation of mechanical ventilation (Table 2).

Figure 1. Delta PaO₂/FiO₂ ratio by 10 minutes after the recruitment manoeuvre in comparison with the control group.

* — $p < 0.017$ compared with the Control group. Data represented as median, 25th–75th interquartile interval



Safety of recruitment manoeuvres

In the CPAP-40 group, 30 seconds after the start of RM, MAP decreased by 33% compared with baseline ($P=0.001$) and by 36% compared with the Control group ($P = 0.0001$; Figure 2). Severe hypotension (MAP below 50 mm Hg) developed in one patient of the PEEP-15 group and in two patients of the CPAP-40 group. The data obtained from these patients during the post-extubation period were excluded from further analysis. In these patients, RM was cancelled prematurely. After RM, MAP returned to the baseline values. There were no significant intergroup differences in HR postoperatively (Table 2).

Recruitment manoeuvres and the postoperative period

All the patients passed the SBT-test successfully. As shown in Table 1, we observed a decrease by 1 hr in the duration of postoperative mechanical ventilation in the PEEP-15 group compared with the control group ($P=0.012$).

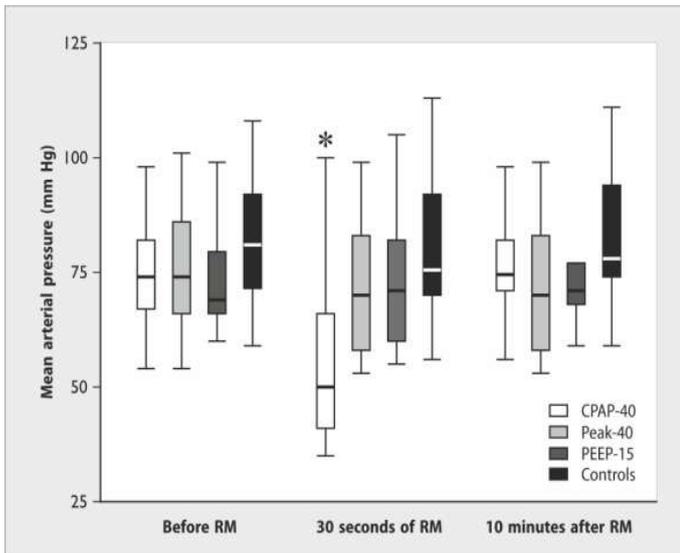
Table 2. Changes of the studied parameters during the recruitment manoeuvres and after extubation

Parameter	Group	Stage					
		Before RM	10 minutes after RM	After SBT	1 hrs after extubation	6 hrs after extubation	12 hrs after extubation
PaO ₂ /FiO ₂ , mm Hg	CPAP-40	240 (195–301)	285 (238–348) †	300 (246–384) †	318 (292–360) †	358 (299–430) †	328 (290–383) †
	PEEP-15	292 (199–370)	352 (220–394) †	322 (210–372) †	312 (292–386) †	322 (302–392) †	343 (306–391) †
	Peak-40	257 (210–350)	311 (260–433) †	298 (236–336) †	352 (279–385) †	357 (290–411) †	314 (270–413) †
	Control	254 (208–354)	260 (224–370)	228 (226–334)	348 (303–384) †	330 (308–464) †	301 (291–356)
Compliance, mL/cm H ₂ O	CPAP-40	34 (30–41)	39 (34–51) †	—	—	—	—
	PEEP-15	34 (29–45)	36 (34–46) †	—	—	—	—
	Peak-40	39 (34–45)	44 (36–53) †	—	—	—	—
	Control	35 (31–41)	36 (32–46)	—	—	—	—
EtCO ₂ , mm Hg	CPAP-40	32 (29–36)	32 (29–35)	39 (35–41) †	36 (35–38) †	36 (35–39)*	35 (32–41)*
	PEEP-15	31 (28–37)	33 (29–36)	38 (35–40) †	38 (34–41) †	35 (31–38)	35 (30–39)*
	Peak-40	32 (28–35)	33 (29–35)	38 (35–43) †	38 (31–41) †	35 (34–38)* †	33 (31–35)
	Control	31 (28–33)	32 (28–32)	38 (35–39) †	35 (33–38)	33 (28–36)	31 (24–32)
PaCO ₂ , mm Hg	CPAP-40	37 (34–41)	37 (35–43)	38,7(36,7–42,1)	36 (34–40)	36 (33–39)	37 (33–41)
	PEEP-15	39 (36–41)	39 (36–41)	39,3(38,3–42,8)	39 (38–42)	37 (35–39)	37 (35–38)
	Peak-40	38 (36–41)	37 (34–43)	39,9 (37,9–42)	39 (36–42)	37 (35–39)	35 (32–38)
	Control	38 (34–41)	39 (35–41)	40 (37–43)	38 (37–41)	37 (34–38)	36 (34–40)
Respiratory rate/min	CPAP-40	14 (12–15)	14 (12–15)	19 (14–22) †	23 (17–24) †	20 (18–21) †	23 (19–24) †
	PEEP-15	14 (12–14)	13 (11–14)	18 (16–21) †	20 (15–22) †	20 (16–24) †	20 (16–23) †
	Peak-40	12 (12–14)	12 (12–14)	18 (16–22) †	18 (15–23) †	19 (17–21) †	20 (18–22) †
	Control	12 (12–14)	12 (12–14)	20 (17–25) †	20 (18–24) †	21 (19–25) †	21 (18–24) †
Heart rate/min	CPAP-40	68 (52–78)	66 (51–82)	89 (78–98) †	95 (72–100) †	83 (74–90) †	78 (75–86) †
	PEEP-15	65 (55–73)	66 (56–72)	77 (70–96) †	89 (81–97) †	84 (73–90) †	81 (69–83) †
	Peak-40	67 (57–72)	69 (54–76)	86 (78–90) †	86 (77–94) †	82 (78–88) †	78 (71–89) †
	Control	61 (54–77)	67 (54–76)	77 (67–92) †	83 (71–97) †	78 (61–91) †	76 (66–88) †

Data represented as median (25th–75th interquartile interval) † — $p < 0.01$ within group compared with baseline (before recruitment manoeuvre), $p < 0.03$ within group compared with baseline (before recruitment manoeuvre) in case of compliance measurements, * — $p < 0.017$ as compared with the control group. EtCO₂ — end-tidal CO₂, SBT—spontaneous breathing trial

Figure 2. Changes in mean arterial pressure during and after recruitment manoeuvre.

* — $p < 0.017$ compared with the Control group. Data represented as median, 25th–75th interquartile interval



The duration of ICU stay ($P > 0.017$) and the incidence of atelectases ($P > 0.017$) did not differ significantly between the groups. All the patients survived beyond Day 28 after the surgery.

Discussion

In the present study, all the three different recruitment manoeuvres resulted in increased dynamic respiratory compliance and improved oxygenation compared with the baseline values. These findings are consistent with those reported by other authors [5,7,15]. Thus, Claxton et al. [15] studied recruitment manoeuvres with PEEP increments to 15 cm H₂O after cardiac surgery and found a significant increase in the PaO₂/FiO₂ ratio in the recruitment group at 30 minutes and one hour after the manoeuvre as compared with groups of zero PEEP and 5 cmH₂O PEEP. In 40 hypoxemic cardiac surgical patients, the investigators also [5] noticed significant improvement in arterial oxygenation during the postoperative period after recruitment manoeuvres (CPAP of 20, 30 and 40 cmH₂O for 30 seconds). Tusman and co-workers also demonstrated improvement of arterial oxygenation 40 minutes after RM, which included repeated increments in inspiratory pressure to 40 cm H₂O over 10 breathing cycles [7]. However, neither the latter studies nor our own investigation aimed at a detection of differences between the recruitment groups; a comparison was made only with the group in which RM was not performed.

One of the major reasons for hypoxemia after OPCAB is the formation of atelectases [1–3]. In ARDS, reduced generation of surfactant, lung consolidation, lung oedema and impairment of hypoxic pulmonary vasoconstriction, all contribute to derangement of oxygenation [16]. However,

to counteract hypoxemia after cardiac surgery, as opposed to ARDS, requires a less vigorous RM to open up collapsed airways. Thus, in adults with healthy lungs, inflations of up to 40 cm H₂O for 7–8 sec may expand the collapsed lung tissue [17]. In contrast, a sustained inflation of up to 45 cm H₂O for 20 sec might be required to improve oxygenation in patients with ARDS [18]. Furthermore, to maintain the beneficial effects of RM, it should be combined with an adequate PEEP level as a part of the open lung concept. Therefore, in coronary surgery patients we used different strategies of RM, including CPAP-40 and Peak-40 that are widely used in ARDS, and a more “gentle” approach including PEEP-15. It has been shown that the open lung concept results in significantly improved lung aeration and oxygenation, both in ARDS and during the perioperative period [1, 19–23]. Meanwhile, it was also shown in a number of studies that the PEEP level of 5 cm H₂O after the manoeuvre is also followed by the oxygenation improvement [24,25]. In addition, in our study the effect of RM was also stimulated by rapid restoration of spontaneous breathing activity of the patients. However, the effects of RM are not always reproducible in different settings and depend on a number of perioperative factors, including pneumoperitoneum in laparoscopic surgery, increased intra-abdominal pressure after laparotomy, or heart failure in cardiac patients [1,10,22,23].

According to recent investigations, the effect of RM persists from 10 minutes to several hours [15]. In our study, we assessed the initial effect of RM on dynamic compliance and oxygenation within the first ten minutes, because the patients restored their spontaneous respiratory activity within 30–60 minutes followed by tracheal extubation within 1–2 hours after RM. The improved arterial oxygenation observed after RM and during the post-extubation period was accompanied by an increase in EtCO₂ after tracheal extubation. This may be explained by a reduction of venous admixture and physiological dead space due to restoration of spontaneous breathing, which is consistent with the findings of previous investigators [27–29]. It is well known that a spontaneous breathing pattern favours alveolar recruitment and is associated with increased oxygenation and improved ventilation in dependent lung areas [26,27]. During spontaneous breathing, the dorsal muscular part of the diaphragm moves more vigorously compared with the tendon plate and promotes the aeration of the dependent lung regions, thereby counteracting the formation of atelectases [27]. Therefore, it is important to preserve spontaneous breathing during postoperative ventilation both after cardiac and non-cardiac interventions.

In our study, RM applying a CPAP of 40 cm H₂O was complicated by arterial hypotension. Consistently, hemodynamic collapse has been described as the most common adverse effect of RM [30]. We interpret the hemodynamic instability during RM as a result of increased

intrapleural pressure and reduced venous return and preload [29]. In parallel, increased alveolar pressure can compress the pulmonary vasculature increasing the pulmonary vascular resistance and, consequently, reduce the right ventricle afterload [31–33]. The decrease in cardiac output and the arterial hypotension after RM may compromise coronary and cerebral blood flow postoperatively in the OPCAB patients. Therefore, the benefits for the respiratory system of postoperative RM should be weighed against the risk of compromising the haemodynamics during the procedure.

In addition, it is important to decide, which type of RM is optimal for the different clinical situations. Despite an ability to open up the lungs, a CPAP of 40 cm H₂O is associated with hemodynamic instability in both ARDS [34] and postoperative patients [35]. In addition to arterial hypotension, investigators recently showed a significant decrease in cardiac index during recruitment with CPAP of 40 H₂O in ARDS patients [36]. By contrast, van den Berg et al. demonstrated that increasing PEEP up to 20 cm H₂O during the postoperative period was associated with minimal deterioration of MAP and cardiac output [31]. Thus, as this study is concerned, we decided to evaluate the mode of RM by increasing PEEP up to 15 cm H₂O, which was not accompanied by significant changes in haemodynamics.

The RM using PEEP-15 for five minutes represents a “gentle” but prolonged type of alveolar recruitment that might impair the pattern of spontaneous breathing to a less extent compared with the CPAP-40 and Peak-40 variants. This effect may explain the decreased time until the restoration of spontaneous ventilation and discontinuation of respiratory support in the PEEP-15 group. Our results are consistent with the findings of investigators who observed that an increase in PEEP up to 30 cm H₂O to recruit the lungs was associated with shortened duration of postoperative respiratory support in cardiosurgical patients [25]. However, a PEEP of 30 cm H₂O can be associated with derangement of haemodynamics, whereas RM employing a PEEP of 15 cm H₂O, as used in our study, provides more stable cardiovascular parameters.

Limitations of the Study

We were unable to demonstrate an effect of RM on the length of the ICU or the hospital stay, but our investigation was not powered for that purpose. Moreover, the duration of the ICU or the hospital stay depends on a variety of confounding factors that are difficult to take into account. Another limitation of our study was the impossibility to make quantitative assessments of atelectatic areas. However, other authors evaluating the effects of RM after CABG using a semi-quantitative assessment, have shown a decreased atelectasis score [15].

Conclusions

After off-pump coronary surgery, alveolar recruitment manoeuvres improved arterial oxygenation and dynamic compliance. The method using a 40 seconds period of CPAP of 40 cm H₂O was accompanied by arterial hypotension whereas a PEEP of 15 cm H₂O for five minutes reduced the duration of respiratory support compared with the control group.

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