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Editorial Board Member of *World Journal of Gastrointestinal Surgery*, Georgios Tsoulfas, AGAF, FACS, FICS, MD, PhD, Professor, Transplant Surgery, Aristotle University of Thessaloniki School of Medicine, Thessaloniki 54124, Greece. tsoulfasg@gmail.com

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WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc.*

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Observational Study

Incidence, characteristics and risk factors for alveolar recruitment maneuver-related hypotension in patients undergoing laparoscopic colorectal cancer resection

Nan-Rong Zhang, Zhi-Nan Zheng, Kai Wang, Hong Li

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Nan-Rong Zhang, Zhi-Nan Zheng, Kai Wang, Hong Li, Department of Anesthesia, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou 510655, Guangdong Province, China

Kai Wang, Hong Li, Guangdong Provincial Key Laboratory of Colorectal and Pelvic Floor Diseases, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou 510655, Guangdong Province, China

Corresponding author: Hong Li, MD, Doctor, Researcher, Guangdong Provincial Key Laboratory of Colorectal and Pelvic Floor Diseases, The Sixth Affiliated Hospital, Sun Yat-sen University, No. 26 Yuancun Erheng Road, Guangzhou 510655, Guangdong Province, China. lihong36@mail.sysu.edu.cn

Abstract

BACKGROUND

Alveolar recruitment maneuvers (ARMs) may lead to transient hypotension, but the clinical characteristics of this induced hypotension are poorly understood. We investigated the characteristics of ARM-related hypotension in patients who underwent laparoscopic colorectal cancer resection.

AIM

To investigate the characteristics of ARM-related hypotension in patients who underwent laparoscopic colorectal cancer resection.

METHODS

This was a secondary analysis of the PROtective Ventilation using Open Lung approach Or Not trial and included 140 subjects. An ARM was repeated every 30 min during intraoperative mechanical ventilation. The primary endpoint was ARM-related hypotension, defined as a mean arterial pressure (MAP) < 60 mmHg during an ARM or within 5 min after an ARM. The risk factors for hypotension were identified. The peri-ARM changes in blood pressure were analyzed for the first three ARMs (ARM_{1,2,3}) and the last ARM (ARM_{last}).

RESULTS

Thirty-four subjects (24.3%) developed ARM-related hypotension. Of all 1027 ARMs, 37 (3.61%) induced hypotension. More ARMs under nonpneumoperitoneum (33/349, 9.46%) than under pneumoperitoneum conditions (4/678, 0.59%)

induced hypotension ($P < 0.01$). The incidence of hypotension was higher at ARM₁ points than at non-ARM₁ points (18/135, 13.3% *vs* 19/892, 2.1%; $P < 0.01$). The median percentage decrease in the MAP at ARM₁ was 14%. Age ≥ 74 years, blood loss ≥ 150 mL and peak inspiratory pressure under pneumoperitoneum < 24 cm H₂O were risk factors for ARM-related hypotension.

CONCLUSION

When the ARM was repeated intraoperatively, a quarter of subjects developed ARM-related hypotension, but only 3.61% of ARMs induced hypotension. ARM-related hypotension most occurred in a hemodynamically unstable state or a hypovolemic state, and in elderly subjects. Fortunately, ARMs that were performed under pneumoperitoneum conditions had less impact on blood pressure.

Key Words: Alveolar recruitment maneuvers; Hypotension; Laparoscopic colorectal cancer resection

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Core Tip: Alveolar recruitment maneuvers (ARMs) may lead to transient hypotension, but clinical characteristics of this hypotension are poorly understood. In the present study, we investigated characteristics of ARM-related hypotension in 140 patients undergoing laparoscopic colorectal cancer resection. The primary endpoint was an ARM-related hypotension. Risk factors for the hypotension were identified. When ARM was repeated intraoperatively, a quarter of subjects developed ARM-related hypotension, but only 3.61% of all the ARMs induced hypotension. ARM-related hypotension events most occurred at a hemodynamic instability or hypovolemic state, and in elderly subjects. Encouragingly, ARMs under pneumoperitoneum conditions had less impact on blood pressure.

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INTRODUCTION

The alveolar recruitment maneuver (ARM) strategy (an ARM or repeated ARMs) has been used to open up collapsed lungs[1] and is an important component of lung-protective ventilation[2-4]. An ARM was also used to predict the fluid response of anesthetized patients[5-8]. However, the strategy is still not broadly used in the operating room[9-11]. This may be partly due to concerns regarding complications[12], especially transient hypotension[13-17] (which we termed ARM-related hypotension). However, in studies[2,13,18-20] on intraoperative lung-protective ventilation that included repeated ARMs, hemodynamic data were usually regarded as safety indicators, with few detailed descriptions of their characteristics. We believe that a comprehensive understanding of the characteristics and risk factors for ARM-related hypotension will promote the proper application of intraoperative lung-protective ventilation strategies.

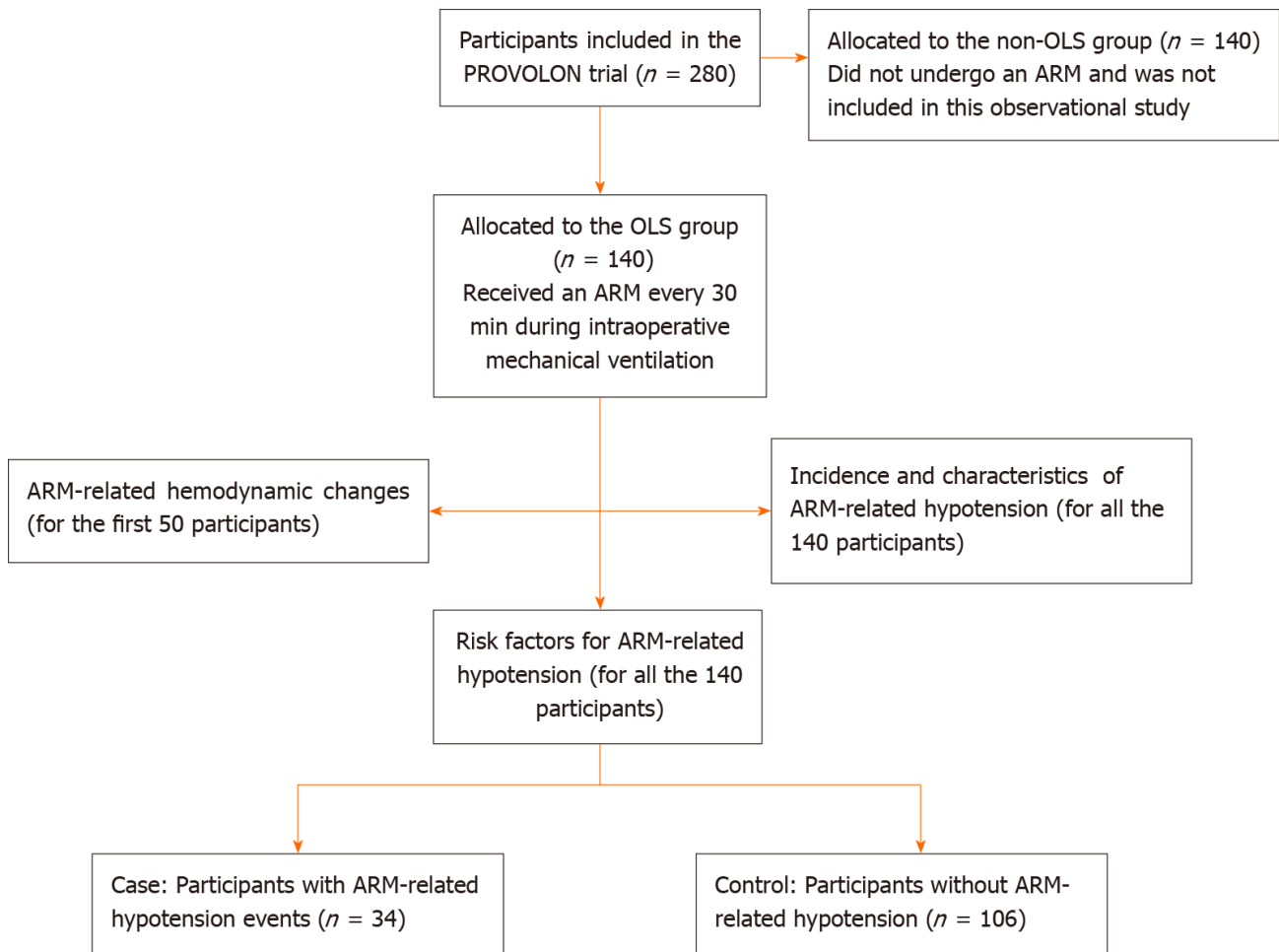
In the PROtective Ventilation using Open Lung approach Or Not (PROVOLON) trial, we investigated the impact of medium positive end-expiratory pressure (PEEP) combined with repeated ARMs on the incidence of major postoperative complications[21]. In this trial, we also intensively recorded the ARM-related hemodynamic changes, which were inconvenient to display in detail in the previously published main results[21]. In this secondary analysis, we investigated the incidence, characteristics and risk factors for ARM-related hypotension. The primary endpoint was ARM-related hypotension, defined as a mean arterial pressure (MAP) < 60 mmHg during an ARM or within 5 min after an ARM.

MATERIALS AND METHODS

Study design and subjects

This was a secondary analysis of the PROVOLON trial. The PROVOLON trial was a prospective, randomized controlled trial conducted in the Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, from January 2017 to October 2018. The trial was approved by the Institutional Ethical Committee of the Sixth Affiliated Hospital, Sun Yat-sen University, on 9 January 2017 (2017ZSLYEC-002) and registered at clinicaltrials.gov (NCT03160144). The trial included two groups: the open-lung strategy (OLS) group and the non-OLS group. In this study, we focused on ARM-related hypotension in the OLS group, which included 140 subjects (Figure 1). Written informed consent was obtained from all subjects before enrollment.

The inclusion and exclusion criteria of the trial have been previously described[21]. Patients were eligible for inclusion if they were aged 40 years or older, had a risk class for postoperative pulmonary complications[2,22] ≥ 2 , were scheduled for laparoscopic colorectal cancer resection with an expected duration of pneumoperitoneum ≥ 1.5 h, and had a body



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Figure 1 Flowchart of the study. Alveolar recruitment maneuver (ARM)-related hypotension means arterial pressure < 60 mmHg during an ARM or within 5 min after an ARM. ARM: Alveolar recruitment maneuver; OLS: Open lung strategy; PEEP: Positive end expiratory pressure; PROVOLON: PROtective Ventilation using Open Lung strategy or Not trial.

mass index (BMI) < 30 kg/m². Patients were excluded if they had an American Society of Anesthesiologists (ASA) physical status ≥ IV, a had pulmonary infection or respiratory failure within the previous one month, or had cardiac failure, severe chronic obstructive pulmonary disease or pulmonary bullae. Subjects were also excluded from the study in the event of conversion to laparotomy within 1 h after the start of the planned surgery.

Respiratory management

All subjects received general anesthesia and low-tidal-volume ventilation [6-8 mL/kg predicted body weight (PBW)][23]. They inhaled 100% oxygen during anesthesia induction. During intraoperative ventilation, the peak inspiratory pressure (PIP) limit was set at 45 cm H₂O, the PEEP was set at 6-8 cm H₂O, the respiratory ratio was 1:2, the inhalation pause time was 30%, and the fraction of inhaled oxygen was 40%-50%. The respiratory rate was adjusted to maintain the end expiratory partial pressure of carbon dioxide within 30-50 mmHg.

An ARM was performed directly after intubation and repeated every 30 min during mechanical ventilation. A stepwise increment of tidal volume was used for each ARM (abbreviated as SITV-ARM) as previously described[21]. We set the PEEP at 12 cm H₂O and the respiratory rate at 6 breaths per minute and then increased the tidal volume in increments of 4 mL/kg of PBW until the plateau airway pressure (P_{plat}) reached 30-35 cm H₂O and held the ventilation settings for 3 breaths. Then, we set the respiratory rate, PEEP, and tidal volume back to the pre-ARM values. An ARM should not be performed when the MAP is ≤ 65 mmHg or the heart rate is ≤ 45 beats per minute, and an ARM should be terminated when the MAP is ≤ 55 mmHg or the heart rate is ≤ 45 beats per minute. In any terminated ARM, when the P_{plat} is ≥ 30-35 cm H₂O and no fewer than two breaths have been taken, the ARM is considered to have been successful.

Anesthesia management

Before anesthesia induction (Datex Ohmeda S/5, GE Healthcare Finland Oy, Helsinki, Finland), 500-700 mL of Ringer's lactate solution was preloaded, invasive arterial blood pressure was conducted *via* the radial artery, an epidural catheter was placed at the T₁₂-L₁ or L₁-L₂ level, and 5 mL of 1% lidocaine was administered to test the intrathecal injection. A central venous access was established, and an intraoperative fluid infusion was administered at 10-12 mL/kg/h.

Anesthesia was induced with midazolam 0.02-0.04 mg/kg, propofol 1.5-2.0 mg/kg, fentanyl 3-4 µg/kg and cisatracurium 0.2 mg/kg, which were administered *via* titration. Anesthesia was maintained with sevoflurane (1%-3%) and a continuous infusion of remifentanyl (0.05-0.15 µg/kg/min) and propofol (1.0-6.0 mg/kg/h). Additional boluses of cisatracurium were administered as necessary. Before the skin incision, morphine (2 mg diluted to 5 mL with 0.9% saline) was administered into the epidural space for preemptive analgesia. Local anesthetics were not given in the epidural space during the operation. Approximately 0.5 h before the end of the surgery, 7-10 mL of ropivacaine (0.1%) was administered into the epidural space as a loading dose for postoperative analgesia. Vasopressors must be given if the MAP is ≤ 55 mmHg intraoperatively.

Measurements, calculations and endpoints

In the first 50 subjects, we recorded the duration of each ARM and the maximum tidal volume of each ARM. Before each ARM, we recorded the subjects' systolic blood pressure (SBP), MAP, diastolic blood pressure (DBP), and heart rate (HR). The extreme values of blood pressure (SBP, MAP, and DBP) and HR during an ARM (intra-ARM) or within 5 min after an ARM (post-ARM) were also recorded (the highest values were recorded when they increased, or the lowest values when they decreased). We calculated the percentage decreases in SBP, MAP, DBP, and HR for the first three ARMs (ARM_{1,2,3}) and the last ARM (ARM_{last}). The calculation of the percentage decrease in MAP was as follows: Percentage decrease in MAP (%) = $(\text{MAP}_{\text{pre-ARM}} - \text{extreme value of MAP}_{\text{intra-ARM or post-ARM}}) \times 100 / \text{MAP}_{\text{pre-ARM}}$.

The primary endpoint was ARM-related hypotension, defined as a MAP < 60 mmHg during an ARM or 5 min after an ARM. For all 140 subjects, ARM-related hypotension and its possible reasons, treatment and relationship with pneumoperitoneum were recorded. We calculated different proportions of ARM-related hypotension (overall, under pneumoperitoneum conditions, under nonpneumoperitoneum conditions, at ARM₁, at non-ARM₁, and at ARM_{last}). Among the subjects who were excluded from the trial, ARMs were not performed after exclusion according to the original study protocol, but their preexclusion hemodynamic data were included in the final analysis.

Risk factors for ARM-related hypotension

According to the presence or absence of ARM-related hypotension, the subjects were divided into two groups: The case (subjects with ARM-related hypotension events) and control (subjects without ARM-related hypotension) groups.

We assessed several perioperative variables as possible risk factors, including baseline characteristics [age, sex, BMI, hemoglobin, white blood cells, C-reactive protein, albumin, saturation of peripheral oxygen (S_pO₂), MAP, ASA physical status, cardiocerebrovascular events, chemotherapy, hypertension, body weight loss ≥ 10%, and diabetes mellitus] and intraoperative variables (duration of mechanical ventilation, nonpneumoperitoneum ventilation time, number of ARMs, prefilling fluids before anesthesia, total fluid administration, blood loss, Trendelenburg position, tidal volume, PIP, driving pressure, respiratory rate, dynamic compliance, urine output, hemoglobin and lactic acid).

Statistical analysis

No power analysis was performed because the incidence of the primary endpoint for the study population was not reported in the literature.

Continuous variables are described as the mean ± SD or as median (25th, 75th percentile) and were compared by an independent *t* test or Mann-Whitney *U* test as appropriate. Categorical variables are reported as counts (proportion) and were compared using Fisher's exact or Pearson χ^2 tests, where appropriate. For the possible risk factors for ARM-related hypotension, a univariate analysis was performed first, and then variables with a *P* < 0.1 or with clinical significance were introduced into the multivariate logistic regression model. Three different models were used to identify risk factors. The identified risk factors are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Statistical analyses were conducted using SPSS statistics for Windows, version 17.0 (SPSS Inc., Chicago, IL, United states). A two-sided *P* value < 0.05 was considered statistically significant.

RESULTS

The mean (SD) age of the subjects was 69.7 (5.8) years (range 55-83). Six subjects met the intraoperative exclusion criteria. The median number of ARMs was 7. A total of 1027 ARMs were actually performed, and 22 of them were not successful (17 for a MAP ≤ 55 mmHg and 5 for anesthesia machine leakage). Eighteen ARMs were not performed (6 for a HR ≤ 45 beats/min, 8 for a MAP ≤ 65 mmHg and 4 for forgetting).

Table 1 shows the occurrence of ARM-related hypotension. Thirty-four subjects (24.3%) developed ARM-related hypotension, and three of them had two hypotensive episodes. Of all 1027 ARMs, 37 (3.61%) induced hypotension. More ARMs under nonpneumoperitoneum (33/349, 9.46%) than under pneumoperitoneum conditions (4/678, 0.59%) induced hypotension (*P* < 0.01). The incidence of hypotension was higher at ARM₁ than at the other ARM points (18/135, 13.3% *vs* 19/892, 2.1%, *P* < 0.01).

As shown in Figure 2, the median percentage decreases in SBP, MAP and DBP at ARM₁ were 19%, 14%, and 8%, respectively, and the median percentage decreases in SBP and MAP at ARM_{last} were 5%. The percentage decreases in SBP, MAP, and DBP at the other ARM points were less than 5%, and the percentage decreases in HR were less than 5% at all points. The duration of ARMs and the maximum tidal volume of ARMs under nonpneumoperitoneum conditions (ARM₁ and ARM_{last}) were higher than those under pneumoperitoneum conditions (ARM₂ and ARM₃).

Table 1 The occurrence of alveolar recruitment maneuver-related hypotension

ARM-related hypotension ¹	MAP < 60 mmHg ²	MAP ≤ 55 mmHg
Patients having hypotension, <i>n</i> (%)	34 (24.3)	17 (12.1)
Patients having hypotension ≥ two times, <i>n</i>	3	2
ARMs with hypotension/total ARMs, No. (%)	37/1027 (3.61)	19/1027 (1.85)
ARM ₁ or ARM _{last} with hypotension, No.	27	12
Recovery without vasopressor, No.	27	NA ³
ARMs under nonpneumoperitoneum conditions	33/349 (9.46) ⁴	16/349 (4.58)
With hypotension/total ARMs, No. (%)		
ARM ₁ with hypotension, No. (%)	18/135 (13.3) ^{5,6}	9/135 (6.7)
ARM _{last} with hypotension, No. (%)	9/134 (6.7) ⁷	3/134 (2.2)

¹Hypotension occurred during an alveolar recruitment maneuver (ARM) or within 5 min after an ARM.

²Primary endpoint: A mean arterial pressure (MAP) < 60 mmHg during an ARM or within 5 min after an ARM.

³NA: No analysis because vasopressors must be given according to the study protocol when MAP ≤ 55 mmHg.

⁴*P* < 0.01 compared with ARMs under pneumoperitoneum conditions (4 of 678, 0.59%).

⁵*P* < 0.01 compared with non-ARM₁ points (19 of 892, 2.13%).

⁶Five participants did not receive ARM₁ because of a MAP ≤ 65 mmHg.

⁷Six participants did not receive ARM_{last} because they met the intraoperative exclusion criteria.

Data are given as counts or counts (proportion). MAP: Mean arterial pressure; ARM: Alveolar recruitment maneuver; ARM₁: The first ARM; ARM_{last}: The last ARM; bpm: Beats per minute; NA: Not available.

Table 2 Univariate analysis of the associations between baseline characteristics and alveolar recruitment maneuver-related hypotension

	ARM-related hypotension		<i>P</i> value
	Yes, <i>n</i> = 34	No, <i>n</i> = 106	
Male	24	78	0.83
Age (yr)	71.7 ± 6.4	69.1 ± 5.5	< 0.01
Age ≥ 74 yr	15	22	< 0.01
Body weight (kg)	60.8 ± 8.8	62.5 ± 9.6	0.36
Body mass index (kg/m ²)	22.54 ± 2.77	23.18 ± 2.63	0.22
Hemoglobin (g/L)	116.1 ± 23.4	121.5 ± 21.5	0.21
White blood cells (× 10 ⁹ /L)	6.84 ± 2.25	6.34 ± 1.94	0.20
C-reaction protein (mg/L)	3.50 (1.39, 7.98)	2.84 (1.02, 6.78)	0.31
Albumin (g/L)	38.4 ± 3.6	39.4 ± 4.0	0.16
S _p O ₂ (%)	96 (96, 97)	97 (96, 97)	0.07
S _p O ₂ (< 96/≥ 96)	8/26	14/92	0.18
Mean arterial pressure (mmHg)	89 ± 8	91 ± 7	0.10
ASA physical status (II/III)	24/10	86/20	0.23
Cardiocerebrovascular events	4	11	0.76
Chemotherapy	5	14	0.78
Hypertension	14	42	> 0.99
Body weight loss ≥ 10%	10	24	0.49
Diabetes mellitus	3	17	0.40

Continuous data are reported as the mean ± SD or median (25th and 75th percentile), and categorical data are given as counts. Alveolar recruitment

maneuver (ARM)-related hypotension: Mean arterial pressure < 60 mmHg during an ARM or within 5 min after an ARM. ARM: Alveolar recruitment maneuver; S_pO_2 : Saturation of peripheral oxygen; ASA: American Society of Anesthesiologists.

Tables 2 and 3 show the results of the univariate analysis of the associations between baseline characteristics or intraoperative data and ARM-related hypotension. Six variables (age ≥ 74 years, preoperative $S_pO_2 < 96\%$, preoperative MAP, blood loss ≥ 150 mL, hemoglobin concentration and PIP under pneumoperitoneum < 24 cm H_2O) with a P value < 0.1 in the univariate analysis and four variables considered clinically relevant (ASA physical status III, number of ARMs, amount of prefilling fluids before anesthesia and nonpneumoperitoneum ventilation > 90 min) were included in the multivariate logistic regression model as independent variables for identifying risk factors for ARM-related hypotension. On multivariate analysis, three independent risk factors (age ≥ 74 years, blood loss ≥ 150 mL and PIP under pneumoperitoneum < 24 cm H_2O) were identified (Table 4).

DISCUSSION

When an ARM was repeated every 30 min during mechanical ventilation for patients undergoing laparoscopic colorectal cancer resection, we found that 24.3% of the subjects developed ARM-related hypotension, but only 3.61% of ARMs induced hypotension, that an ARM after anesthesia induction was prone to inducing hypotension, and that ARMs under pneumoperitoneum conditions had less impact on blood pressure. We further found that age ≥ 74 years, blood loss ≥ 150 mL and PIP under pneumoperitoneum < 24 cm H_2O were risk factors for ARM-related hypotension. To our knowledge, this is the first study to specifically investigate ARM-related hypotension in surgical patients.

We first clearly defined ARM-related hypotension and found that 24.3% of the subjects developed such hypotension. Similar to other studies[13,18-20], we previously reported[21] intraoperative hypotension and vasopressor requirements as adverse events of the study but did not analyze the relationship between ARM and hypotension. The incidence of intraoperative hypotension was 31.6% in the PROBESE trial[19], in which the frequency of ARMs (once an hour) was close to that in the present study; however, it may include the impact of a high PEEP (12 cm H_2O)[13]. The IMPROVE trial [2], in which lung-protective ventilation also included ARMs repeated every 30 min, did not report a high incidence of hypotension. In that trial, the definition of hypotension (SBP < 70 mmHg) reduced the probability of its detection. However, the authors mentioned the effects of ARM-induced transient hypotension. Altogether, ARM-induced hypotension cannot be ignored.

Only 3.61% of ARMs induced hypotension, suggesting that the incidence of hypotension due to repeated ARMs was low overall. One advantage of the current study that may reduce the occurrence of ARM-related hypotension is the use of SITV-ARM, which might have a smaller hemodynamic impact[24]. Although SITV-ARM was performed in the PROVHILO trial[13], it was accompanied by a significant increase in hypotension. Possible explanations may be the sensitive definition of hypotension (SBP < 90 mmHg) and the high PEEP (12 cm H_2O) used in that trial[13].

Unlike findings in ARDS patients[25], our results (only three subjects developed two or more hypotensive episodes, and the number of ARMs was not a risk factor for ARM-related hypotension) implied that one person was less likely to experience multiple ARM-related hypotensive episodes when repeated ARMs were performed. The difference may have been related to a negative fluid balance, which may last for a longer time in ARDS patients but only occurs during special periods in surgical patients.

The incidence of hypotension at ARM₁ was 13.3%, and the median percentage decreases in SBP and MAP at ARM₁ were 19% and 14%, respectively, which were evidently higher than those at the other points, suggesting that an ARM after anesthesia induction (ARM₁) is prone to inducing hypotension. ARM₁-related hypotension may be associated with a hemodynamic instability and/or hypovolemia state caused by circulatory depression and vasodilator effects of anesthetics and/or with fasting and bowel cleansing before abdominal surgery. ARM_{last}-related hypotension (6.7%) may also be associated with a hypovolemic state caused by local anesthetics in the epidural space at that moment. In addition, we found that blood loss ≥ 150 mL was a risk factor for ARM-related hypotension. Altogether, these data suggest that ARM-related hypotension is more likely to develop in a hemodynamically unstable or hypovolemic state.

We did not find that the number of prefilling fluids was a protective factor. The prefilling fluids might have reduced the incidence of ARM₁-related hypotension in the current study, but such a volume was not infused within a short time. Consequently, the subjects may have remained in a relatively hypovolemic state. Atelectasis can immediately develop after anesthesia induction[26,27], and an ARM should be performed soon after that[28]. Therefore, how to safely perform an ARM after anesthesia induction is still a challenge. Considering the ARM₁-related decrease in MAP, that ARM-related hypotension was transient and that an intraoperative MAP < 55-60 mmHg may be related to postoperative outcomes[29, 30], it may be safe to perform an ARM at a MAP of 70-75 mmHg or higher.

More ARMs under nonpneumoperitoneum conditions (9.46%) than under pneumoperitoneum conditions (0.59%) induced hypotension, suggesting that ARMs under pneumoperitoneum conditions have less impact on blood pressure. This is a surprising finding since atelectasis is prone to developing under pneumoperitoneum conditions[31], which makes it more appropriate to perform ARMs under this condition. A possible explanation may be that the SITV-ARM requires a relatively small tidal volume and a shorter time under pneumoperitoneum conditions (Figure 2), which may have a slight impact on intrathoracic pressure and venous return; additionally, the abdominal venous system is compressed by pneumoperitoneum, and its role in blood storage is reduced; therefore, the circulating blood volume is sufficient, and the hemodynamic fluctuation is slight under this condition. Conversely, SITV-ARM under nonpneu-

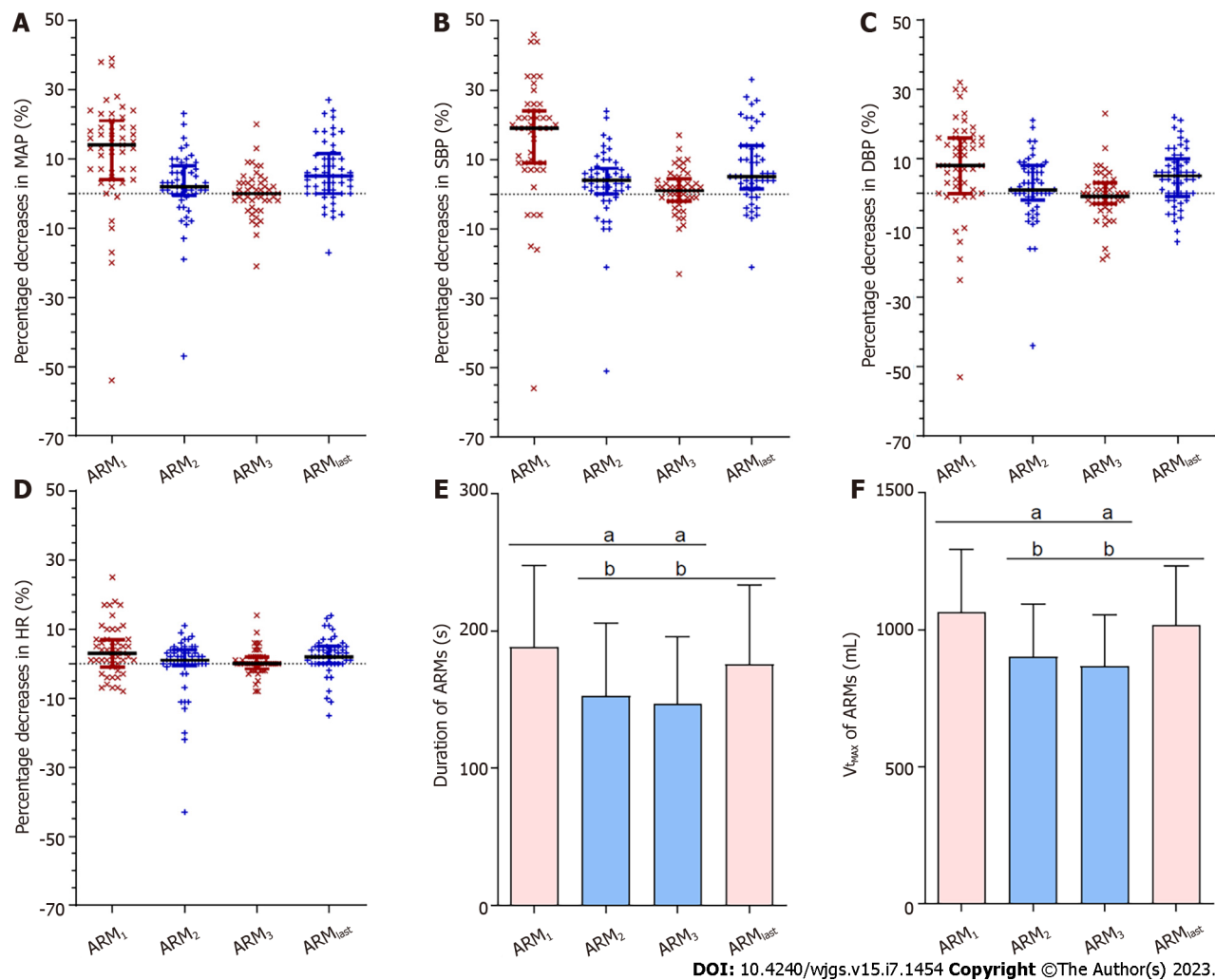


Figure 2 Alveolar recruitment maneuver-related hemodynamic changes and characteristics of alveolar recruitment maneuvers. A-D: Individual values (dots) and medians with interquartile ranges (line and error line) for the percentage decreases in mean arterial pressure (MAP) (A), systolic blood pressure (B), diastolic blood pressure (C), and heart rate (D); E and F: Mean (bar) and SD (error bar) of the duration of ARMs and the maximum tidal volume of ARMs. The blue bar indicates the pneumoperitoneum conditions, and the pink bar indicates the nonpneumoperitoneum conditions. ^a $P < 0.05$ vs ARM₁; ^b $P < 0.05$ vs ARM_{last}. Percentage decrease in MAP (%) = $(\text{MAP}_{\text{pre-ARM}} - \text{extreme value of MAP}_{\text{intra-ARM or post-ARM}}) \times 100 / \text{MAP}_{\text{pre-ARM}}$. An extreme value was defined as the highest value when a variable increased or as the lowest value when the variable decreased. ARM: Alveolar recruitment maneuver; post-ARM: Within 5 min after an ARM; ARM₁: The first RM; ARM_{last}: The last ARM; MAP: Mean arterial pressure; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; V_{Tmax}: Maximum tidal volume.

moperitoneum conditions requires a larger tidal volume and a longer time, which has a greater impact on intrathoracic pressure and venous return, thus reducing cardiac output and making the subjects prone to developing hypotension. SITV-ARM under pneumoperitoneum in a PIP < 24 cm H₂O state also requires a large tidal volume; therefore, it is a risk factor for ARM-related hypotension. However, the hypotensive events that occurred under nonpneumoperitoneum conditions were also related to a hypovolemic state, since 73% of them occurred at ARM₁ and ARM_{last}.

Older age is a risk factor for pulmonary complications[22], and atelectasis is prone to develop in elderly patients. Meanwhile, elderly patients often have cardiocerebrovascular diseases and easily suffer damage from hemodynamic fluctuations. We found that age 74 years or older was a risk factor for ARM-related hypotension. Therefore, the application of repeated ARMs in older patients may be more beneficial but needs to be performed with more caution.

Seventy-three percent (27/37) of ARM-related hypotension episodes recovered to the pre-ARM level soon without using vasopressors in this study, suggesting that most ARM-related hypotension episodes were transient and self-limited, *i.e.*, they could disappear with the return of normal intrathoracic pressure after the completion of an ARM. There are still some ARM-related hypotension events requiring vasopressors, suggesting the importance of dynamic blood pressure monitoring during the peri-ARM periods.

This study had several limitations. First, the PROVOLON trial was not specifically designed to investigate the characteristics of ARM-related hypotension. However, the current study was exhaustive with respect to prospective data collection. Second, ARM-related hypotension events were recorded in real time but were not predefined in detail. However, this would reduce subjective bias in the determination of ARM-related hypotension. Third, it may be too arbitrary to define ARM-related hypotension as a MAP < 60 mmHg. However, this represents the defined level of complications from ARMs in a previous study[25], and it is also a threshold of intraoperative hypotension that may

Table 3 Univariate analysis of the associations between intraoperative variables and alveolar recruitment maneuver-related hypotension

	ARM-related hypotension		P value
	Yes, <i>n</i> = 34	No, <i>n</i> = 106	
Non-PPT ventilation \geq 90 min	9	17	0.31
Duration of ventilation (min)	233 \pm 67	229 \pm 84	0.76
Amount of infusion (mL)	3414 \pm 799	3181 \pm 611	0.13
Recruitment maneuver (times)	7 (6, 8)	7 (5, 8)	0.88
Prefilling fluids before anesthesia (mL)	678 \pm 140	696 \pm 144	0.52
Blood loss \geq 150 mL	12	15	0.01
Trendelenburg position	25	79	0.82
V_t at T_1 < 7 mL/kg of PBW	8	20	0.62
V_t at T_2 < 7 mL/kg of PBW	21	51	0.24
PIP at T_1 (cm H ₂ O)	17 \pm 2	17 \pm 2	> 0.99
PIP at T_2 (cm H ₂ O)	24 \pm 3	25 \pm 2	0.076
PIP at T_2 < 24 cm H ₂ O	15	23	0.02
Respiratory rate at T_1 (bpm)	12 (12, 12)	12 (12, 12)	0.97
Respiratory rate at T_2 (bpm)	17 (16, 18)	16 (15, 18)	0.15
Driving pressure at T_1 (cm H ₂ O)	6 \pm 2	6 \pm 2	0.94
Driving pressure at T_2 (cm H ₂ O)	13 \pm 2	13 \pm 2	0.14
C_{dyn} at T_1 (mL/cm H ₂ O)	48 \pm 9	51 \pm 14	0.38
C_{dyn} at T_2 (mL/cm H ₂ O)	24 \pm 5	24 \pm 5	0.95
Urine output < 1.2 mL/kg/h	7	23	0.82
Hemoglobin at T_2 (g/L)	97 \pm 20	103 \pm 18	0.10
lactic acid at T_2 (mmol/L)	0.66 \pm 0.18	0.69 \pm 0.23	0.58

Continuous data are reported as the mean \pm SD or median (25th, 75th percentile), and categorical data are given as counts. Alveolar recruitment maneuver (ARM)-related hypotension: Mean arterial pressure < 60 mmHg during an ARM or within 5 min after an ARM. PPT: Pneumoperitoneum; ARM: Alveolar recruitment maneuver; PBW: Predicted body weight; T_1 : Immediately before induction of pneumoperitoneum; T_2 : 0.5 h after induction of pneumoperitoneum; PIP: Peak inspiratory pressure; bpm: Breaths per minute; C_{dyn} : Dynamic compliance; V_t : Tidal volume.

Table 4 Multivariate analysis: Adjusted risk factors for alveolar recruitment maneuver-related hypotension

Risk factors	OR (95%CI)	P value
Age < 74 yr	1 (Reference)	
Age \geq 74 yr	2.97 (1.24, 7.09)	0.014
Intraoperative blood loss < 150 mL	1 (Reference)	
Intraoperative blood loss \geq 150 mL	2.88 (1.13, 7.30)	0.012
PIP at T_2 \geq 24 cm H ₂ O	1 (Reference)	
PIP at T_2 < 24 cm H ₂ O	3.06 (1.28, 7.31)	0.026

Alveolar recruitment maneuver (ARM)-related hypotension: Mean arterial pressure < 60 mmHg during an ARM or within 5 min after an ARM. Three different models (A, B, and C) were used to identify risk factors, and all models identified the above three risk factors. Here, we list the results of model C. Model A includes ten variables (six variables with a *P* value < 0.1 in univariate analysis and four variables considered clinically relevant) using forward conditional stepwise variable elimination. Model B included six variables (three risk factors in model A, American Society of Anesthesiologists physical status, the number of ARMs and the amount of loading fluids before anesthesia) using an enter method. Model C included five variables (three risk factors in model A, number of ARMs and number of prefilling fluids before anesthesia) using backward likelihood ratio stepwise variable elimination. T_2 : 0.5 h

after induction of pneumoperitoneum; OR: Odds ratio; CI: Confidence interval; ARM: Alveolar recruitment maneuver; PIP: Peak inspiratory pressure.

increase postoperative complications[29,30]. Fourth, the conclusions need to be further validated in other populations. However, the conclusions drawn in elderly patients should be safe when applied to younger patients. Last, the number of positive cases (with ARM-related hypotension events) is not sufficient to identify risk factors for ARM-related hypotension, and we need to validate these risk factors in a larger cohort study.

CONCLUSION

When an ARM was repeated intraoperatively, a quarter of subjects developed ARM-related hypotension events, but less than 4% of ARMs induced hypotension. ARM-related hypotension occurred mostly in a hemodynamically unstable state or a hypovolemic state, and in elder subjects. Fortunately, ARMs under pneumoperitoneum conditions had less impact on blood pressure.

ARTICLE HIGHLIGHTS

Research background

The alveolar recruitment maneuver (ARM) strategy, an important component of lung-protective ventilation, is still not broadly used in the operating room, partly due to its transient hypotension effect.

Research motivation

To promote the proper application of intraoperative lung-protective ventilation.

Research objectives

To investigate the characteristics and risk factors for ARM-related hypotension in patients undergoing laparoscopic colorectal cancer resection.

Research methods

This was a secondary analysis of the PROtective Ventilation using Open Lung approach Or Not trial and included 140 subjects. An ARM was repeated every 30 min during intraoperative mechanical ventilation. The primary endpoint was ARM-related hypotension, defined as a mean arterial pressure (MAP) < 60 mmHg during an ARM or within 5 min after an ARM. The risk factors for hypotension were identified. The peri-ARM changes in blood pressure were analyzed for the first three ARMs (ARM_{1,2,3}) and the last ARM (ARM_{last}).

Research results

Thirty-four subjects (24.3%) developed ARM-related hypotension. Of all 1027 ARMs, 37 (3.61%) induced hypotension. More ARMs under nonpneumoperitoneum (33/349, 9.46%) than under pneumoperitoneum conditions (4/678, 0.59%) induced hypotension ($P < 0.01$). The incidence of hypotension was higher at ARM₁ points than at non-ARM₁ points (18/135, 13.3% vs 19/892, 2.1%; $P < 0.01$). The median percentage decrease in the MAP at ARM₁ was 14%. Age ≥ 74 years, blood loss ≥ 150 mL and peak inspiratory pressure under pneumoperitoneum < 24 cm H₂O were risk factors for ARM-related hypotension.

Research conclusions

When an ARM was repeated intraoperatively, a quarter of subjects developed ARM-related hypotension, but only 3.61% of ARMs induced hypotension. ARM-related hypotension most occurred in a hemodynamically unstable state or a hypovolemic state, and in elderly subjects. Fortunately, ARMs that were performed under pneumoperitoneum conditions had less impact on blood pressure.

Research perspectives

The proper application of the ARM strategy warrants further investigations in a more complicated clinical settings.

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FOOTNOTES

Author contributions: Li H contributed to study design; Zhang NR, Zheng ZN, and Wang K contributed to data collection; Li H, Zhang NR, and Wang K contributed to data analysis and manuscript preparation; and all authors contributed to manuscript review.

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Country/Territory of origin: China

ORCID number: Nan-Rong Zhang 0000-0002-2998-0722; Kai Wang 0000-0003-0543-859X; Hong Li 0000-0003-0296-7242.

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