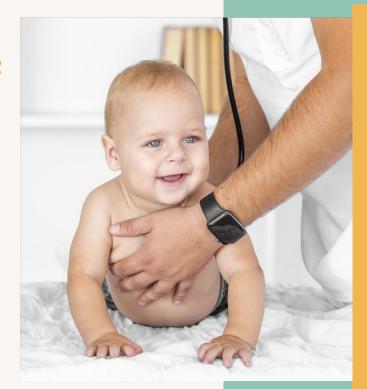
Effect of regular alveolar recruitment on intraoperative atelectasis in pediatric patients ventilated in the prone position:
A randomised controlled trial

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Background

- Desaturation frequently occurs in infants after GA in the prone position.
- Aimed to evaluate the effect of regular alveolar recruitment in preventing atelectasis in infants and children after GA in the prone position.



- Infants and young children: small thoracic outward recoil of the chest wall, the cartilaginous rib cage, an underdeveloped diaphragm and respiratory muscles.
- Smaller FRC and are susceptible to anesthesia induced atelectasis and oxygen desaturation.



Background

- Prone position is typically used in ARDS as it increases the FRC and reduces the ventilation/perfusion mismatch, consolidation, and atelectasis.
- Previous studies have reported that alveolar recruitment manoeuvre and PEEP decrease the incidence of anesthesia-induced atelectasis in children.
- Recent study used the electric impedance tomography of the ventilation and reported that a higher PEEP (9 cm H2O) is required to avoid alveolar collapse in adult patients in the prone position.
- Observed that oxygen desaturation occurs after GA in the prone position.



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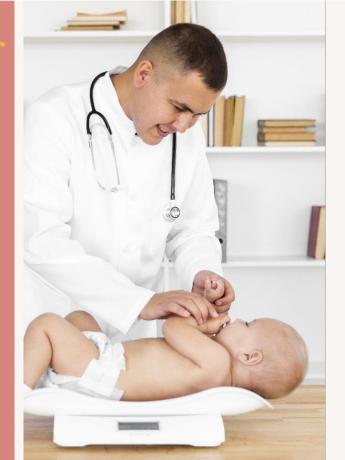
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Objective

Compare the effect of regular recruitment vs single alveolar recruitment, in preventing atelectasis in infants and young children after GA in the prone position using lung ultrasound.





Hypothesis

"Regular alveolar recruitment during GA would be more effective in preventing significant atelectasis in infants and children after surgery in the prone position with PEEP (7 cm H2O) in comparison with single alveolar recruitment whilst inducing general anesthesia."



Methods



Study design

- This prospective, parallel-arm RCT was a single-site study.
- At a tertiary teaching children's hospital in the Republic of Korea between March 2018 and July 2019.
- Approved by the Seoul National University Hospital Institutional Review Board, Seoul, Republic of Korea (Prof. Byung-Joo Park, chairperson) on March 3, 2018.



Subjects

- Registered before patient enrolment at clinicaltrials.gov.
- Eligibility of the pediatric patients and individually approached the parents or guardians of the children to acquire written informed consent to enroll the participants before surgery.

Inclusion criteria

• Infants and children (age <3y) scheduled to undergo elective noncardiac surgery in the prone position under GA(>2 h) requiring tracheal intubation and mechanical ventilation.





Exclusion criteria

- Previous thoracic surgery
- Pulmonary disease
- Airway anomaly
- Airway infection
- Abnormal preoperative chest X-ray findings, such as atelectasis, pneumothorax, pleural effusion, or pneumonia.





Randomisation

- Allocation ratio of 1:1 via block randomisation generated by computer-generated randomisation software (https://www.randomizer.org).
- Sealed in opaque envelopes, opened by one trained study personnel after the induction of GA.

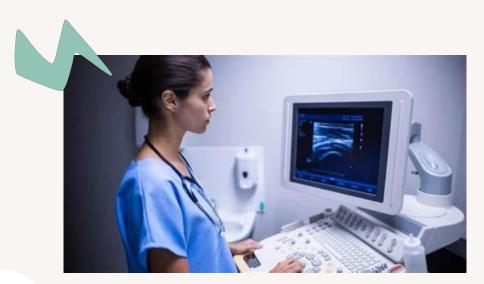






Randomisation

The operator of the lung ultrasound (Y-EJ) and the reviewer of the lung ultrasound image (S-HJ) were blinded to the patients' group allocation.







- Age, weight, and sex : recorded.
- I.V. cannula was placed before transferring to OR.
- Standard monitoring (Electrocardiography, Noninvasive blood pressure, and Pulse oximetry, EtCO2 and Body temperature).
- Induced: Atropine 0.02 mg/kg, Propofol 2 mg/kg, and Rocuronium 0.6 mg/kg.



- Preoxygenation: 100% O2 with face-mask ventilation for 3 min and underwent tracheal intubation with a cuffed reinforced endotracheal tube of an appropriate size.
- Cuff pressure: 25-30 cm H2O to ensure no significant leakage.
- Mechanical ventilation: VCV mode to TV of 6 ml/kg without PEEP and RR 20-40 /min to maintain 4.7e5.3 kPa of EtCO2, FIO2 0.4 and I:E ratio = 1:2.





- Baseline lung ultrasound was performed in the supine (baseline, supine) and prone (baseline, prone) positions.
- FIO2 to 100% 3 min before changing position, and ETT disconnected and reconnected within 10 s.
- Prone position, the chest and pelvis were supported by positioning pads, free movement of abdominal wall.
- The arms are placed near the trunk, and the hip and knee joints were semi-flexed.



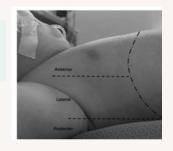
- Neuromuscular block: monitored by TOF-Watch SX acceleromyography device.
- After tracheal intubation
- Intraoperative MEP monitoring: not receive additional NMB.
- Not need intraoperative MEP monitoring: i.v. rocuronium of 0.1-0.2 mg/kg (TOF count of 0-1 twitch) (moderate-to-deep block).

Lung Ultrasound

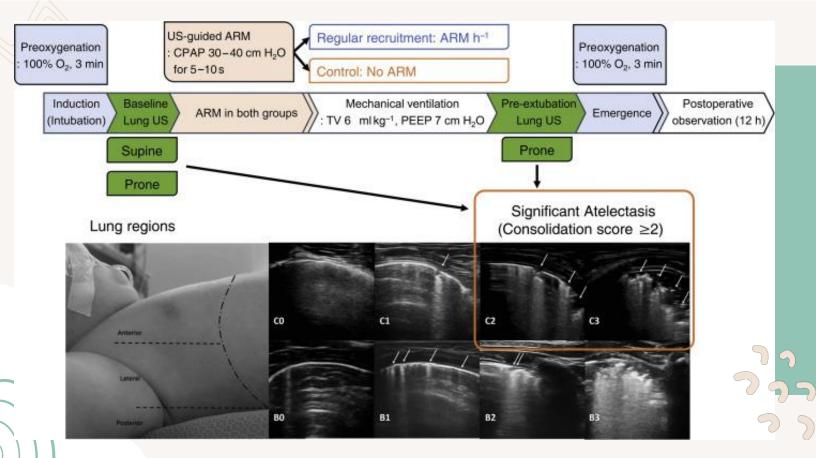
- Lung ultrasound (1.baseline, supine)(2.baseline, prone)(3.pre-extubation) in both groups.
- One anesthesiologist (Y-EJ): experience of more than 100 lung ultrasound scans in pediatric patients performed all lung ultrasound scans, and he was blinded to the group allocation.
- We used an E-CUBE i7™ unit
 (ALPINION Medical Systems, Seoul, Republic of Korea)
 with a 3e12 MHz linear L3-12T probe
 (ALPINION Medical Systems).



Lung Ultrasound



- Described by Acosta and colleagues.
- The anterior and posterior axillary lines divide: the anterior, lateral, and posterior regions of the chest.
- A linear probe placed parallel to the ribs, and two-dimensional images of the lung, all intercostal spaces were scanned.
- The degree of consolidation and B-line were categorised into four grades (0-3).
- Significant atelectasis was defined as a consolidation score≥2.



Study Intervention

- Both groups: real-time US alveolar recruitment to restore FRC after baseline lung US with 30-40 cm H2O of continuous positive airway pressure via a closed system for approximately 5-10 s until no collapsed lung areas were detected.
- After recruitment, PEEP of 7 cm H2O in both groups.
- During mechanical ventilation, the regular recruitment group received recruitment once an hour, the control group did not.



Study Protocol



 Lung US at the end of anesthesia in the prone position (pre-extubation) to evaluate the incidence of significant atelectasis.

After lung US >> FIO2 100% for 3 min and position changed to supine.

 Reversed by : Atropine 0.02 mg/kg and Neostigmine 0.05 mg/kg , and TOF ratio >0.9 was confirmed.

Study Protocol



• Extubation: gained complete consciousness and adequate spontaneous breathing.

 PACU: supplemental O2 6 L/min via a simple face mask with a reservoir and tapered to room air when the SpO2 ≥ 95%.

PACU for 1 h and followed-up until 12 h after operation.

Outcome Variables

Primary outcome

Incidence of significant atelectasis on pre-extubation lung ultrasound.

Secondary outcomes

- (1) Lung ultrasound measurements in each lung region.
- (2) The incidence of desaturation (SpO2<95%) during mechanical ventilation, emergence from GA, and the postoperative period (<12hr).

Safety of Intervention

- Assessed side-effects
- 1. Transient hypotension (<80% of baseline blood pressure) and
- 2. Oxygen desaturation (SpO2 <95%)), following regular alveolar recruitment.





Statistical Analysis

- All data as mean (standard deviation) or median (inter-quartile range) unless otherwise specified.
- Distribution : ShapiroeWilk test.
- The baseline characteristics: independent t-test and ManneWhitney Utest.
- The primary outcome: the c2 test.
- The secondary outcomes: the c2 test, independent t-test, and ManneWhitney U-test.
- A two-sided P-value < 0.05 indicated statistical significance.
- •
- Statistical analyses: R software version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria).

Sample size

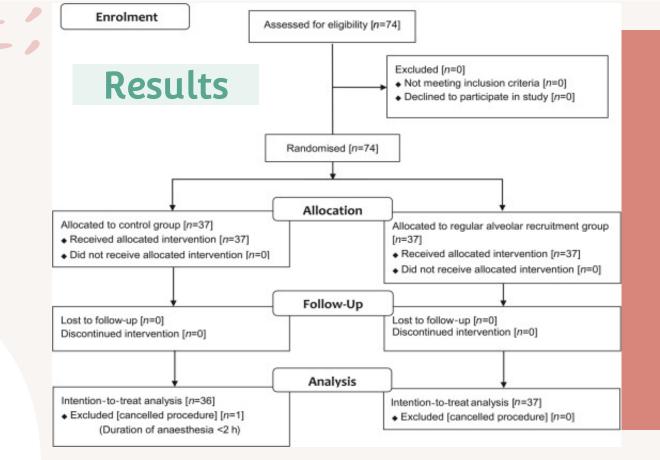
- The sample size for each group was calculated as 33.
- 74 patients in total were required.





Results





Subject characteristics

Table 1 Subject characteristics. Values are median (inter-quartile range) [range], n (%), or mean (standard deviation).

	Control (<i>n</i> =36)	Regular recruitment (<i>n</i> =37)
Age (month)	6.5 (4.0–14.8) [2–29]	4.0 (2.5–6.5) [1–21]
Male	20 (55.6)	20 (54.1)
Weight (kg)	9.0 (2.3)	7.2 (1.6)
Duration of anaesthesia (min)	232.5 (201.3–350.0) [145–520]	245 (202.5–350.0) [125–605]

Result: Primary Outcome

Incidence of significant atelectasis before extubation was **lower** in the **regular recruitment group** than the standardised care (control) group (8.1% vs 47.2%); P<0.0001.



Result: Secondary Outcome

1.Regional lung collapse

- Significant atelectasis: more frequently occurred in the dependent posterior chest regions at the supine position after induction of anesthesia.
- After changing the position to prone: significant atelectasis at the dependent anterior chest increased in both groups compared with the supine position.
- At the end of the anesthesia: the incidence of significant atelectasis at the non-dependent lateral and posterior chest decreased in the control group(P<0.001).



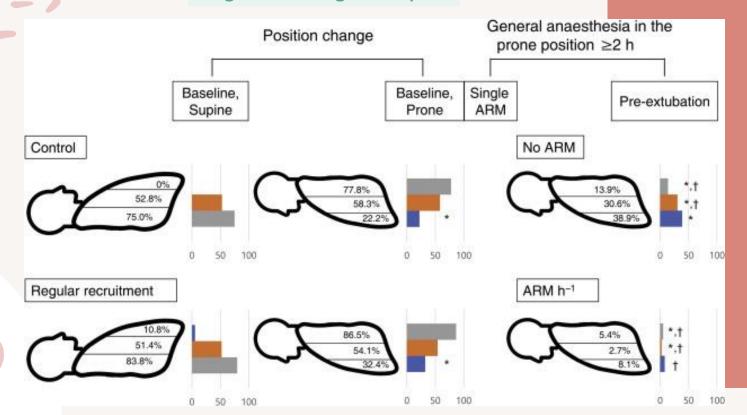
Result: Secondary Outcome

1.Regional lung collapse

- Significant atelectasis was similar between groups in the dependent anterior chest region.
- In the regular recruitment group, the incidence of significant atelectasis decreased in all chest regions at the end of the anesthesia (P<0.0001).



Regional lung collapse



Result: Secondary Outcome

2.Oxygen desaturation

- The incidence of oxygen desaturation during emergence was significantly lower in the regular recruitment group (P=0.028) than the control group.
- There was **no** difference in the intra- (P>0.99) and postoperative oxygen desaturation (13.9% vs 21.6%; P=0.577).



Result

Safety of intervention

No side-effect of alveolar recruitment: including hypotension and desaturation in both groups (Table 2).



Table 2 Lung ultrasound measurements and incidence of desaturation of control (single alveolar recruitment) group and the regular recruitment manoeuvre group. Values are median (inter-quartile range) [range], n (%), or mean (standard deviation). ARR, absolute risk reduction; CI, confidence interval. *P-value <0.05.

	Control (n=36)	Regular recruitment (n=37)	Odds	95% CI of odds or mean difference	ARR, %	95% CI of ARR	P-value
Baseline, supine after induction							
Significant atelectasis (consolidation score ≥2)	30 (83.3)	31 (83.8)	1.03	0.300-3.56	-0.45	-17.5 to 16.6	>0.99
Total consolidation score	9.5 (5.0-12.0) [1-18]	10.0 (5.5–12.0) [0–20]	N/A	N/A	N/A	N/A	0.921
Total B-line score	11.3 (5.4)	13.3 (4.9)	N/A	-4.4 to 0.4	N/A	N/A	0.098
Baseline, prone after position change							
Significant atelectasis (consolidation score ≥2)	32 (88.9)	34 (91.9)	1.42	0.294-6.83	-3.0	-16.5%-10.5%	0.711
Total consolidation score	10.3 (4.0)	11.7 (5.4)	N/A	-3.7 to 0.8	N/A	N/A	0.198
Total B-line score	11.0 (8.0—14.5) [0—23]	16.0 (12.5–20.0) [4–28]	N/A	N/A	N/A	N/A	0.058
Pre-extubation							
Significant atelectasis (consolidation score \geq 2)	17 (47.2)	3 (8.1)	0.099	0.026-0.380	39.1	20.6-57.6	<0.0001*
Total consolidation score	4.0 (1.0-9.0) [0-16]	3.0 (1.0-4.5) [0-16]	N/A	N/A	N/A	N/A	0.104
Total B-line score	8.6 (5.6)	7.6 (4.3)	N/A	-1.3 to 3.3	N/A	N/A	0.401
Desaturation (SpO ₂ <95%)							
During operation	1 (2.8)	2 (5.4)	2.0	0.173 - 23.1	-2.7	-11.7 to 6.3	>0.99
During emergence	14 (38.9)	5 (13.5)	0.246	0.077-0.78	25.4%	6.0-44.7%	0.028*
Postoperative period (within 1 h)	5 (13.9)	8 (21.6)	1.71	0.50-5.8	-7.7%	-25.2 to 9.7	0.577
Hypotension and desaturation during alveolar recruitment	0 (0)	0 (0)	N/A	N/A	N/A	N/A	N/A



- Our data, the first time, regular alveolar recruitment during GA safely prevents atelectasis in infants and children <3 yr old after GA in the prone position.
- Atelectasis is a major complication associated with GA and can persist for more than 24 h after operation.
- Anesthesia-induced atelectasis impairs gas exchange by shunting pulmonary blood flow, it decreases the oxygen reservoir resulting in intra- and postoperative hypoxemia.
- Correlation poorer clinical outcomes.
- Previous studies have reported that the incidence of significant atelectasis after induction of anesthesia is approximately 80-90%.

- Lung ultrasonography used for monitor and improve pulmonary conditions.
- Intra- and postoperative atelectasis can be evaluated by lung ultrasound, and alveolar recruitment can be performed to eliminate atelectasis using real-time ultrasound guidance.
- Lung-ultrasound guided monitoring and alveolar recruitment decreased the postoperative desaturation and duration of mechanical ventilation in congenital heart disease patients.
- Data concerning the use of lung ultrasound in pediatric patients undergoing surgery in the prone position have not been reported.

- Several mechanisms contributing to atelectasis GA: raised transmural pressure, absorption of oxygen by blood flow, and loss of pulmonary surfactant.
- Preoxygenation with 100% oxygen via positive-pressure ventilation to increase the oxygen reservoir during tracheal intubation, associated absorption atelectasis.
- Incidence of significant atelectasis does not appear to differ after induction with preoxygenation of 60% compared with 100% oxygen.
- Loss of positive airway pressure and FRC during tracheal intubation may play a critical role in the formation of significant atelectasis after induction of anesthesia and position change in the present study.

- To restore FRC, we performed ultrasound-guided alveolar recruitment in both groups at the beginning of mechanical ventilation, and used the same FIO2 (0.4) and PEEP (7 cm H2O) throughout the GA.
- Previous studies: Younger age and longer procedure time are the most important risk factors for the development of intraoperative atelectasis and oxygen desaturation in pediatric patients.
- Infants: Thoracic outward recoil cannot sufficiently maintain counterbalance to the inward recoil of the lungs and resting FRC is physiologically low.
- Vulnerable to external compression of the thorax : more susceptible to internal collapse of the small airway and oxygen desaturation occurs more rapidly.

- Re-expand the atelectatic lung via alveolar recruitment and prevent atelectasis by optimal PEEP after inducing GA.
- Elastic recoil of the lung decreases and compliance increases with an increase in age.
- In Thorax, the rib cage becomes stiffer and larger, and is capable of offering a strong counterbalance to the lung, development of respiratory muscles with an increase in age.
- Thoracic outward recoil stabilises the resting FRC and can offer some resistance to external compression.

- Prone position: increase intrathoracic and abdominal pressure by external compression, and decrease respiratory compliance and peripheral aeration.
- Recent study: Intra-tidal compliance analysis and electric impedance tomography showed that PEEP of 6 cm H2O, sufficient to avoid intra-tidal de-recruitment during the supine position, was insufficient during the prone position in adult patients.
- Increase PEEP to 9 cm H2O to reduce end-expiratory alveolar collapse during prone ventilation, and a PEEP level above the one that is typically used in the supine position to avoid the alveolar collapse in the prone position.
- Similarly, PEEP of 7 cm H2O was not enough to prevent significant atelectasis in the control group of the present study.

- In present study: Atelectasis was most frequently in the dependent regions of the lung, consistent with the previous studies.
- All lung regions was eliminated by ultrasound guided alveolar recruitment in both groups,
- Control group: higher incidence of significant atelectasis in the dependent anterior chest at the end of anesthesia.
- Regular recruitment group: did not.
- Compressive atelectasis at the dependent anterior chest is the main cause of significant atelectasis in the prone position.
- Low incidence of significant atelectasis at the dependent anterior chest increase the O2 reservoir and contribute to the prevention of O2 desaturation during emergence in the regular recruitment group.

Limitations

- 1. Only included infants and children with normal respiratory physiology, and lung disease or critically ill were not evaluated.
- 2. lung ultrasound is operator dependent and reviewer dependent. Only one anesthesiologist (Y-EJ) performed lung ultrasound.
- 3. the time interval of regular alveolar recruitment was relatively short (1 h). Not confirm the effect of alveolar recruitment lasts for more than 1 h.

Limitations

- 4. Effect of higher TV (>6 ml kg1), higher PEEP (>7 cm H2O), or PCV on prevention of atelectasis after GA in the prone position was not evaluated, and not be sure that this strategy might be the best choice to prevent atelectasis in prone position.
- There are several studies on adult patients undergoing GA in the prone position, as adults have larger FRC and their rib cage is more resistant to external compression, these results are not applicable to pediatric patients.
- 5. Causes of oxygen desaturation after extubation, such as upper airway obstruction, apnea, inadequate spontaneous ventilation, and laryngospasm, were not categorised.
- We primarily focused on the decrease in the oxygen reservoir by significant atelectasis on lung ultrasound before extubation.

Conclusions

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 Infants and children are vulnerable to atelectasis during GA in the prone position.

 Regular recruitment effectively prevented significant atelectasis at the end of surgery in the prone position and oxygen desaturation during emergence in infants and children.





