



Research article

Effects of incentive spirometry respiratory trainer device on lung recruitment in non-intubated mechanical ventilation moderate ARDS patients: A retrospective study

Pingping Zeng, Yanping Lin, Yongqiang Chen, Guoliang Tan *

Department ICU of the Second Affiliated Hospital of Fujian Medical University, China



ARTICLE INFO

Keywords:

Lung recruitment
Moderate ARDS
Respiratory trainer device
Non-intubated

ABSTRACT

Objectives: A retrospective study was performed to investigate the effects of incentive spirometry (IS) respiratory trainer device on lung recruitment in non-intubated moderate ARDS patients.

Method: Moderate ARDS patients who non-intubated from January 2019 to October 2022 were enrolled to the lung recruitment group and the control group. Compared the PaO₂/FiO₂ (P/F) ratio, lung ultrasound (LUS) score, APACHE-II score, Maximum inspiratory volume during three days (baseline, Day1, Day2, Day3) and the rate of intubation, mean hospital stay, the 28-day in-hospital mortality and the 90-days in-hospital mortality between the two groups.

Results: The lung recruitment group 118 patients (73 males, 47.6 ± 16.5y) and the control group 103 patients (62 males, 50.2 ± 14.8y) were included. The P/F ratios, APACHE-II scores, LUS scores, and the maximum inspiratory volume (ml) were significantly different between the two groups (P = 0.000, P = 0.014, P = 0.013 and P = 0.001, respectively). The P/F ratios were higher (252.6 ± 55.6 v.s. 166.96, p = 0.035, day2), (269.8 ± 75.7 v.s 183.9 ± 68.6, p = 0.027, day3), the APACHE-II scores were lower (10.0 ± 2.4 v.s 15.3, p = 0.025, day2), (8.0 ± 1.4 v.s 14.1 ± 2.7, p = 0.000, day3), the LUS scores were higher (16.2 v.s 21.6, p = 0.043, day2), (11.4 ± 5.9 v.s 20.3 ± 6.9, p = 0.004, day3), the maximum inspiratory volumes were higher (1722.3 ± 432.2 v.s 1310.7, p = 0.044, day2), (1913.5 v.s 1299.7, p = 0.018, day3) in Lung Recruitment group than that in Control group. These data at day1, day2, and day3 were significantly improvement than baseline in Lung Recruitment group. Only 36 patients (30.5%) in Lung Recruitment group needed to intubation, while 48 patients (46.6%) in Control group (p = 0.014). The mean hospital stay in lung recruitment group was lower (12.6 ± 4.6 v.s, 18.4 ± 5.3, P = 0.018). The 28-days and the 90-days in-hospital mortality were no statistical significance between the two groups (P = 0.414 and P = 0.418, respectively).

Conclusions: Using IS to perform lung recruitment in moderate ARDS patients can improve maximum inspiratory volume, PaO₂/FiO₂ ratio, LUS scores, and APACHE-II score and reduce the rate of intubation and the mean hospital stay, but the 28 days and the 90-days in-hospital mortality were not improved.

* Corresponding author. Department ICU of the Second Affiliated Hospital of Fujian Medical University, Quanzhou City, Fujian Province, 362000, China.

E-mail address: annan1125@sina.com (G. Tan).

<https://doi.org/10.1016/j.heliyon.2023.e16073>

Received 31 January 2023; Received in revised form 3 May 2023; Accepted 4 May 2023

Available online 6 May 2023

2405-8440/© 2023 Published by Elsevier Ltd.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Acute respiratory distress syndrome (ARDS) is life-threatening. Hypoxemia, dyspnea, or respiratory failure are the main manifestations of ARDS since many functional units of the lungs deteriorate or become nonaerated due to collapse, flooding, or consolidation. In ARDS patients, the proportion of patients that needed to receive invasive ventilation was 42–58% [1,2], and the overall in-hospital mortality rate of 35–65% indicated a serious problem [3–5]. Invasive mechanical ventilation may lead to many complications, including worsening hypoxemia, Hemodynamics, ventilator-associated pneumonia, biological trauma, tracheobronchial stenosis, and airway loss, and even death [6]. Therefore, the key to treatment is preventing ARDS from increasing in severity. Patients with ARDS had severe hypoxemia due to massive alveolar collapse and poor lung ventilation. Prone ventilation has improved oxygenation in some of these patients [7,8], but it is difficult for some patients who underwent thoracoabdominal surgery to tolerate a prone position. Lung recruitment maneuvers (RMs) are also frequently used to improve oxygenation in ARDS patients, which are primarily used to increase in transpulmonary pressure to reopen partially ventilated or under ventilated alveoli [9]. However, current methods of lung recruitment such as sustained inflation (SI), pressure control method (PCV), maximal recruitment strategy (MRS) and prolonged recruitment maneuver (PRM) are aimed at patients receiving invasive mechanical ventilation for moderate to severe ARDS [10]. Continuous positive airway pressure (CPAP) increases the airway pressure high level (SIGH) in a short period of time to retract collapsed alveoli and improve oxygenation for some patients with Non-invasive ventilator assisted ventilation [11]. However, these methods may have a significant impact on hemodynamics and may be associated with the risk of ventilator-associated pneumonia and pneumothorax [12,13] and some patients cannot tolerate enhancing the intrathoracic high level positive pressure in a short period of time [14].

An incentive spirometer (IS) is a respiratory trainer device that uses visual and/or auditory feedback to help patients achieve sustained maximal inspiration for improving perioperative respiratory function in patients with COPD [15,16]. It can increase the negative intrathoracic pressure to expand or prevent the collapse of alveoli to inhale [17–19], therefore, it can be considered used for lung recruitment in some ARDS patients who do not receive invasive mechanical ventilation. However, at present, there are no relevant reports on the use of respiratory trainer device for lung recruitment maneuvers. So we performed a retrospective study to investigate the would use of respiratory trainer device to perform lung recruitment maneuvers to those moderate ARDS patients who non-intubated and receive invasive mechanical get more benefit than those with no lung recruitment maneuvers.

2. Patients and methods

The Institutional Research and Ethics Committee of our Hospital approved this study for human subjects (#2022172). Written informed consent was obtained from all patients or next of kin before data were included in the study.

2.1. Study sample

Moderate ARDS patients who non-intubated in our hospital from January 2019 to October 2022. Inclusion criteria: a) Age ≥ 17 years, b) Moderate ARDS (according to the 2012 Berlin diagnostic criteria for ARDS) [20], c) No previous history of lung disease, d) No serious hemodynamic abnormalities, and e) Clear-minded.

Exclusion criteria: a) Age < 17 years, b) Endotracheal intubation at admission, c) Patients with incomplete data.

The planned moderate ARDS patients were enrolled and assigned to the lung recruitment group and the control group according to whether they used IS a device to perform lung recruitment. Both groups were given continuous high-flow nasal oxygen (HFNO) during treatment. We collected physiological data in a data file, including the $\text{PaO}_2/\text{FiO}_2$ (P/F) ratio, the lung ultrasound (LUS) score, the Acute Physiology and Chronic Health Evaluation (APACHE-II) score and the maximum inspiratory volume at baseline and day1, day2, day3 between the two groups. And compared the mean hospital stay and the 28-days in-hospital mortality and the 90-days in-hospital mortality between the two groups.

2.2. Incentive spirometry

Incentive spirometry (IS) is widely used by a respiratory therapist in clinical practice to increase alveolar ventilation and functional residual capacity. Patient data recorded before training represents baseline. IS is an inspiratory flow device and has three spaces, marked with a different color pellet in each space. The three spaces represent three different inspiratory flow: 600 ml/s, 900 ml/s, and 1200 ml/s. When the patient inhales, the gas enters the balloon chamber, flows through the sphere chamber, and moves the pellet based on inspiratory flow. The inspiratory flow at this time represents when the pellet reaches the apex of each space, and maximum inspiratory volume (ml) = inspiratory flow rate (ml/sec) \times time (the length of time the pellet remained at the apex, sec). For example, “600 ml/s” indicates that the inspiratory flow rate that moves the pellet to the apex is 600 ml per second, and when the inspiratory flow rate reaches 900 ml per second, the 1st and 2nd pellets move to the apex. The highest inspiratory flow rate reached 1200 ml/s, therefore indicating that all three pellets reached the apex [21].

The patients were trained for 15 min at 2-h intervals during the day and 4–6 h intervals at night.

2.3. ARDS lung ultrasound score

Patients were examined by a Versana Premier ultrasound equipped with a 3.5–5 MHz convex array probe (GE, USA). The chest

walls were divided into twelve zones. First, the chest walls were divided into upper and lower zones by the nipple level, and then each chest wall zone was divided into three small zones (anterior, lateral, and posterior) by the sternum, anterior axillary line, posterior axillary line and spine as the boundaries. Therefore, the bilateral chest walls were divided into 12 zones. Each zone was scored according to the following signs: 1) normal ventilation (N): 0 score, presence of lung sliding with A-line, and occasionally an isolated B-line; 2) mild reduction of lung aeration (discrete B-line, B1): 1 score, multiple B-lines with clear boundary, regular distribution and spacing above 7 mm or irregular distribution can be seen; 3) severely reduced lung aeration (fused B-lines, B2): 2 score, continuous fused B-lines diffusely distributed and within 3 mm of the distance; 4) signs of lung consolidation (C): 3 score, echogenicity like liver and bronchial inflation sign. When multiple sonographic signs were present within the same area, the highest score (most severe sign) was recorded [22]. All patients were examined and evaluated by intensive care unit (ICU) physicians who had received ultrasound training and obtained qualifications.

2.4. Statistical analysis

Quantitative continuous variables were given as either means (\pm standard deviations [SD]) or medians (with interquartile ranges [IQR]). Analysis of Variance (ANOVA) Tests or Wilcoxon rank sum tests for continuous variables, General linear Model (Multivariate) for multiple comparison. The Kaplan–Meier was used to estimate survival probabilities at 28 days and 90 days, and the log-rank test was used to calculate the differences between groups and trends. Probability values of <0.05 were considered statistically significant. All data analyses were performed with commercially available statistical analysis software packages (SPSS version 15.0; SPSS, Chicago, Illinois, USA).

3. Results

3.1. Characteristics of the clinically

Fig. 1 shows the patient flowchart. Of the 221 non-intubated moderate ARDS patients who were admitted to our hospital from

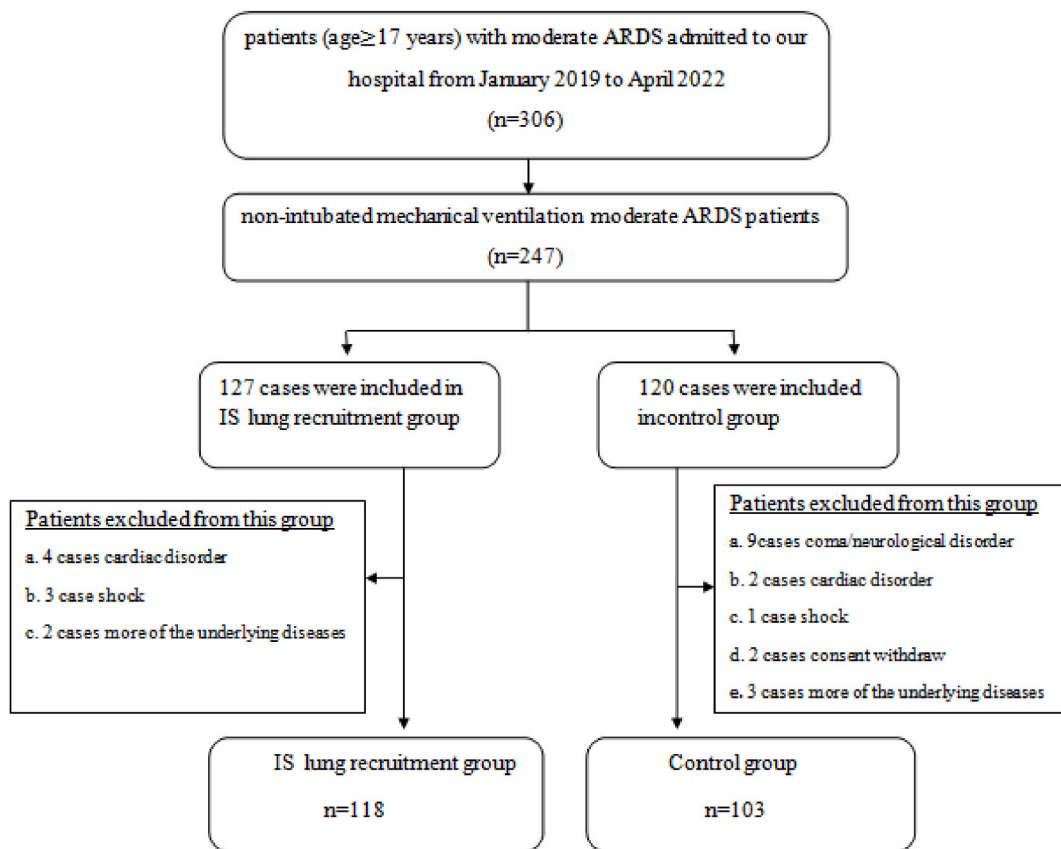


Fig. 1. Flowchart of the inclusion/exclusion process. Of the 221 non-intubated moderate ARDS patients who were admitted to our hospital from January 2019 to oct 2022, including 112 cases with pulmonary origin and 109 cases with pulmonary exogenous origin. The treatment group (LUNG recruitment group) was 118 patients (73 males and 45 females) and the control group was 103 patients (62 males and 41 females).

January 2019 to October 2022, including 112 cases with pulmonary origin and 109 cases with pulmonary exogenous origin. The treatment group (LUNG recruitment group) was 118 patients (73 males and 45 females) and the control group was 103 patients (62 males and 41 females), $P = 0.467$. The average age was 47.6 years (SD 16.5 years) in the Lung Recruitment group and 50.2 years (SD 14.8 years) in the Control group, $P = 0.489$. The number of obese patients (BMI, kg/m²) was 27.5 ± 2.6 in the Lung Recruitment group and 28.2 ± 2.2 in the Control group, $P = 0.512$. The main patients' characteristics are summarized in [Table 1](#).

3.2. The PaO₂/FiO₂(P/F)ratios, APACHE-II scores, LUS scores, and the median maximum inspiratory volume (ml) at different time between the two groups

The PaO₂/FiO₂(P/F)ratios, APACHE-II scores, LUS scores, and the median maximum inspiratory volume (ml) were significantly different among the two groups ($P = 0.000$, $P = 0.014$, $P = 0.013$ and $P = 0.001$, respectively). The LUS scores in the LUNG recruitment group were lower than those in the control group (17.6 ± 3.8 v.s. $22.32.3n$, $p = 0.046$, day1), (16.2 ± 2.9 v.s. $21.61.6\pm$, $p = 0.043$, day2), (11.4 ± 5.9 v.s. $20.30.34$, $p = 0.004$, day3). The P/F ratios in the LUNG recruitment group were higher than those in the control group (252.6 ± 55.6 v.s. 166.9 ± 72.8 , $p = 0.035$, day2), (269.8 ± 75.7 v.s. $183.93.9 \pm 7$, $p = 0.027$, day3). The APACHE-II score in the IS lung recruitment group were higher than that in the control group (10.0 ± 2.4 v.s. $15.35.3P$, $p = 0.025$, day2), (8.0 ± 1.4 v.s. $14.14.11$, $p = 0.000$, day3). The median maximum inspiratory volume in the LUNG recruitment group were higher than that in the control group (1722.3 ± 432.2 v.s. $1310.7.722.5$, $p = 0.044$, day2) and (1913.5 ± 467.2 v.s. $1299.79452.5$, $p = 0.018$, day3). The median maximum inspiratory volumes were higher than baseline in the lung recruitment group (1722.3 ± 432.2 v.s. $1133.7.73.7a$, $p = 0.045$, day2) and (1913.5 ± 467.2 v.s. $1133.773.73.$, $p = 0.035$, day3). In Lung Recruitment group, the P/F ratios at day2 and day3 were higher than those at baseline ($P = 0.042$, $P = 0.033$), the LUS scores at day1, day2, day3 were significantly lower than baseline ($p = 0.043$, $P = 0.031$, $p = 0.023$, respectively), and the APACHE-II scores at day2, and day3 were lower than baseline ($P = 0.046$, $P = 0.026$). [Table 2](#).

3.3. Compared with the rate of intubation to mechanical ventilation at the end

During treatment, some patients in both groups needed to intubation due to the deterioration of their condition. At the end, 48 (46.60%) patients in the control group received intubation mechanical ventilation, while only 36 (30.51%) patients in the LUNG recruitment group received intubation mechanical ventilation ($p = 0.014$). There was no significant Hemodynamics change or pneumothorax during lung recruitment. [Fig. 2](#).

Table 1
Patients characteristics.

Characteristics (Baseline)	IS Lung Recruitment Group (n = 118)	Control Group (n = 103)	P value
Leukocyte ($\times 10^9/L$)	12.6 ± 3.5	13.4 ± 5.6	$P=0.667(NS)$
Sex (male/female)	73/45	62/41	$P=0.467(NS)$
Age (years)	47.6 ± 16.5	50.2 ± 14.8	$P=0.489(NS)$
Body mass index (BMI, kg/m ²)	27.5 ± 2.6	28.2 ± 2.2	$P=0.512(NS)$
Total leukocyte count	16.78 ± 4.88	15.98 ± 6.76	$P=0.525(NS)$
APACHE-II score	15.36 ± 2.58	16.76 ± 2.63	$P=0.530(NS)$
P/F Ratio (ratio of PaO ₂ /FiO ₂)	165.56 ± 48.47	159.86 ± 55.58	$P=0.537(NS)$
PaCO ₂ (mmHg)	31.56 ± 4.47	34.23 ± 5.65	$P=0.525(NS)$
Respiratory rate (RR)	22 ± 3	21 ± 4	$P=0.489(NS)$
Lung ultrasound (LUS) score	24.79 ± 2.59	25.38 ± 3.29	$P=0.478(NS)$
Heart Rate (HR)	92 ± 12	89 ± 9	$P=0.534(NS)$
Mean arterial pressure (MAP)	87 ± 8	85 ± 10	$P=0.557(NS)$
Causes of ARDS			
DIRECT LUNG INJURY			$P=0.923(NS)$
Pneumonia (bacterial, viral, fungal)	36	27	
Aspiration	6	8	
Lung contusion	8	12	
Inhalation Injury	4	3	
Fat embolism	2	1	
Pulmonary vasculitis	3	1	
Near-drowning	1	0	
INDIRECT LUNG INJURY			
Serious infection	15	16	
Nonthoracic trauma	11	11	
Acute pancreatitis	10	7	
Upper abdominal surgery	9	8	
Chest Surgery	9	6	
Blood transfusion	3	2	
Drug overdose	0	1	
Burn injury	1	0	

N = number of subjects, $p \leq 0.05$ significance, NS = not significant.

Table 2Comparison of SpO₂/FiO₂ (P/F) ratio, APCHII score, LUS score, and Maximum inspiratory volume between the two groups.

	Baseline	Day1	Day2	Day3	F value	P value
P/F Ratio						
Lung Recruitment Group	165.6 ± 48.5	226.5 ± 45.4	252.6 ± 55.6*	269.8 ± 75.7**	279.14	0.000
Control Group	159.9 ± 55.6	163.7 ± 62.3	166.9 ± 72.8	183.9 ± 68.6		
P value	P = 0.658(NS)	P = 0.087(NS)	P = 0.035	P = 0.027		
APACHE-II score						
Lung Recruitment Group	15.4 ± 2.6	12.1 ± 2.3	10.0 ± 2.4 [#]	8.0 ± 1.4 ^{##}	26.28	0.014
Control Group	16.8 ± 2.6	16.3 ± 2.4	15.3 ± 2.3	14.1 ± 2.7		
P value	P = 0.687(NS)	P = 0.223(NS)	P = 0.025	P = 0.000		
LUS score						
Lung Recruitment Group	24.8 ± 2.6	17.6 ± 3.8 [@]	16.2 ± 2.9 ^{@@}	11.4 ± 5.9 ^{@@@}	35.75	0.013
Control Group	25.4 ± 3.3	22.3 ± 4.7	21.6 ± 4.8	20.3 ± 6.9		
P value	P = 0.726(NS)	P = 0.046	P = 0.043	P = 0.004		
Median maximum inspiratory volume (ml)						
Lung Recruitment Group	1133.7recruit	1586.2ec22.9	1722.3e432.2 ^{&}	1913.5e467.2 ^{&&}	140.65	0.001
Control Group	1089.81379.4	1285.71379.4	1310.71322.5	1299.71452.5		
P value	P = 0.787(NS)	P = 0.323(NS)	= 0.044	P = 0.018		

P/F Ratio: Partial pressure of oxygen/fraction of inspired oxygen. LUS: Lung ultrasound.

P ≤ 0.05 significance, NS = not significant. General linear Model (Multivariate) for multiple comparison. *V. S Baseline, P = 0.042. **V. S Baseline, P = 0.033. #V. S Baseline, P = 0.046. ##V. S Baseline, P = 0.026. @V. S Baseline, P = 0.043. @@V. S Baseline, P = 0.031. @@@V. S Baseline, P = 0.023. @@@V. S @, P = 0.040. &V.S. Baseline, P = 0.045. &&V.S. Baseline, P = 0.035. No adjustments were made for multiple comparisons.

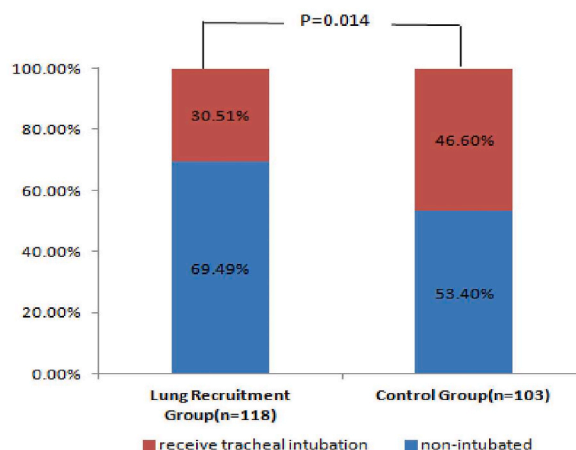


Fig. 2. Comparison of the rate of received tracheal intubation mechanical ventilation between two groups at the end. P ≤ 0.05 significance, NS = not significant. 48 (46.60%) patients in the control group received tracheal intubation mechanical ventilation, while only 36 (30.51%) patients in the LUNG recruitment group received tracheal intubation mechanical ventilation (p = 0.014) at end.

3.4. Compared of the mean hospital stay and the 28 days in-hospital mortality the 90-days in-hospital mortality between the two groups

The mean hospital stay in the lung recruitment group was lower than that in the control group, 12.6 ± 4.6 v.s 18.4 ± 5.3, P = 0.018, Fig. 3. Compared with the 28-day in-hospital mortality and the 90-day in-hospital mortality, there were no statistical significance between the two groups, (the 28-day in-hospital mortality 6.8% v.s 7.8%, P = 0.414 and the 90-day in-hospital mortality 21.2% v.s 25.2%, P = 0.490, log-rank test), Fig. 4.

4. Discussion

This study was designed to assess the effects of an incentive spirometry respiratory trainer device on lung recruitment in non-intubated moderate ARDS patients. According to the results obtained by this study, We found that the PaO₂/FiO₂(P/F)ratios, the maximum inspiratory volume (ml), APACHE-II scores and LUS scores were significantly different between the two groups. The ratios of PaO₂/FiO₂ at day2 and day3 were significantly higher than baseline in the LUNG recruitment group. And the ratios of PaO₂/FiO₂ in the LUNG Recruitment group were higher than in the Control group at day2, day3. The APACHE-II scores in the LUNG recruitment group were lower than in the control group. In the LUNG recruitment group, the APACHE-II scores at day2 and day3 were lower than baseline.

Invasive mechanical ventilation may lead to an increased risk of ventilator-associated pneumonia and prolonged use of medical

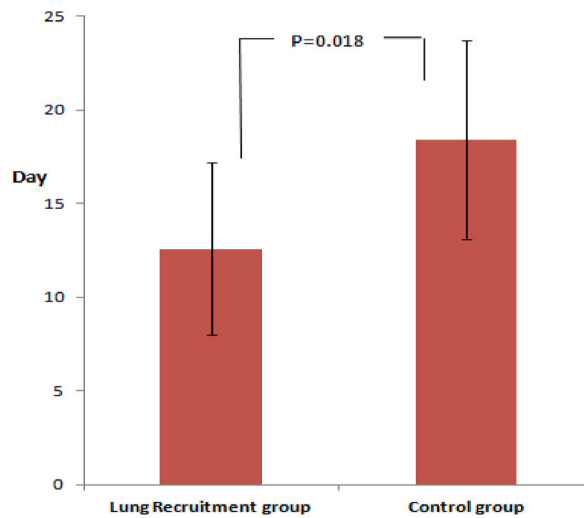


Fig. 3. Compared the mean length of hospital stay (days) in surviving patients between the two groups. $P \leq 0.05$ significance. The mean hospital stay in the lung recruitment group was lower than that in the control group, 12.6 ± 4.6 v.s 18.4 ± 5.3 , $P = 0.018$.

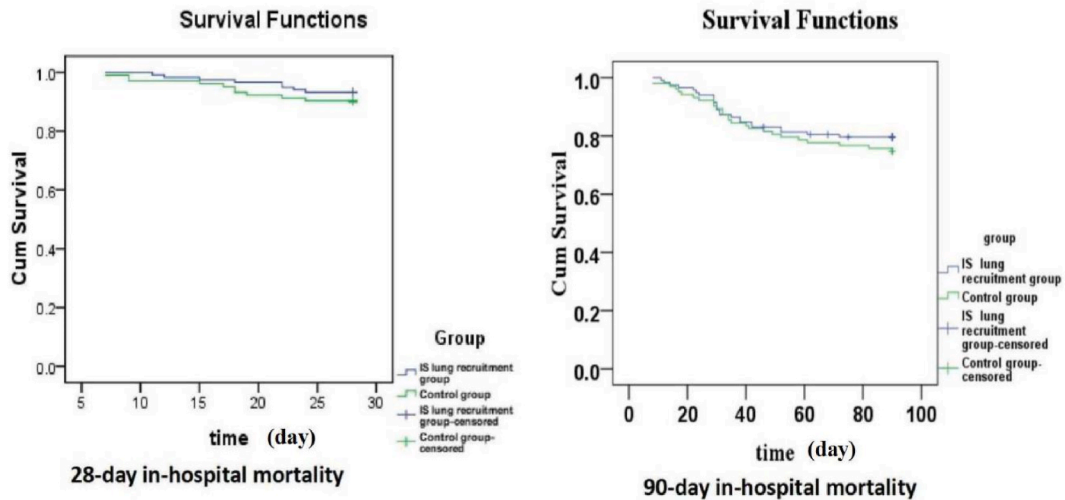


Fig. 4. Compared of the 28-day in-hospital mortality between the two groups. $P \leq 0.05$ significance, NS = not significant. Kaplan-Meier estimate of the 28-day in-hospital mortality and the 90-day in-hospital mortality. There were no statistical significance between the two groups (the 28-day in-hospital mortality 6.8% v.s 7.8%, $P = 0.414$ and the 90-day in-hospital mortality 21.2% v.s 25.2%, $P = 0.490$, log-rank test). (that IS, Incentive spirometry).

resources, which may be associated with higher mortality [6]. Therefore, reducing the rate of tracheal intubation is essential, the key point of treatment is to avoid the progression of mild to moderate to severe ARDS. Some studies found the early use of noninvasive ventilation (NIV) can reduce the need for intubation of mild ARDS patients. Patel et al. [23] found that to non invasive ventilation (NIV) delivered via helmet reduced intubation rates in patients with ARDS more significantly, compared to NIV delivered via facial mask (from 61% to 18%, respectively), as the helmet in this case seems to be a more effective and tolerable interface. In a few observational studies [24–26] the rates of intubation were seen lower in hypoxemic patients receiving high-flow nasal cannula (HFNC) than those receiving NIV. Non invasive ventilation delivered via helmet and HFNC provides a lower transpulmonary pressure (TPP) potentially. However, NIV and HFNC do not adequately address the underlying pathology of ARDS. Combining prone positioning (PP) with these noninvasive respiratory supports in ARDS may result in better physiological effects on ventilation–perfusion mismatch, better drainage of purulent lung infection-induced ARDS, and greater homogeneity in ARDS mechanics while receiving positive pressure support. Scaravilli et al. [27] showed a significant improvement in PaO_2/FiO_2 with prone positioning in awake, non-intubated, spontaneously breathing patients with hypoxemic ARF. Shoma et al. [28] describe 13 cases of non hypercapnic acute hypoxemic respiratory failure of varied etiology, who were treated successfully by prone positioning without the need for intubation and increasing the Oxygenation index PaO_2/FiO_2 ratio and Alveolar to arterial (A-a) O_2 gradient. More recently, early added to HFNO

or NIV avoided the need for intubation in up to half of the patients with moderate to severe ARDS, including those with viral pneumonia [29]. Nevertheless, ventilation in the prone position must be continuously maintained for at least 4 h or longer to be effective, such a long periods of time may be difficult to tolerate for some moderate ARDS patients.

Incentive spirometry (IS) respiratory trainer can help patients achieve sustained maximal inspiration through visual and/or auditory feedback and aims to promote adequate alveoli ventilation and increase transpulmonary pressure. Its benefits include helping to enhance lung ventilation by increasing the expansion of the chest wall, maintaining or increasing appropriate lung volume and capacity, and eventually reducing the incidence of pulmonary function loss and its related complications [30–32]. It was primarily designed to be used in clinical practice to increase alveolar ventilation and functional residual capacity to prevent atelectasis and reverse postoperative hypoxemia in surgical patients and improve lung ventilation in patients with chronic lung diseases. However, there have been no reports related to the use of respiratory trainers for lung recruitment in ARDS patients. Incentive spirometry can cause diaphragmatic displacement and increase negative intrathoracic pressure by deep inspiration, prevent postoperative alveolar collapse, or allow the collapsed alveoli to reexpand. Therefore, it can be used to perform lung recruitment maneuvers for patients with alveolar collapse caused by various diseases. The difference is that lung recruitment by the RESPIRATORY trainer device can increase intrathoracic negative pressure to improve alveolar collapse, while the others allow the collapsed alveoli to relax by increasing positive alveolar pressure, so the former has less impact on hemodynamics because more consistent with respiratory physiology [33–35].

Our study showed that lung recruitment maneuvers with a respiratory trainer device (incentive spirometry) on 118 moderate ARDS patients achieved better lung recruitment. The LUS scores in LUNG recruitment group were better than in the control group at day1, day2, and day3. The median maximum inspiratory volume in the LUNG recruitment group was higher than that in the control group at day2 and day3 and the LUS scores were significantly lower at day1 day2 and day3 than baseline in the LUNG recruitment group. The mean hospital stay in the lung recruitment group was lower than that in the control group. In addition, during treatment, some patients needed to intubation mechanical ventilation due to the deterioration of their condition. At the end, compared with the control group, the proportion of cases that progressed to severe ARDS and needed to intubation mechanical ventilation was significantly lower (30.51% V. S 46.60%, $P = 0.014$), which showed that lung recruitment by IS can be significantly reduced the rate of intubation in moderate ARDS patients and a better clinical treatment effect was achieved. However, the 28 days in-hospital mortality and the 90 days in-hospital mortality were not improved.

Several limitations of our study exist. First, the small sample size was prone to bias, yielding spurious findings on statistical analysis. Increasing the sample size and collecting more cases in further studies may avoid this limitation. Second, in addition, patient inclusion was conducted without calculating the sample size. Third, this study was carried out in only one hospital, and it may not represent the general situation. However, our study informs the design of a future multicenter prospective randomized controlled trial of lung recruitment by non-intubated moderate ARDS patients to answer this question.

5. Conclusions

The use of incentive spirometry to perform lung recruitment maneuvers in moderate ARDS patients achieved better effects. Patients' maximum inspiratory volume, $\text{PaO}_2/\text{FiO}_2$ ratio, LUS score, and APACHE-II score were significantly improved and effectively reduced the rate of intubation mechanical ventilation and the mean hospital stay in these patients. However, the 28 days in-hospital mortality and the 90 days in-hospital mortality were not improved.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author on reasonable request, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Ethics approval and consent to participate

This study was approved by the Institutional Research and Ethics Committee of the Hospital (No. 2022172). Written informed consent was obtained from all patients or the patient's next of kin before data were included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for publication

Not applicable.

Production notes

Author contribution statement

Tan Guoliang: Conceived and designed the experiments.

Zeng pingping: Performed the experiments, Analyzed and interpreted the data; Wrote the paper.

Lin Yanping: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Chen Yongqiang: Performed the experiments.

Data availability statement

Data will be made available on request.

Additional information

No additional information is available for this paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

This study was sponsored by the Research Project of Science and Technology Department of Fujian Province, China (Grant 2021J01123491). Guoliang Tan.

Abbreviations

ARDS	Acute Respiratory Distress Syndrome
RMs	Lung recruitment maneuver
SI	sustained inflation
PCV	pressure control method
MRS	Maximal recruitment strategy
PRM	Prolonged recruitment maneuver
IS	Incentive spirometry
BMI	Body mass index
LUS	Lung ultrasound
APACHE-II	Acute Physiology and Chronic Health Evaluation
HFNO	High-Flow Nasal Oxygen

References

- [1] J.P. Frat, A.W. Thille, A. Mercat, et al., High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure, *N. Engl. J. Med.* 372 (2015) 2185–2196, <https://doi.org/10.1056/NEJMc1508390>.
- [2] A. Bajaj, S. Kumar, A.H. Inamdar, et al., Noninvasive respiratory support in acute hypoxic respiratory failure in medical intensive care unit: a study in rural medical college, *Int. J. Crit. Illn. Inj. Sci.* 9 (2019) 36–42, https://doi.org/10.4103/IJCIIS.IJCIIS_40_18.
- [3] A. Esteban, A. Anzueto, F. Frutos, I. Alia, et al., Mechanical Ventilation International Study Group Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study, *JAMA* 287 (2002) 345–355, <https://doi.org/10.1001/jama>.
- [4] A. Esteban, N.D. Ferguson, M.O. Meade, et al., Evolution of mechanical ventilation in response to clinical research, *Am. J. Respir. Crit. Care Med.* 177 (2008) 170–177, <https://doi.org/10.1164/rccm>.
- [5] L.B. Ware, M.A. Matthay, The acute respiratory distress syndrome, *May 4, N. Engl. J. Med.* 342 (18) (2000) 1334–1349, <https://doi.org/10.1056/NEJM200005043421806>.
- [6] A. Esteban, F. Frutos-Vivar, A. Muriel, et al., Evolution of mortality over time in patients receiving mechanical ventilation, *Am. J. Respir. Crit. Care Med.* 188 (2013) 220–230, <https://doi.org/10.1164/rccm>.
- [7] L. Ding, L. Wang, W. Ma, et al., Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study, *Crit. Care* 24 (2020) 28, <https://doi.org/10.1186/s13054-020-2738-5>.
- [8] Tan Wei, Xu Dong-yang, Xu Meng-jiao, et al., The efficacy and tolerance of prone positioning in non-intubation patients with acute hypoxemic respiratory failure and ARDS: a meta-analysis, *Ther. Adv. Respir. Dis.* 15 (2021 Jan-Dec), <https://doi.org/10.1177/17534666211009407>.
- [9] S.E. Lapinsky, S. Mehta, Bench-to-bedside review: recruitment and recruiting maneuvers, *Crit. Care* 9 (1) (2005) 60–65, <https://doi.org/10.1186/cc2934>.
- [10] Anup Das, Oana Cole, Marc Chikhani, et al., Evaluation of lung recruitment maneuvers in acute respiratory distress syndrome using computer simulation, *Crit. Care* 19 (1) (2015) 8, <https://doi.org/10.1186/s13054-014-0723-6>.
- [11] Stefano Isgro, Alberto Zanella, Chiara Sala, Giacomo Grasselli, et al., Continuous flow biphasic positive airway pressure by helmet in patients with acute hypoxic respiratory failure: effect on oxygenation, *Intensive Care Med.* 36 (10) (2010 Oct) 1688–1694, <https://doi.org/10.1007/s00134-010-1925-2>.
- [12] Antonio Anzueto, Fernando Frutos-Vivar, Andres Esteban, Inmaculada Alía, et al., Incidence, risk factors and outcome of barotrauma in mechanically ventilated patients, *Intensive Care Med.* 30 (4) (2004 Apr) 612–619, <https://doi.org/10.1007/s00134-004-2187-7>.
- [13] Wajih Khan, Adnan Safi, Muhammad Muneeb, Mehwish Mooghal, et al., Complications of invasive mechanical ventilation in critically ill Covid-19 patients - a narrative review, *Ann. Med. Surg. (Lond)* 80 (2022 Aug) 104201, <https://doi.org/10.1016/j.amsu.2022.104201>.
- [14] Gianmaria Cammarota, Rosanna Vaschetto, Emilia Turucz, et al., Influence of lung collapse distribution on the physiologic response to recruitment maneuvers during noninvasive continuous positive airway pressure, *Intensive Care Med.* 37 (7) (2011 Jul) 1095–1102, <https://doi.org/10.1007/s00134-011-2239-8>.
- [15] R.D. Restrepo, R. Wettstein, L. Wittnebel, M. Tracy, Incentive spirometry: 2011, *Respir. Care* 56 (10) (2011) 1600–1604, <https://doi.org/10.4187/respcare.01471>.

- [16] Liliane Patrícia de Souza Mendes, Larissa Faria Borges, Letícia Mendonça, et al., Incentive spirometer: aspects of the clinical practice of physical therapists from Minas Gerais working with patients with respiratory dysfunction, *Braz. J. Phys. Ther.* 25 (5) (2021 Sep-Oct) 632–640, <https://doi.org/10.1016/j.bjpt>.
- [17] R. Sebio, M.I. Yáñez-Brage, E. Giménez-Moolhuyzen, M.C. Valenza, G. Reyhler, L.P. Cahalin, Impact of a pre-operative pulmonary rehabilitation program on functional performance in patients undergoing video-assisted thoracic surgery for lung cancer, *Arch. Bronconeumol.* 52 (5) (2016 May) 231–232, <https://doi.org/10.1016/j.arbres>.
- [18] A.S. Kumar, G.K. Alaparthi, A.J. Augustine, Z.C. Pazhyaottayil, A. Ramakrishna, S.K. Krishnakumar, Comparison of flow and volume incentive spirometry on pulmonary function and exercise tolerance in open abdominal surgery: a randomized clinical trial, *J. Clin. Diagn. Res.* 10 (1) (2016 Jan 1) KC01–6, <https://doi.org/10.7860/JCDR/2016/16164.7064>.
- [19] R.H. Bartlett, P. Krop, E.L. Hanson, F.D. Moore, Physiology of yawning and its application to postoperative care, *Surg. Forum* 21 (1970) 222–224.
- [20] ARDS Definition Task Force, V.M. Ranieri, G.D. Rubenfeld, et al., Acute respiratory distress syndrome: the Berlin Definition, *JAMA* 307 (2012) 2526–2533, <https://doi.org/10.1001/jama.2012.5669>.
- [21] Emily Franklin, Fatima Anjum, *Incentive Spirometer and Inspiratory Muscle Training*, Jan. 2022 Jul 28. PMID: 34283480. Bookshelf ID: NBK572114, StatPearls Publishing, 2022.
- [22] Francesco Rizzetto Noemi Perillo, Diana Artioli, et al., Correlation between lung ultrasound and chest CT patterns with estimation of pulmonary burden in COVID-19 patients, *Eur. J. Radiol.* 138 (2021 May) 109650, <https://doi.org/10.1016/j.ejrad.2021.109650>. Published online 2021 Mar 11.
- [23] B.K. Patel, K.S. Wolfe, A.S. Pohlman, J.B. Hall, J.P. Kress, Effect of noninvasive ventilation delivered by helmet vs face mask on the rate of endotracheal intubation in patients with acute respiratory distress syndrome: a randomized clinical trial, *JAMA* 315 (2016) 2435–2441.
- [24] J.P. Frat, A.W. Thille, A. Mercat, C. Girault, S. Rago, S. Perbet, G. Prat, T. Boulain, E. Morawiec, A. Cottreau, et al., High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure, *N. Engl. J. Med.* 372 (23) (2015) 2185–2196, <https://doi.org/10.1056/NEJMoa1503326>.
- [25] J.P. Frat, B. Brugiere, S. Rago, D. Chatellier, A. Veinstein, V. Goudet, R. Coudroy, F. Petitpas, R. Robert, A.W. Thille, et al., Sequential application of oxygen therapy via high-flow nasal cannula and noninvasive ventilation in acute respiratory failure: an observational pilot study, *Respir. Care* 60 (2) (2015) 170–178, <https://doi.org/10.4187/respcare.03075>.
- [26] J. Messika, K. Ben Ahmed, S. Gaudry, R. Miguel-Montanes, C. Rafat, B. Sztymf, D. Dreyfuss, J.D. Ricard, Use of high-flow nasal cannula oxygen therapy in subjects with ARDS: a 1-year observational study, *Respir. Care* 60 (2) (2015) 162–169, <https://doi.org/10.4187/respcare.03423>.
- [27] V. Scaravilli, G. Grasselli, L. Castagna, A. Zanella, S. Isgro, A. Lucchini, Prone positioning improves oxygenation in spontaneously breathing nonintubated patients with hypoxemic acute respiratory failure: a retrospective study, *J. Crit. Care* 30 (2015) 1390–1394, <https://doi.org/10.1016/j.jcrc.2015.07.008>.
- [28] Shoma V. Rao, R. Udhayachandar, Vasudha B. Rao, et al., Voluntary prone position for acute hypoxemic respiratory failure in unintubated patients, *Indian J. Crit. Care Med.* 24 (7) (2020 Jul) 557–562, <https://doi.org/10.5005/jp-journals-10071-23495>.
- [29] L. Ding, L. Wang, W. Ma, H. He, Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study, *Crit. Care* 24 (2020) 28.
- [30] Renault Já, R. Costa-val, M.B. Rossetti, et al., Comparison between deep breathing exercises and incentive spirometry after CABG surgery, *Rev. Bras. Cir. Cardiovasc.* 24 (2009) 165–172, <https://doi.org/10.1590/s0102-76382009000200012>.
- [31] P. Pasquina, M.R. Tramèr, J.M. Granier, et al., Respiratory physiotherapy to prevent pulmonary complications after abdominal surgery: a systematic review, *Chest* 130 (2006) 1887–1899, <https://doi.org/10.1378/chest.130.6.1887>.
- [32] M.M. Guimarães, R. El Dib, A.F. Smith, et al., Incentive spirometry for prevention of postoperative pulmonary complications in upper abdominal surgery, *Cochrane Database Syst. Rev.* 2009 (3) (2009), CD006058, <https://doi.org/10.1002/14651858>.
- [33] Bo Li, Duoling Li, Wei Huang, Yuan yuan Che. Effect of lung recruitment on blood gas index, hemodynamics, lung compliance, and rehabilitation index in children with acute respiratory distress syndrome, *Che. Trans. Pediatr.* 9 (6) (2020 Dec) 795–801, <https://doi.org/10.21037/tp-20-383>.
- [34] András Lovas, Tamás szakmány. Haemodynamic effects of lung recruitment manoeuvres, *BioMed Res. Int.* 2015 (2015) 478970, <https://doi.org/10.1155/2015/478970>.
- [35] Ignacio Garutti, Guillermo Martinez, Patricia Cruz, et al., The impact of lung recruitment on hemodynamics during one-lung ventilation, *J. Cardiothorac. Vasc. Anesth.* 23 (4) (2009 Aug) 506–508, <https://doi.org/10.1053/j.jvca>.