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Effect of a cough assist device on hemodynamic status and oxygen saturation in mechanically ventilated adults with pneumonia; a double-blind randomized clinical trial study

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Abstract

Introduction: Pneumonia often leads to impaired airway clearance and reduced oxygenation. Conventional physiotherapy has limited benefits, whereas newer approaches such as cough assist devices may play a more effective role in secretion clearance and improvement of oxygenation status.

Objectives: This study aimed to comparatively evaluate the effect of a cough assist device versus physiotherapy on hemodynamic status and oxygen saturation (O_2Sat) in patients with pneumonia.

Materials and Methods: This double-blind clinical trial study was conducted on patients with pneumonia undergoing mechanical ventilation (MV) at Firouzgar hospital in Tehran from July 2025 to February 2026. A total of 92 eligible patients were enrolled and randomly assigned to two groups: an intervention group (cough assist device, 45 patients) and a control group (chest physiotherapy, 47 patients). Hemodynamic indices (heart rate and respiratory rate) were monitored using cardio–pulmonary monitoring, and arterial blood gas (ABG) parameters (PCO_2, pH, O_2Sat, and HCO_3^-) were measured to assess gas exchange and acid–base balance. Outcomes were evaluated at three time points; before the intervention, one day after the intervention, and two days after the intervention, and the results were compared between the two groups using statistical tests.

Results: The findings indicated that, compared with physiotherapy, the cough assist device improved arterial O_2Sat status, leading to increased O_2Sat, improved pH, and reduced PCO_2 ($P<0.05$), whereas no significant differences were observed between the two groups in HCO_3 levels or hemodynamic indices such as heart rate and respiratory rate ($P>0.05$).

Conclusion: The results indicate that, compared with chest physiotherapy, cough assist devices can significantly improve arterial O_2Sat status and pH balance in mechanically ventilated patients with pneumonia, without adverse effects on hemodynamic stability. These findings support the integration of cough assist devices as a safe and effective adjunct in respiratory care in the intensive care unit (ICU).

Trial Registration: The trial protocol was approved by the Iranian Registry of Clinical Trials with code (IRCT20251111067960N1), and ethical code from Iran University of Medical Sciences (IR.IUMS.FMD.REC.1404.198).

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Introduction

Mechanical ventilation (MV) is a critical life-supporting intervention widely used in the intensive care unit (ICU); however, it exposes patients to a significant risk of serious infectious complications, the most clinically important of which is ventilator-associated pneumonia (VAP) (1,2). Ventilator-associated pneumonia is defined as pneumonia occurring 48–72 hours or more following endotracheal intubation, characterized by the presence of new or progressive pulmonary infiltrates, systemic signs of infection, changes in sputum characteristics, and identification of a causative microorganism (1,3,4). The estimated incidence of VAP ranges from 9% to 27% among mechanically ventilated patients, with event rates of 1.2 to 8.5 episodes per 1,000 ventilator days and the greatest risk concentrated in the first five days of ventilation (1,5). VAP is associated with prolonged duration of MV, extended ICU length of stay, and an estimated attributable mortality of approximately 10%, with higher mortality in surgical ICU patients and those with intermediate illness severity scores on admission (6). The predominant pathogenic mechanism involves microaspiration of oropharyngeal secretions colonized by pathogenic microorganisms, facilitated by the endotracheal tube which circumvents the natural cough reflex and mucociliary

Key point
Our study found that the cough assist device improved arterial oxygen saturation (O_2Sat), pH, and PCO_2 levels compared with physiotherapy, while HCO_3 levels and hemodynamic indices (heart rate and respiratory rate) remained similar between groups, indicating no adverse impact on cardiovascular stability. Collectively, these findings suggest that cough assist can be safely integrated as an adjunctive airway-clearance strategy in mechanically ventilated pneumonia patients to enhance gas exchange without compromising hemodynamic status.

defenses of the lower respiratory tract (1). Acutely ill mechanically ventilated patients exhibit significantly impaired mucociliary clearance, further reducing the capacity of the airways to expel colonized secretions and thereby increasing susceptibility to lower respiratory tract infection (7).

Effective airway secretion clearance is a fundamental component of respiratory management in mechanically ventilated patients; however, the inability to generate an adequate cough, attributable to sedation, neuromuscular compromise, or severe respiratory failure, represents a major clinical barrier in the ICU setting (8,9). The mechanical insufflation-exsufflation (MI-E) device, commonly referred to as the cough assist device, addresses this deficit by delivering controlled positive pressure to inflate the lungs, followed by a rapid transition to negative pressure, thereby simulating the physiological mechanics of a cough and generating sufficient peak expiratory flow to mobilise and transport secretions toward the proximal airway (8,10). This technique has been most extensively validated in patients with neuromuscular diseases, where it has been demonstrated to augment peak cough flow, reduce the frequency of respiratory tract infections, and improve patient outcomes (11). In mechanically ventilated critically ill patients, MI-E has been proposed as a more controlled and potentially safer alternative to manual hyperinflation and conventional endotracheal catheter suctioning, both of which carry risks of airway mucosal trauma, haemodynamic fluctuation, and transient oxygen desaturation (12). A retrospective cohort study demonstrated that the use of MI-E in ICU patients with impaired cough was independently associated with a significantly reduced incidence of VAP compared with conventional chest physiotherapy (13).

The cardiovascular and respiratory safety profile of any airway clearance manoeuvre must be rigorously evaluated in critically ill mechanically ventilated patients, as even transient haemodynamic instability or oxygen desaturation can carry grave clinical consequences (6). A randomized clinical trial found that use of the cough assist device did not produce significant changes in blood pressure, heart rate, or peripheral oxygen saturation (O_2Sat) compared with conventional endotracheal suctioning (14). Results reported from a preliminary observational study of intubated ICU patients found that MI-E was not associated with clinically relevant hemodynamic adverse events and led to a significant post-procedure rise in arterial oxygen partial pressure, likely reflecting alveolar recruitment during the positive-pressure insufflation phase (12). A randomized crossover trial further demonstrated that high-pressure MI-E (±50 cmH_2O) combined with endotracheal suctioning maintained systolic blood pressure, diastolic blood pressure, and peripheral O_2Sat at baseline levels while simultaneously improving respiratory compliance and augmenting the volume of secretions removed (15). Despite these encouraging findings, the existing evidence is largely derived from heterogeneous ICU populations with varied primary diagnoses, and targeted data examining the haemodynamic and oxygenation effects of the cough assist device specifically in mechanically ventilated adults with confirmed pneumonia remain scarce. Given the high clinical burden of VAP, the established physiological rationale for MI-E use, and the absence of high-quality randomized evidence in this specific patient subgroup, a double-blind randomized clinical trial investigating the effect of a cough assist device on hemodynamic status and O_2Sat in mechanically ventilated adults with pneumonia is both scientifically warranted and clinically imperative.

Objectives

The objective of this study is to compare the effects of a cough assist device and conventional chest physiotherapy on hemodynamic status and arterial oxygenation, including arterial blood gas (ABG) parameters, in mechanically ventilated adult patients with pneumonia.

Materials and Methods

Study design and participants

This double-blind, randomized clinical trial used a parallel-group design to compare a cough assist device with conventional chest physiotherapy in adult patients with pneumonia undergoing invasive MV in the ICU of Firouzgar hospital in Tehran, Iran, from July 2025 to February 2026. This study included 92 patients in two groups: a control group of 47 patients who received conventional chest physiotherapy, and an intervention group of 45 patients who received airway clearance with a cough assist device in addition to standard care. Eligible participants were hemodynamically stable adults with a confirmed diagnosis of pneumonia who were intubated and expected to remain on MV for at least 48 hours and who met predefined inclusion and exclusion criteria to minimize confounding respiratory or cardiovascular conditions.

Inclusion criteria

Adult patients aged 18 years or older, written informed consent for participation obtained from the patient's legal guardian, radiologic evidence of pneumonia on chest X-ray or a positive sputum culture, endotracheal intubation with invasive MV for at least 24 hours, and no history of pneumothorax during the month before enrollment.

Exclusion criteria

Inconsistency of the intervention with the study protocol; implementation of therapeutic measures requiring interruption of the intervention, or any change in the patient's clinical condition that posed an immediate threat to life. Deterioration of the patient's condition or death from any cause before completion of the follow-up period. Initiation of new medications that could interfere with the action of the cough assist device, extubation before the end of the study period and voluntary withdrawal from the study at the request of the patient's legal guardian.

Sample size

The sample size was calculated based on a 95% confidence interval, 90% statistical power, and the results of a similar study (16), yielding a minimum of 36 patients per group (72 patients in total). Considering the possibility of attrition according to the study's exclusion criteria, the required sample size was adjusted by assuming a 20% dropout rate, resulting in a final target of 90 patients, with 45 patients in each group.

Randomization/allocation

Block randomization was used in this study to maintain balance in the number of participants in each group. First, the block size, typically consisting of four participants, was determined. Then, all possible allocation permutations to the two groups (cough assist device and physiotherapy) within each block were generated. Each block was randomly selected from these permutations, and participants were assigned sequentially according to the allocation sequence within the selected block.

Blinding

Blinding in this double-blind clinical trial was maintained at the level of both participants' care teams and outcome assessors. Treating ICU staff responsible for routine patient management were not informed of group allocation and did not participate in delivering the study interventions, which were administered by a separate team following a standardized protocol to minimize discernible differences in procedure between the cough assist and physiotherapy arms. Outcome assessors who recorded hemodynamic parameters and ABG measurements were blinded to treatment assignment, and data were coded so that statisticians performed all analyses without knowledge of group identity until the completion of primary analyses.

Intervention

Cough assist device: In this study, a mechanical cough assist device was used in the intervention group to enhance airway secretion clearance. The device delivers positive pressure during inspiration to inflate the lungs to near-maximal volume and then abruptly switches from positive to negative pressure to simulate the natural cough mechanism, thereby promoting more effective expulsion of secretions. The device used was the Philips T70 Cough Assist (USA). Initially, the percussor mode was applied for five minutes with a frequency of 300–400 Hz, positive pressure of 20–40 cmH_2O, and flow intensity ranging from minimum to maximum in order to loosen secretions. Subsequently, in Auto-Sync mode, the device was set to a positive pressure of 20–40 cmH_2O, a negative pressure of −20 to −40 cmH_2O, oxygen flow up to 15 L/min, inspiratory time of 1.5 seconds, expiratory time of 2.5 seconds, and a pause between inspiration and expiration of 0.3–1 second. In this mode, five insufflation–exsufflation cycles were performed and, after 20 seconds of rest, the sequence was repeated three to five times; the total duration of the procedure was five minutes. A one-second pause was also provided between each cycle to facilitate drainage of secretions through the endotracheal tube. All patients were placed in a semi-sitting position during device use, and the device circuit was connected directly to the endotracheal tube. Within the specified ranges, device settings were individualized according to hemodynamic status, patient tolerance, and secretion volume. Each patient received one treatment session per day, with no additional physiotherapy interventions; the number of sessions was determined by the physician and delivered by a physiotherapist or trained nurse. At the end of each intervention, lung auscultation and ventilator waveform assessment were performed to confirm adequate secretion clearance (17,18).

Chest physiotherapy: In the control group, chest physiotherapy in mechanically ventilated patients was performed stepwise and in accordance with safety principles to improve pulmonary ventilation and facilitate effective secretion clearance. First, the patient was positioned appropriately, usually in a semi-sitting posture or in targeted postural drainage positions so that gravity could assist mucus mobilization. Manual techniques, including percussion (rhythmic clapping with cupped hands over the chest wall) and vibration (rapid, controlled oscillations during expiration), were then applied to loosen airway secretions. Next, in coordination with the ventilator, lung volume–expanding maneuvers were carried out by the care team to recruit poorly ventilated lung regions. When feasible, endotracheal suctioning was performed after secretions had been loosened to achieve more complete airway clearance. Throughout the procedure, vital signs, O_2Sat, ventilator pressures, and the patient's clinical response were continuously monitored to ensure safety and tolerability. The physiotherapy session was typically delivered in several short cycles and concluded once the patient had returned to a stable condition with adequate ventilation (19).

Data collection

The sampling method in this study was simple random sampling. The research procedure was explained to the patients' legal guardians, including its advantages and

disadvantages, and written informed consent was obtained from them for participation in the study. Data collection included demographic characteristics such as age, gender, body mass index (BMI), history of smoking and opium, and clinical data including hospitalization time, intubation time, check ejection fraction (EF), and pulmonary artery pressure (PAP). These data were gathered through observational and interview-based methods, including questioning patients' companions, reviewing clinical records, and using the hospital information system. Outcome assessment in this study was performed using repeated and systematic measurements at three time points: before the intervention, one day after the intervention, and two days after the intervention. Hemodynamic parameters, including heart rate and respiratory rate, were recorded via cardiopulmonary monitoring. In addition, ABG analysis was performed to evaluate O_2 saturation (O_2Sat), pH, partial pressure of carbon dioxide ($PaCO_2$), and bicarbonate (HCO_3), allowing precise assessment of changes in gas exchange and acid–base balance.

Outcomes measurement

The primary outcome was comparing ABG analysis parameters, including O_2Sat, $PaCO_2$, PH, and HCO_3, as well as hemodynamic indices (heart rate and respiratory rate) measured at baseline, one day after the intervention, and two days after the intervention between two groups of physiotherapy and cough assist. The secondary outcome was assessing change in these parameters between baseline and post-intervention time points.

Statistical analysis

Statistical analyses were performed using SPSS software, version 27.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed with the Kolmogorov–Smirnov test to evaluate the assumption of normality. For each outcome, both parametric and corresponding non-parametric tests were initially explored, and because the direction and significance of P-values were concordant across these approaches, parametric tests were selected for the final analyses owing to their greater statistical efficiency and precision. Between-group comparisons of continuous variables were conducted using independent samples T-tests, while within-group changes over time (post-intervention vs. baseline) were evaluated using paired T-tests; categorical variables were analyzed using the chi-square test. A two-sided *P* value of less than 0.05 was considered statistically significant.

Results

At the beginning, 114 individuals were assessed for eligibility for the study. Of those, 12 were excluded; 7 did not meet the inclusion criteria, and 5 refused to participate. Consequently, 102 participants were randomly allocated to two groups; 49 were assigned to the cough assist group, all of whom received the intervention using the cough assist device, and 53 were assigned to the physiotherapy group, all of whom received the allocated physiotherapy. In the cough assist group, 4 participants did not complete the follow-up period (3 due to non-adherence to the study protocol and 1 due to voluntary withdrawal), resulting in 45 participants being included in the final analysis. In the physiotherapy group, 6 participants did not complete the follow-up period (4 due to non-adherence to the study protocol and 2 due to voluntary withdrawal), resulting in 47 participants being included in the final analysis (Figure 1).

This study included 92 patients in two groups; a control group (47 patients) who received physiotherapy, and an intervention group (45 patients) who received a cough assist device. The results showed that the frequency distribution of demographic and clinical characteristics of the studied patients, such as age, sex, BMI, history of tobacco and opium use, EF level, PAP level, length of hospital stay, and duration of intubation, did not differ significantly between the cough assist and physiotherapy groups (Table 1).

Across all three time points, ABG indices were broadly comparable between the physiotherapy and cough assist groups, with similar baseline values before the intervention, and no statistically significant differences in O_2Sat, pH, $PaCO_2$, HCO_3, and hemodynamic parameters were observed. The cough assist group showed a progressive advantage in arterial O_2Sat status over time, which became significant by the second day after the intervention, whereas oxygenation in the physiotherapy group improved more modestly over the same period. Hemodynamic parameters, including heart rate and respiratory rate, remained largely stable and did not differ significantly between groups at any time point, indicating that neither intervention adversely affected cardiovascular or respiratory stability while the cough assist approach conferred superior improvement in oxygenation by the end of follow-up (Table 2 and Figure 2).

One day after the intervention, both physiotherapy and cough assist were associated with improved arterial O_2Sat status compared with baseline, but the magnitude of improvement was greater and statistically more robust in the cough assist group. In the physiotherapy group, oxygenation gains were accompanied by a significant reduction in arterial $PaCO_2$ without meaningful changes in pH, HCO_3, or hemodynamic indices, suggesting modest enhancement of gas exchange without hemodynamic compromise. In contrast, patients treated with the cough assist device not only demonstrated a similarly favorable reduction in $PaCO_2$ but also a small yet statistically significant rise in pH and a trend toward increased HCO_3, again without significant alterations in heart rate or respiratory rate. Overall, these within-group comparisons indicate that while both strategies improved oxygenation over the first 24 hours, cough assist provided a somewhat more pronounced correction of oxygenation and acid–base status, with no evidence of adverse hemodynamic

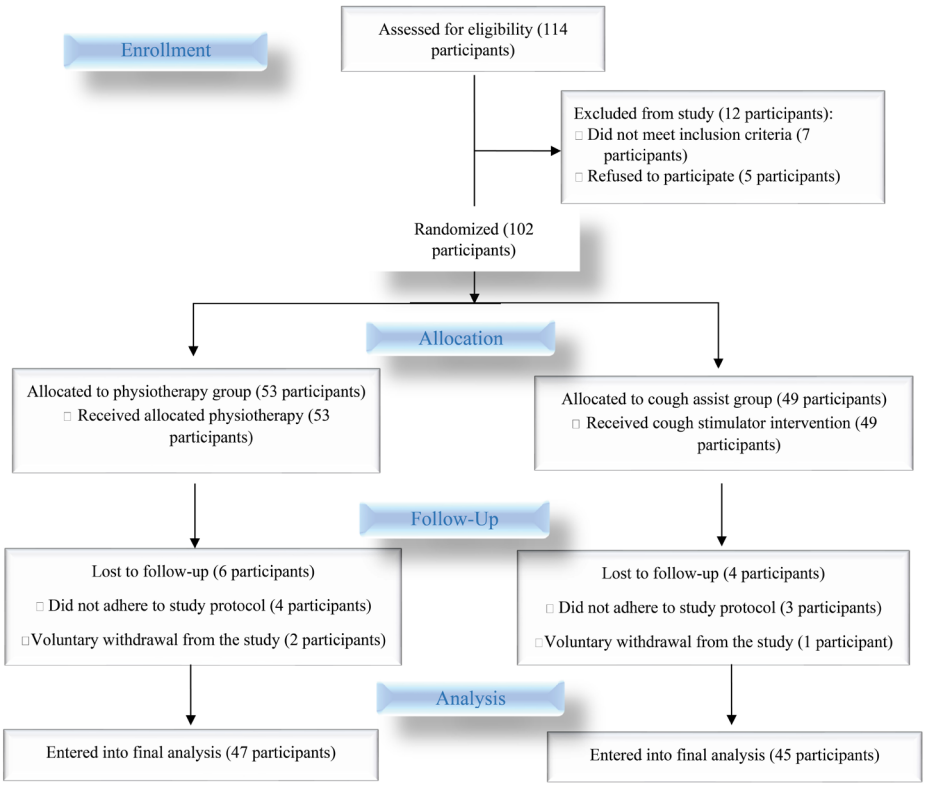

Figure 1. CONSORT flow diagram of the study.

effects in either group (Table 3).

Two days after the intervention, both groups demonstrated sustained improvements in arterial O_2Sat status compared with baseline, with the cough assist group showing a slightly greater relative increase than the physiotherapy group. In both arms, pH exhibited a small but statistically significant rise, while HCO_3 levels remained essentially unchanged, indicating modest correction of acid–base balance without major shifts in buffer status. In the physiotherapy group, $PaCO_2$ levels showed a nonsignificant reduction, whereas the cough assist group experienced a marked and statistically significant decline in $PaCO_2$, suggesting a more pronounced enhancement of alveolar ventilation. Heart rate and respiratory rate tended to increase modestly in both groups, but these changes did not reach statistical significance, implying that neither intervention adversely affected hemodynamic stability over the two-day period (Table 4).

Table 1. Demographic characteristics and clinical data comparison between the physiotherapy and cough assist groups

Qualitative variables		Treatment group				*P* value*
		Physiotherapy (n = 47)		Cough assist (n = 45)		
		N	%	N	%	
Gender	Female	17	36.2	14	31.1	0.608
	Male	30	63.8	31	68.9	
Smoking	No	32	68.1	26	57.8	0.306
	Yes	15	31.9	19	42.2	
Opium	No	39	83	31	68.9	0.113
	Yes	8	17	14	31.1	
Quantitative variables		**Mean**	**SD**	**Mean**	**SD**	***P* value****
Age (year)		67.79	14.82	70.67	15.04	0.358
BMI (kg/m²)		26.55	3.84	25.34	4.87	0.158
EF (%)		44.68	10.65	46.22	13.01	0.535
PAP (mm Hg)		31.91	7.59	33.67	9.39	0.327
Hospitalization time (day)		11.12	9.70	8.93	10.50	0.305
Intubation time (day)		7.66	8.69	6.22	10.30	0.471

BMI: Body mass index, EF: Ejection fraction, PAP: Pulmonary artery pressure, SD: Standard Deviation, *Chi-square, **Independent T-test.

Table 2. Comparison of ABG analysis and hemodynamic parameters between the physiotherapy and cough assist groups during the study duration

Parameters		Treatment group				*P* value*
		Physiotherapy (n = 47)		Cough assist (n = 45)		
		Mean	SD	Mean	SD	
Before intervention						
ABG	O_2Sat (%)	90.96	3.46	91.69	3.37	0.308
	pH	7.38	0.06	7.36	0.06	0.097
	$PaCO_2$ (mm Hg)	40.36	8.75	43.64	9.45	0.088
	HCO_3 (mEq/L)	25.54	6.61	23.88	6.20	0.216
Hemodynamic	HR (N)	87.02	10.24	89.56	16.53	0.382
	RR (N)	17.38	2.55	17.47	3.43	0.895
One day after the intervention						
ABG	O_2Sat (%)	94.60	3.06	95.96	3.30	0.044
	pH	7.39	0.05	7.38	0.06	0.194
	$PaCO_2$ (mm Hg)	37.51	7.45	40.96	9.65	0.057
	HCO_3 (mEq/L)	24.25	6.33	25.12	6.27	0.510
Hemodynamic	HR (N)	89.36	14.62	90.71	14.69	0.660
	RR (N)	18.53	4.32	19.00	6.50	0.684
Two days after the intervention						
ABG	O_2Sat (%)	94.68	2.69	69.20	3.38	0.019
	pH	7.41	0.05	7.39	0.05	0.070
	$PaCO_2$ (mm Hg)	38.63	4.99	36.38	3.95	0.019
	HCO_3 (mEq/L)	25.37	5.89	25.08	6.70	0.828
Hemodynamic	HR (N)	90.60	14.56	91.20	10.27	0.819
	RR (N)	17.87	3.94	19.40	3.67	0.058

ABG: Arterial blood gas, O_2Sat: Oxygen saturation, $PaCO_2$: Partial pressure of carbon dioxide, HCO_3: Bicarbonate, HR: Heart rate, RR: Respiratory rate, SD: Standard deviation. *Independent T-test.

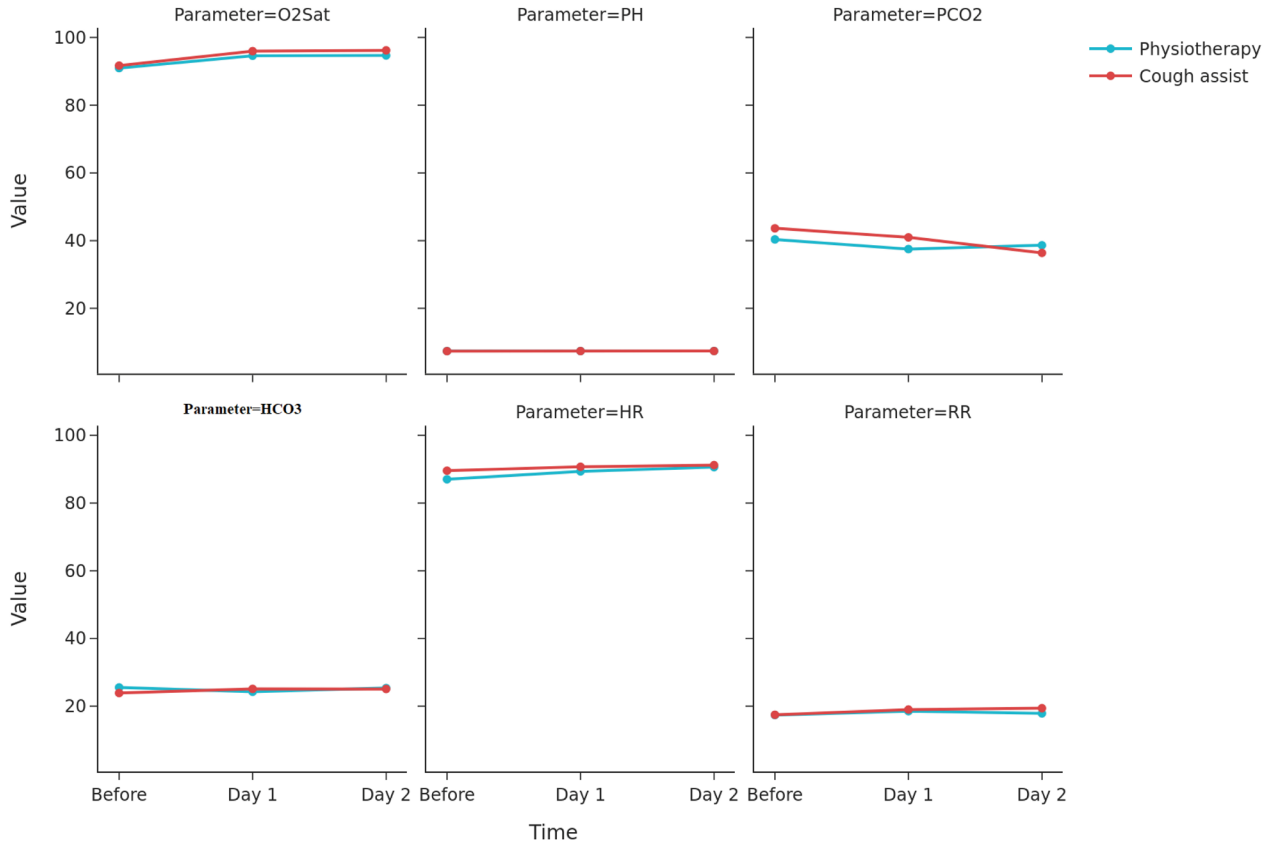

Figure 2. Comparison of ABG and hemodynamic parameters between the physiotherapy and cough assist groups during the study duration. O_2Sat: Oxygen saturation, $PaCO_2$: Partial pressure of carbon dioxide, HCO_3: Bicarbonate, HR: Heart rate, RR: Respiratory rate.

Discussion

The present double-blind randomized clinical trial demonstrated that, compared with conventional chest physiotherapy, the application of a cough assist device in mechanically ventilated adults with pneumonia was associated with a statistically significant improvement in arterial O_2Sat, an increase in arterial pH, and a reduction in PCO_2. These findings are consistent with the broader physiological rationale underpinning MI-E; by generating high transthoracic pressure differentials, the device mobilizes retained bronchopulmonary secretions, thereby reducing ventilation-perfusion mismatch, decreasing airway resistance, and facilitating more effective alveolar gas exchange. Prior evidence has supported the beneficial effects of MI-E on respiratory mechanics and secretion clearance in critically ill mechanically ventilated patients (20). In a single-center randomized controlled trial of 180 adult ICU patients, Ferreira de Camillis et al reported that MI-E application led to significantly improved secretion clearance as measured by the weight of aspirated secretions, alongside improved lung compliance (21). Similarly, Nunes et al demonstrated in a randomized crossover trial that high-pressure MI-E (±50 cmH_2O) combined with endotracheal suctioning improved respiratory mechanics and was associated with greater volumes of removed secretions, which indirectly supports the oxygenation improvements observed in the present study (15). An analogous finding was reported by Siriwat et al in a study of pneumonic children on MV with cerebral palsy, where the MI-E, compared to physiotherapy groups, demonstrated

Table 3. Comparative analysis of ABG analysis and hemodynamic parameters, one day after the intervention versus before, within each of the physiotherapy and cough assist groups

Parameters		Mean difference			Percentage change	*P* value*
		Mean	Standard error	95% CI (Lower–Upper)		
Physiotherapy (n = 47)						
ABG	O_2Sat (%)	3.64	0.45	2.77–4.55	↑ 4%	<0.001
	pH	0.01	0.009	-0.01–0.03	↑ 0.13%	0.247
	$PaCO_2$ (mm Hg)	-2.85	1.04	- 4.97 – [- 0.74]	↓ 7.06%	0.009
	HCO_3 (mEq/L)	-1.29	0.83	-2.97–0.39	↓ 5.05%	0.130
Hemodynamic	HR (N)	2.34	1.88	-1.44–6.12	↑ 2.68 %	0.220
	RR (N)	1.15	0.7	-0.26–2.56	↑ 6.61%	0.108
Cough assist (n = 45)						
ABG	O_2Sat (%)	4.27	0.51	3.22–5.30	↑ 4.65%	< 0.001
	pH	0.02	0.008	0.001–0.04	↑ 0.27%	0.032
	$PaCO_2$ (mm Hg)	-2.68	1.48	- 5.68–0.32	↓ 6.14 5	0.079
	HCO_3 (mEq/L)	1.24	1.08	-0.94–3.43	↑5.19%	0.257
Hemodynamic	HR (N)	1.15	2.01	-2.89–5.20	↑ 1.28%	0.568
	RR (N)	1.53	1.06	-0.62–3.68	↑ 8.75%	0.158

ABG: Arterial blood gas, O_2Sat: Oxygen saturation, $PaCO_2$: Partial pressure of carbon dioxide, HCO_3: Bicarbonate, HR: Heart rate, RR: Respiratory rate, *Paired T-test.

Table 4. Comparative analysis of ABG analysis and hemodynamic parameters, two days after the intervention versus before, within each of the physiotherapy and cough assist groups

Parameters		Mean difference			Percentage change	*P* value*
		Mean	Standard error	95% CI (Lower–Upper)		
Physiotherapy (n = 47)						
ABG	O_2Sat (%)	3.72	0.54	2.62 – 4.82	↑ 4.08 %	<0.001
	pH	0.03	0.01	0.001 – 0.04	↑ 0.40%	0.041
	$PaCO_2$ (mm Hg)	- 1.73	1.22	-4.19 – 0.73	↓ 4.28%	0.164
	HCO_3 (mEq/L)	-0.18	0.69	-1.57 – 1.21	↓ 0.7%	0.798
Hemodynamic	HR (N)	3.57	2.19	-0.84 – 7.99	↑ 4.10%	0.110
	RR (N)	0.49	0.57	-0.67 – 1.65	↑ 2.81%	0.401
Cough assist (n = 45)						
ABG	O_2Sat (%)	4.51	0.58	3.41 – 5.68	↑ 4.97%	< 0.001
	pH	0.03	0.01	0.01 – 0.05	↑ 0.40%	0.012
	$PaCO_2$ (mm Hg)	- 7.26	1.49	-10.22 – [-4.28]	↓ 16.63 %	< 0.001
	HCO_3 (mEq/L)	1.20	1.25	-1.32 – 3.72	↑ 5.02%	0.343
Hemodynamic	HR (N)	1.64	1.95	-2.30 – 5.59	↑ 1.83%	0.406
	RR (N)	1.93	0.75	-0.41 – 3.45	↑ 11.04%	0.054

ABG: Arterial blood gas, O_2Sat: Oxygen saturation, $PaCO_2$: Partial pressure of carbon dioxide, HCO_3: Bicarbonate, HR: Heart rate, RR: Respiratory rate, *Paired T-test.

significant improvements in atelectasis (22).

The significant improvement in arterial pH and reduction in PCO_2 observed in the cough assist group, compared to physiotherapy, suggests that effective secretion removal by MI-E reduces the degree of functional dead-space ventilation and enhances alveolar ventilation efficiency in patients with pneumonia. This is mechanistically plausible, as accumulated tracheobronchial secretions in mechanically ventilated patients with pneumonia impair mucociliary clearance and increase airway resistance, leading to progressive CO_2 retention and respiratory acidosis, a pathophysiological process well characterized in the critical care literature (20). The absence of a significant between-group difference in HCO_3^- levels in the present study is in keeping with the understanding that serum bicarbonate, as a slower-acting metabolic compensatory mechanism, may not demonstrate significant change within a brief post-intervention window of one to two days, irrespective of the intervention applied (23). Swingwood et al, in a scoping review of 28 studies on MI-E use in invasively ventilated critically ill adults, noted that outcomes reported across studies are highly heterogeneous and that the specific effects of MI-E on acid-base balance, particularly HCO_3^-, are infrequently measured and reported, further underscoring the novelty of systematically examining this parameter in the present study (24).

A key safety finding of the present trial was the absence of statistically significant differences between the cough assist device group and the physiotherapy group in hemodynamic indices, specifically heart rate and respiratory rate. This finding corroborates the results reported by Coutinho et al in a randomized crossover trial of 43 mechanically ventilated ICU patients, in which MI-E application did not produce statistically significant changes in mean arterial pressure, heart rate, or peripheral O_2Sat compared with conventional endotracheal suctioning, suggesting an overall favorable cardiovascular safety profile for the device (14). Sánchez-García et al similarly reported no clinically significant hemodynamic adverse events in a preliminary observational study of intubated ICU patients treated with MI-E, reinforcing the conclusion that, when applied with appropriate settings, the cough assist device does not impose a deleterious hemodynamic burden (12). Further confirmed in a crossover trial that even high-pressure MI-E (±50 cmH_2O) maintained systolic blood pressure, diastolic blood pressure, and peripheral O_2Sat at baseline levels throughout the intervention period (15). Collectively, the present findings and the existing body of evidence consistently indicate that MI-E can be applied in mechanically ventilated patients, including those with pneumonia, without inducing clinically meaningful hemodynamic instability, which is a critical prerequisite for safe adoption of this technique in the ICU setting.

The superiority of the cough assist device over chest physiotherapy in improving oxygenation and gas exchange, as demonstrated in the present study, highlights an important limitation of conventional physiotherapy in mechanically ventilated patients. In a retrospective cohort study, Kuroiwa et al reported that the use of MI-E in ICU patients with impaired cough was independently associated with a significantly reduced incidence of VAP compared with conventional chest physiotherapy alone (26.4% vs. 84.2%), suggesting that beyond immediate physiological effects, MI-E may offer broader protective benefits against nosocomial complications in this population (13). Goetz et al noted that while various cough augmentation strategies, including high-frequency chest wall oscillation, intrapulmonary percussive ventilation, and MI-E, have been studied in mechanically ventilated patients, the evidence base remains insufficiently robust to identify a single superior modality, and the present study, by directly comparing the cough assist device with physiotherapy using a rigorous double-blind RCT design, makes an important methodological contribution to this field (20). Cough augmentation techniques for extubation or weaning, reviewed by Rose et al in the Cochrane Database, found limited high-quality evidence on the superiority of specific cough augmentation methods over others in critically ill patients (25), underscoring the significance of the present study's positive findings for a specific high-risk subgroup like mechanically ventilated adults with pneumonia.

Overall, the findings of the present trial support the integration of the cough assist device as a safe and effective adjunct to standard respiratory care in the ICU for mechanically ventilated adults with pneumonia. The demonstrated improvements in arterial O_2Sat and acid-base balance, without adverse hemodynamic effects, provide clinicians with a physiologically grounded evidence base for incorporating MI-E into airway clearance protocols in this patient population. However, several limitations should be acknowledged. The heterogeneity of critically ill patients, differences in pneumonia severity, ventilator settings, and sedation protocols may influence the generalizability of the present findings, and future multi-center trials with larger samples and extended follow-up periods are warranted to confirm these results and examine clinically important endpoints such as duration of MV, ICU length of stay, and mortality.

Conclusion

The results of this randomized clinical trial showed that, in mechanically ventilated adult patients with pneumonia, use of a cough assist device was more effective than conventional physiotherapy in improving oxygenation. The intervention produced significant improvements in arterial O_2Sat status, normalization of pH, and reductions in PCO_2, without adverse effects on hemodynamic status, thereby confirming the safety of this approach in critically ill patients. Overall, these findings suggest that cough assist devices can serve as a valuable adjunct to standard

respiratory care in the pulmonary ICU by yielding measurable improvements in pulmonary gas exchange. Multicenter studies with larger sample sizes and longer follow-up are recommended to confirm these results and to assess their potential impact on reducing complications, shortening the duration of MV, and improving long-term outcomes.

Limitations of the study

First, it was conducted in a single center, which may limit the generalizability of the results to other intensive care settings with different case mixes, staffing patterns, or respiratory care protocols. Second, the sample size, although calculated a priori and adequate for detecting differences in arterial oxygenation, may have been underpowered to demonstrate smaller but clinically relevant effects on some secondary outcomes, such as hemodynamic changes or bicarbonate levels. Third, the follow-up period was relatively short and restricted to the first 48 hours after initiation of the intervention, so potential longer-term benefits or harms, such as effects on duration of MV, ICU length of stay, or mortality, could not be fully assessed. Fourth, because the study relied on protocolized physiotherapy and cough assist settings tailored by the clinical team, some variability in technique and intensity between providers is possible, which may have introduced performance bias despite the double-blind design. Finally, the study did not systematically evaluate patient-centered outcomes such as comfort, dyspnea, or cough effectiveness, nor did it include objective measures of secretion volume, which would have provided a more comprehensive assessment of airway clearance efficacy.

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Authors' contribution

Conceptualization: Mahdi Yadollahzadeh and Afrooz Kargaran Dehkordi.
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Methodology: Mahdi Yadollahzadeh and Nader Rezaie.
Project management: Afrooz Kargaran Dehkordi.
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Supervision: All authors.
Validation: Afrooz Kargaran Dehkordi and Nader Rezaie.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Conflicts of interest

The authors declare no conflict of interest.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

While preparing this work, the authors utilized AI (Grammarly, and Perplexity) to refine grammar points and language style. Subsequently, they thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

The research was conducted in accordance with the principles of Declaration of Helsinki. The study was conducted at Firouzgar Hospital, Tehran, Iran, and derived from the thesis of Afrooz Kargaran Dehkordi (Thesis No. 33573). The study was approved by Iran University of Medical Sciences (Ethical Code IR.IUMS.FMD.REC.1404.198; https://ethics.research.ac.ir/form/64qx8ysz7b7soshn.pdf) on July 11, 2025. The study protocol was also registered as a clinical trial at the Iranian Registry of Clinical Trials (identifier: IRCT20251111067960N1). Accordingly, informed written consent was taken from all participants before any intervention. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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