Physical Therapy Management of Ventilated Patients with Acute Respiratory Distress Syndrome or Severe Acute Lung Injury

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INTRODUCTION

Acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) are serious respiratory conditions characterized by bilateral pulmonary infiltrates and severe hypoxemia in the absence of cardiogenic pulmonary edema and left atrial hypertension.¹⁻³ The diagnosis of ARDS/ALI can be defined by the ratio of the partial pressure of oxygen in the patient's arterial blood (PaO_2) to the fraction of oxygen in the inspired air (FIO_2), which in ARDS is less than 200 and in ALI is less than 300.¹ Patients with ARDS/ALI are often cared for by physical therapists in Canadian intensive-care units. The purpose of this article is to review the literature on physical therapy interventions for these conditions and to discuss limitations of this literature.

Among ARDS and ALI patients, the leading pathophysiologic event and medical history often differ, but both conditions are associated with high mortality and morbidity.^{3,4} Alveolar-capillary damage in ARDS may be induced by physical or chemical injury or by development of innate inflammatory responses, leading to leaky alveolar-capillary barriers and resulting in widespread alveolar flooding.³ Thus a variety of injuries may result in damage either to the vascular endothelium or to the alveolar epithelium, leading to ARDS,^{1,5} which in turn results in progressive hypoxemia as a result of ventilation/perfusion mismatching causing intrapulmonary shunt.^{1,3}

PATIENT PROFILE

A patient with ARDS or ALI has severe hypoxemia ($\text{PaO}_2/\text{FIO}_2 < 300$) and is being cared for in an intensive-care unit (ICU) and maintained on a ventilator at low

tidal volume.⁶ Generally the patient has minimal airway secretions; therefore, the treatment focus will be on physiotherapy interventions to improve oxygenation, decrease the risk of ventilator-associated pneumonia (VAP), and gradually increase mobility.

THE CLINICAL QUESTION

What is the most appropriate physiotherapy treatment for this severely hypoxemic, ventilated patient who has minimal airway secretions?

CURRENT OPINION

Recently, the European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients highlighted the need for standardized guidelines and pathways for the management of such patients.⁷ They proposed the following targets for physiotherapy management: avoiding atelectasis, impaired airway clearance, general deconditioning, intubation, and weaning failure where possible.

It is important to note, however, that the task force reported that some of these recommendations were based on low-quality studies⁷ with many methodological problems. Such an evidence base might lead to erroneous conclusions.^{8,9} For example, one study used a paired *t*-test for between-group analysis,¹⁰ while another used an unpaired *t*-test for within-group analysis.¹¹ One study reported an increase in ventilation parameters when mobilizing from supine to standing, but there was a serious confounding factor: the patients were on a ventilator while supine and were removed from the ventilator during mobilization.¹² Another study reported a statistically

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significant improvement of only 1.1% in SpO_2 in all three of their intervention groups.¹³ A survey of the use of a tilt table was quoted to support the conclusion that upright position increases lung volume and gas exchange,¹⁴ but the actual study¹⁵ reported no improvement in gas exchange and a only short-term increase in ventilation. These examples highlight the need to view such narrative reviews with caution, especially when recommendations are supported by low-quality studies.

The European review⁷ also outlined guidelines for safe mobilization of critically ill patients, but other studies^{16–18} showed that these mobilization guidelines may be too restrictive and that mobilizations are still tolerated by patients who have vital signs or laboratory values outside the proposed safety levels.

EVIDENCE AND APPROACH TO TREATMENT

The Patient: Ventilated, with Severe Hypoxemia ($\text{PaO}_2/\text{FiO}_2 < 300$)

The patient may be put on a newly advanced mode of ventilation, such as high-frequency oscillatory ventilation or pressure-control ventilation, and require heavy sedation, analgesia, or even full paralysis to facilitate ventilation and decrease overall oxygen consumption.^{19–22} The Richmond Agitation–Sedation Scale (RASS) is frequently used in assessing the sedation level of ventilated patients.^{23,24} With this type of patient, sedation levels likely range from light sedation, meaning brief (<10 seconds) wakefulness and eye contact in response to voice stimulation (RASS score of –2), to unarousable, meaning no response to voice or physical stimulation (RASS score of –5).

Physiotherapy targets for these patients aim to improve oxygenation, decrease incidence of VAP, and initiate gradual mobilization. Basic and subsequent physiotherapy interventions may consist of turns every 2 hours; maintaining the head of the bed at $>30^\circ$ most of the time; good oral care (often from nursing staff); subglottic suctioning to decrease the risk of VAP; maintaining proper body alignment while in bed; positioning for prevention of pressure sores; passive range-of-motion exercise to limbs; and adjusting the head of the bed up to 45° for 30–60 minutes twice a day.^{25–32}

The optimal turning protocol for critically ill patients has not been well established, and kinetic therapy (systematic mechanical rotation of patients with 40° – 60° turns) has been proposed to decrease pulmonary complications relative to the standard of turning patients every 2 hours.^{33–38} In the largest recent randomized controlled trial (RCT),³⁸ patients on kinetic therapy were kept at 40° on each side for 10 minutes and supine for 5 minutes; unfortunately, head-of-bed angles were not reported. The study reported a lower incidence of VAP and lobar atelectasis, but no change in gas exchange, in

the kinetic therapy group relative to the control group. Other studies on the effects of side-lying and gas exchange also reported no improvement.^{39–41}

Recently two separate systematic reviews with meta-analyses on kinetic therapy have been published.^{42,43} Complications associated with rotational therapy include disconnection of intravascular catheters, patient intolerance of the rotation, adverse effects on intracranial pressure, and arrhythmias.⁴³ The systematic review by Delaney et al. reported that kinetic therapy decreased the incidence of nosocomial pneumonia but had no effect on mortality, duration of mechanical ventilation, or duration of ICU and hospital stays.⁴² The systematic review by Goldhill et al. reported that kinetic therapy decreased the incidence of pneumonia but had no effect on duration of mechanical ventilation, number of days in ICU, or hospital mortality.⁴³ Each review included 15 trials, of which 13 were common to both reviews; therefore, it is not surprising that both studies reported the same findings from the meta-analyses, with the exception that Goldhill et al. did not consider duration of hospital stay. Interestingly, however, their conclusions differed. Delaney et al. suggested that given the lack of consistent benefit and the poor methodological quality of the trials included in their analysis, definitive recommendations on the use of kinetic therapy could not be made.⁴² In contrast, Goldhill et al. concluded that kinetic therapy may be useful for preventing and treating respiratory complications in selected critically ill patients receiving mechanical ventilation.⁴³

An observational study by Chandy et al. reviewed more than 6,000 ICU admissions and concluded that the introduction of kinetic beds with vibration, percussion, and rotation modules did not decrease the incidence of atelectasis in mechanically ventilated patients.⁴⁴

Turning patients into prone lying is a labour-intensive protocol^{33,45–47} that has been reported to improve oxygenation relative to supine lying^{33,47–49} and sitting.⁵⁰ Four to six staff and an average of 10 minutes are generally required to turn the patient.⁴⁷ In 2008, three separate systematic reviews with meta-analyses on severely hypoxemic patients were published.^{47–49} The systematic review on ARDS⁴⁸ included five trials. No significant differences were found between prone-positioned patients and controls with respect to mortality, number of days on mechanical ventilation, or incidence of VAP. In a sub-group analysis of two studies, a review of prone positioning showed a significant reduction in mortality in patients with higher illness severity relative to controls; prone positioning also showed significant and persistent improvement in the $\text{PaO}_2/\text{FiO}_2$ ratio (weighted mean difference of 51.5; 95% CI: 6.95–96.05). The systematic review on acute hypoxemic respiratory failure,⁴⁷ which included 13 trials with good overall methodological quality, reported that prone positioning did not reduce either mortality or the duration of mechanical

ventilation but that the ratio of $\text{PaO}_2/\text{FiO}_2$ was higher (~34%) among patients in the prone position than among those who remained supine.⁴⁷ Prone positioning was also associated with a reduced risk of VAP and an increased risk of pressure ulcers.⁴⁷ The third systematic review⁴⁹ included both ARDS and ALI but reviewed only five trials, four of which were identical to those examined in the review on ARDS.⁴⁸

Possible mechanisms^{51–58} by which the prone position may improve oxygenation include (1) production of more uniform pleural pressures between dorsal and ventral lung lobes through increased recruitment of dorsal lung regions; (2) equal perfusion in the dorsal and ventral lung regions between the supine and prone positions, resulting in a more uniform ventilation-perfusion distribution in the dorsal lung region; (3) avoidance of ventilator-associated lung injury by preventing repeated opening and closing of small airways and/or excessive stress at the margins between opened and atelectatic dorsal lung units; (4) anterior chest wall constriction between the bed surface and the weight of the body above it, which may result in some redistribution of tidal volume to dorsal lung units close to the diaphragm; and (5) improved oxygenation, leading to decreased FiO_2 and, at least theoretically, decreasing the risk of oxygen toxicity to allow time for other medical treatments to have an effect.⁴⁷

The Patient: Still Ventilated But Now More Medically Stable and Less Hypoxemic

Depending on the patient's sedation level, cognition, limb strength, and pain level, further mobilization may now be possible.^{25–32} In particular, sedation vacations and optimal sedation are associated with improved patient outcomes.^{19,59–61} RASS may be used to target sedation level and decrease over-sedation.^{23,24} When the patient is more conscious (RASS level > -2) but not agitated (RASS level < +2), able to follow some simple verbal commands, with pain under control, the basic physical therapy intervention may include encouraging the patient to help with turns, bed positioning, additional exercises, and mobilization as appropriate.^{25,26,29–32} Mobilization may include use of a cardiac chair, tilt table, dangle, or mechanical lift to chair for 30 to 60 minutes a few times a day. When the patient has anti-gravity arm movements, mobility can be progressed (in addition to the previous physiotherapy programme) to encourage independence with bed mobility as much as possible and work on attaining side sitting on the side of the bed, body control, and sitting balance exercises. When the patient has anti-gravity leg (knee-extension) movements, he or she can work on sit to stands at bedside and progressive mobilization in addition to the previous physiotherapy programme.^{25,29,31,32} At this point the patient's

medical condition may have stabilized sufficiently that a lower level of medical care is required and transfer off ICU to a ward where therapy can be progressed as appropriate.

Safety Considerations

For safe mobilization, it is important to review the patient's previous mobility status to ensure that no factors that might limit mobilization are present.^{29,31,32} Table 1 presents a summary of factors that might limit safe mobilization, based on recent RCTs on the safety of mobilizing ICU patients.^{29,32} Because such patients and their conditions are diverse, and because different ICUs may also have their own sets of contraindications, it is essential to speak with the patient-care team if there is any doubt as to whether a patient can be mobilized safely. An excellent time to do this is during multidisciplinary patient-care rounds.

Table 1 Summary of Factors That May Limit Mobilization of ICU Patients*

<i>System Status</i>	<i>Factors That May Limit Mobilization**</i>
Cardiovascular	
MAP (mm Hg)	< 65 ^{29,32}
HR (beats/min)	< 40 ³² or > 130 ³²
Hemodynamic	Administration of a new pressor agent ²⁹ Active bleeding ³²
Cardiac status	New myocardial infarct ^{29,32} Dysrhythmia requiring new medications ² Active cardiac ischemia ³²
Respiratory	
SpO ₂	< 88% ^{29,32}
RR (breaths/min)	< 5 or > 40 ³²
Ventilator issues	Increased positive end expiratory pressure or change in ventilator mode ²⁹ Ventilator asynchrony ³² Unsecure airway ³² Pressure-control ventilation ³¹
FiO ₂	> 60% ³¹
Neurological	
Patient status	Severely agitated, distressed, or combative ³²
ICP	Significantly increased ³²
Other	Intermittent hemodialysis ³² Unstable spinal-cord injury or vertebral fracture ³¹

MAP = mean arterial pressure; HR = heart rate; SpO₂ = percutaneous oxygen saturation level; RR = respiratory rate; FiO₂ = fraction of inspired oxygen; ICP = intracranial pressure

* The author (FC) is currently working with Fraser Health Critical Care Practice Council²⁵ and the SAFEMOB working group on a more detailed mobilization protocol. The SAFEMOB working group is a collaboration between the Physiotherapy Association of British Columbia, the University of British Columbia Department of Physical Therapy, and the BC Rehabilitation Sciences Research Network whose goal is to create practice guidelines for the safe prescription of mobilization for patients in acute-care settings.

** Specialized ICUs may have specific lists of contraindications.

Issues and Gaps in the Evidence and Directions for Future Research

Diagnosing ARDS requires confirming the presence of bilateral pulmonary infiltrates, using radiographs, and the absence of left atrial hypertension, using pulmonary artery occlusion pressure; both of these measures may be unreliable, however.^{62–65} Furthermore, various pathophysiologies are represented in ARDS/ALI, such that diverse groups of patients are grouped into a single syndrome diagnosis. Additional sources of heterogeneity in the literature include diverse leading causes, variation with respect to the phases of ARDS in which specific treatments were given, and variability in the mechanisms of lung injury.^{66,67} As a recent systematic review indicated,⁴⁸ therapy that benefits one sub-group of patients with ARDS may not benefit another sub-group. Recently it has been proposed that a more precise and research-focused definition of ARDS/ALI is needed to help better understand these conditions and conduct research focused on this topic.^{5,66,67}

Two systematic reviews on kinetic therapy, despite the similarity of the trials included and the results of their meta-analyses, offered differing conclusions.^{42,43} VAP is known to be associated with a longer duration of mechanical ventilation and ICU length of stay;^{28,42,68,69} however, no significant reduction in these important outcomes was reported. Delaney et al. added that the reduction in VAP with kinetic therapy may be an artefact of methodological deficiencies in the included clinical trials.⁴² In the largest clinical trial on kinetic therapy, for example, blinding and allocation concealment were not used.³⁸ Furthermore, in the group receiving kinetic therapy, about 18% of individuals (21/118) could not tolerate kinetic therapy, and data on VAP and lobar atelectasis for this group were not reported. Intention-to-treat analysis was not used; the data from these 21 individuals were not included in the statistical analysis.

Hypoxemia is one of the main clinical concerns in ARDS/ALI, but the leading cause of mortality is multi-organ failure.^{2,3,58} The mechanisms leading to multi-organ failure are as diverse as the leading cause and subsequent pathophysiologies. One such mechanism is further lung injury caused by vigorous mechanical ventilation to manage hypoxemia, which can induce the production of pro-inflammatory cytokines, endotoxins, or bacteria, resulting in multi-organ failure.^{2,3,58} Thus, prone positioning may improve oxygenation yet not contribute significantly to decreasing mortality in ARDS patients.^{47,58,70}

Many clinicians in clinical trials^{71,72} were aware of the positive effects of prone position on oxygenation (e.g., “co-investigators considered it unethical not to allow severely hypoxemic patients to be placed in a prone position”^{72(p.2384)}). As a result, many patients in the supine group in these trials (almost 21% in one study⁷²)

were placed in prone position at some point, and many patients in the prone-lying group were not turned as scheduled.^{71,72} Another study was terminated early because of slow recruitment, which was largely due to clinicians’ unwillingness to forgo the use of prone positioning.⁷¹ Duration of prone lying was also an issue in one systematic review, which reported that patients were placed in the prone position for a median duration of 12 hours per day over a median duration of 4 days;⁴⁷ the total time spent in prone lying may have been too short for any significant long-term benefit to be achieved.^{47,49,58,72,73}

While both kinetic therapy and prone-lying studies reported a reduction in VAP relative to supine lying, these studies did not control head-of-bed angles. Keeping the head of the bed $>30^\circ$ is known to decrease the incidence of VAP.^{27,28} Further studies of kinetic therapy and prone position need to compare the incidence of VAP with that among patients in supine position but with head-of-bed angles $>30^\circ$. For reasons of safety, however, many kinetic beds allow lateral rotation only if the head of the bed is kept low.

Both recent RCTs on early ICU treatments had very stringent admission criteria, yielding an inclusion rate of about 10% into the trials.^{29,32} Based on this small, selected group of patients, it may be difficult to generalize the research findings to the usual clinical setting.^{74,75} Patients with ALI represented $>55\%$ of participants, and patients with chronic obstructive pulmonary disease (COPD) about 10%; patients with neuromuscular conditions were excluded.^{29,32} Group assignment and interventions were not blinded, as masking is difficult in a clinical setting.^{29,32} Therefore, potential bias may be associated with the physicians, nurses, physiotherapists, and respiratory therapists who cared for patients in both arms of the studies. Intention-to-treat analysis was not used, and only the outcomes of responders (survivors) were used for statistical analysis.²⁹ It is important to note that both studies were done in the United States, where neither the availability⁷⁶ nor the practice of physiotherapy services^{29,32,77} is necessarily the same as in Canada. Earlier studies had reported that for patients with similar severity of illness and discharge outcomes, ICU usage was more than double and ICU lengths of stay were greater in the United States than in Canada.^{78,79} Also, because of differences in referral practices, physiotherapy care of ICU patients that would be routine in Canada may be delayed or limited in the United States.^{29,32} A 2009 study found that up to 89% of ICUs in the United States where physical therapists were employed required a physician consultation to initiate physiotherapy.⁷⁷

ICU and hospital lengths of stay have frequently been used as outcome measures in RCTs and systematic reviews on this topic. However, many other issues—such as medical, social, psychological, and institutional

factors; severity of illness; length of ward stay before ICU admission; and presence or absence of full-time ICU physician involvement in care—also play an important role in a patient's length of stay.^{80,81}

There was some heterogeneity in most trials and systematic reviews, which may have affected the validity of the findings.^{82–84} For example, the improvement in oxygenation reported by Alsaghir and Martin was associated with a high level of heterogeneity ($I^2 = 90\%$),⁴⁸ while Sud et al. used a ratio of oxygenation between groups and reported improved oxygenation with low heterogeneity ($I^2 = 0\%$).⁴⁷ The finding of decreased mortality in severely ill ARDS patients in prone position⁴⁸ was based on a sub-group analysis and needs to be verified in large RCTs.

Clinical trials funded by for-profit organizations are more likely than those funded by not-for-profit organizations to report positive findings and more positive conclusions.^{85–87} Some of the trials on kinetic therapy^{34,37,38} and one of the authors in the systematic review by Goldhill et al.⁴³ reported industry support.⁴³ There was less industrial funding in prone-positioning trials, and no conflicts of interest were reported in systematic reviews on prone positioning and trials on ICU mobilization.^{29,32,47–49} However, it is not known to what degree industry funding affected the validity of the findings.

SUMMARY

The early use of prone positioning, longer duration in prone lying (i.e., sufficient dosage), and use of prone positioning over a sufficient number of days are important components of the prone-positioning protocol for ventilated patients with ARDS/ALI.^{47–49,70,72,73} Kinetic therapy or lateral positioning with head of bed $> 30^\circ$ and sitting with head of the bed $> 30^\circ$ may be used for routine positioning of patients with ventilated ARDS/ALI.^{28,42,43}

Step-wise early mobilization of ICU patients is safe and is associated with favourable outcomes in terms of both hospital length of stay and functional ability of the patient.^{29,30,32} Early intervention of sufficient frequency and duration and over an adequate period are the key to success for many physiotherapy interventions for ventilated ARDS/ALI patients.

This review provides a starting point for physiotherapy guidelines in the management of patients with ARDS/ALI, but more clinical research is needed, and, of course, the patient's best interest is paramount when research findings are incorporated into clinical practice.^{88,89} Even given the complexity involved in clinical research on ICU care of severely ill patients, there may be some simple but important treatment interventions for physical therapists to use that may save lives when properly administered.⁹⁰

ADDITIONAL COMMENTARY

A late addition to the literature on this topic was published by Taccone et al. in winter 2009.⁹¹ Their RCT assessed the effects of prone positioning on moderately or severely hypoxemic patients with ARDS and concluded that prone positioning does not provide significant survival benefit in patients with ARDS or in subgroups of patients with moderate and severe hypoxemia. Unfortunately, as noted by Taccone et al., this study was likely underpowered; with a sample size of 342 patients, it did not have enough statistical power to detect any absolute mortality difference below 15%. This limitation is even more evident with respect to the sub-groups of patients with severe hypoxemia ($n = 74$ prone, $n = 76$ supine), in whom previous studies have shown prone lying to improve pathophysiology.^{47,48} This new study showed an 11% absolute reduction in mortality in the prone-lying group at 6 months, not high enough to be significant for the statistical power of this RCT. When we added the data from Taccone et al. to those of a previous meta-analysis,⁴⁸ (Fig. 3) however, the results affirmed that the use of prone position is associated with lower ICU mortality in severely ill patients (OR = 0.47, 95% CI: 0.24–0.93). This is another example of the importance of critically reviewing the literature and of the danger of basing clinical decisions on a study's conclusions alone.

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