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Mobility Interventions to Improve Outcomes in Patients Undergoing Prolonged Mechanical Ventilation: A Review of the Literature

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Abstract

Survivors of critical illness often undergo an extended recovery trajectory. Reduced functional ability is one of several adverse outcomes of prolonged bed rest and mechanical ventilation during critical illness. Skeletal muscle weakness is known to be one of the major phenomena that account for reduced functional ability. Although skeletal muscle weakness is evident after prolonged mechanical ventilation, few studies have tested the benefits of various types of mobility interventions in this population. The purpose of this article is to review the published research on improving mobility outcomes in patients undergoing prolonged mechanical ventilation. For this review, published studies were retrieved from MEDLINE, PubMed, CINAHL, and the Cochrane Database of Systematic Reviews from January 1990 to July 2007. A total of 10 relevant articles were selected that examined the effect of whole body physical therapy, electrical stimulation, arm exercise and inspiratory muscle training. Overall, there is support for the ability of mobility interventions to improve outcomes in patients on prolonged mechanical ventilation but limited evidence of how to best accomplish this goal. Generating more data from multicenter studies and randomized controlled trials is recommended.

Keywords

prolonged mechanical ventilation; long-term mechanical ventilation; critical illness; rehabilitation; physical therapy; exercise; ambulation; mobility; respiratory muscle training; muscle strength; functional status; psychosocial; physiological; movement; weaning

Patients who require prolonged mechanical ventilation (PMV) experience high rates of mortality and morbidity and decreased quality of life, which often necessitates substantial assistance from family caregivers (Chelluri et al., 2003; Combes et al., 2003; Gracey, Naessens, Krishan, & Marsh, 1992; Spicher & White, 1987). Over 50% of 1-year PMV survivors require assistance in basic activities in daily life (Chelluri et al., 2004). For this reason, there is growing interest in ways to improve long-term physical and psychosocial outcomes directly linked with overall quality of life in this population (Carson, 2006; Morris, 2007).

Skeletal muscle weakness and, consequently, decreased functional status are widely recognized problems in persons on bed rest and receiving PMV (Larsson, 2007). The major cause of these problems is a decrease in both skeletal muscle strength and mass due to disuse. In healthy adults, approximately 45% of total body weight consists of muscle (Topp, Ditmyer, King, Doherty, & Hornyak, 2002). During absolute bed rest, muscle mass decreases by up to 5% per week (Bloomfield, 1997). With such a decrease in muscle mass, skeletal muscle strength decreases by 1–1.5% per day (De Jonghe et al., 2002; Siebens, Aronow, Edwards, & Ghasemi, 2000; Topp et al., 2002) and by a total of 40% during the first week (Topp et al., 2002). Other factors that can cause muscular weakness include catabolism from the underlying illness, poor nutritional status and medications, e.g. neuromuscular blockade or corticosteroids (Kim et al., 2006).

Preventing loss of muscle function during the early stage of critical illness is important. However, few studies have tested interventions designed for this purpose (Timmerman, 2007). In the early phase of critical illness, patients are typically viewed as “too sick” or “too physiologically unstable” to initiate mobility interventions to improve skeletal muscle strength (Bailey et al., 2007). Therefore, mobility interventions are delayed until patients have recovered sufficiently to be transferred to a rehabilitation-focused setting (Morris, 2007). However, the need for PMV often extends for weeks or months (Carson, 2006), thus further delaying such interventions. Considering that skeletal muscle strength decreases significantly during the first week of bed rest (Topp et al., 2002), such delays can lead to a significant loss of functional ability. For this reason, earlier introduction of mobility interventions is important (Morris & Herridge, 2007).

In spite of the increasing awareness of the importance of early mobility interventions in PMV patients, there are no specific guidelines for changing current clinical practice in order to prevent deconditioning and promote mobility in critically ill patients, including those who require PMV. Two previous systematic reviews (Clini & Ambrosino, 2005; Stiller, 2000) focused on evidence supporting use of a broad spectrum of physiotherapy techniques, including suctioning, chest physiotherapy and positioning practices, as well as mobility therapy in intensive care units. Neither of these reviews specifically focused on patients receiving PMV, and both reported a lack of sufficient evidence to develop specific guidelines to improve mobility in patients on PMV.

The purpose of this article is to review the published research on improving mobility outcomes in patients undergoing PMV in order to explore the characteristics of mobility interventions and examine their effects on physiological and clinical outcomes. We also highlight directions for future research.

Methods

Search Strategy

We conducted a comprehensive search of the electronic databases MEDLINE, PubMed, CINAHL, and the Cochrane Database of Systematic Reviews from January 1990 to July 2007. To ensure the rigor of the literature search, two of us (JC and LAH) were involved in the process. The keywords or text words used in various combinations were “prolonged mechanical ventilation,” “long-term mechanical ventilation,” “critical illness,” “rehabilitation,” “physical therapy,” “exercise,” “ambulation,” “mobility,” “respiratory muscle training,” “muscle strength,” “functional status,” “psychosocial,” “physiological,” “movement,” “weaning.” The definition of *prolonged* in PMV varied from 2 to 29 days in the literature (Chelluri et al., 2003; Combes et al., 2003; Gracey et al., 1992; Spicher & White, 1987). Therefore, rather than predetermining a definition of *prolonged* for our search, we included a study if the author(s) used “prolonged mechanical ventilation,” “long-term

mechanical ventilation” or “difficulty to wean” as one of the sample inclusion criteria. We limited the search to studies published in the English language involving human subjects 18 years or older. To identify additional studies, we also manually searched the reference lists of retrieved articles. We did not include abstracts of conference presentations, personal communications or scholarly dissertations and theses. After the search of each database, we imported all records of interest into the bibliographical software package EndNote 8, deleting duplicates. We reviewed titles and abstracts to screen for relevance and obtained and reviewed full text for all potentially relevant articles.

For the purposes of this review, we defined *mobility interventions* as a class of interventions designed to improve respiratory or limb muscle strength and endurance in patients who underwent PMV, such as positioning and exercise protocols that focused on upper or lower limb muscles or the respiratory muscles. We used the following inclusion criteria for the final selection of articles: 1) randomized or nonrandomized intervention study that examined the effect of a mobility intervention on outcomes in patients who underwent PMV or 2) prospective or retrospective study to observe outcomes after a mobility intervention. For each study selected, we extracted and summarized data on sample characteristics, methods, interventions and outcomes.

Results

We found 10 studies that met our inclusion criteria. These are presented in Table 1 in chronological order. Of the 10, 4 studies (Bailey et al., 2007; Chiang, Wang, Wu, Wu, & Wu, 2006; U. J. Martin, Hincapie, Nimchuk, Gaughan, & Criner, 2005; Nava, 1998) examined only whole-body physical therapy, which is already a part of routine care. The other 6 tested electrical stimulation (Zanotti, Felicetti, Maini, & Fracchia, 2003), arm exercise (Porta et al., 2005) and inspiratory muscle training (Aldrich et al., 1989; Caruso et al., 2005; A. D. Martin, Davenport, Franceschi, & Harman, 2002; Sprague & Hopkins, 2003) as additional interventions to whole-body physical therapy. We identified the study by Aldrich et al. (1989) while reviewing the study by Martin et al. (2002). Because the Aldrich study reported data from the research group that first introduced inspiratory muscle training as an intervention to improve weaning outcome, we considered this study to be of importance for this review even though its publication date was 1 year earlier than the lower limit of our literature search.

Whole body physical therapy

The ultimate goal of whole-body physical therapy in patients on PMV is to minimize loss of mobility, maximize functional independence and facilitate weaning (Perme, Southard, Joyce, Noon, & Loebe, 2006). Whole-body physical therapy consists of various activity events, ranging from passive range of motion to walking with or without assistance (Clini & Ambrosino, 2005; Stiller, 2000). Although the potential benefits of whole-body physical therapy in critically ill patients were described over a decade ago (Dean & Ross, 1992), our search revealed few randomized controlled trials testing the effects of this intervention. The 4 included studies that involved whole-body physical therapy include 2 randomized controlled studies (Chiang et al., 2006; Nava, 1998), 1 nonrandomized retrospective analysis (U. J. Martin et al., 2005) and 1 nonrandomized prospective cohort study (Bailey et al., 2007).

Nava (1998) investigated the effects of inpatient pulmonary rehabilitation in patients who experienced acute respiratory failure secondary to an exacerbation of chronic obstructive pulmonary disease (COPD). The intervention consisted of a progressive four-step regimen; control subjects only received Steps 1 and 2 whereas intervention subjects received all four steps. Progression was dependent on patient tolerance. The intervention group improved significantly in their ambulation distance. However, there was no difference between the groups in total RICU length of stay, mortality, or weaning outcome. This study had several

critical limitations. First, the inclusion and exclusion criteria were too broad, resulting in a heterogeneous sample. Patient management was not limited to either invasive or noninvasive ventilation at enrollment, thus, both groups included patients receiving both types of treatment. Also, patients' prior number of days on mechanical ventilation was not clearly stated. Second, the additional steps provided to intervention subjects (Steps 3 and 4) focused on improving exercise capacity for individuals able to ambulate independently. Based upon the completion rate for Step 3 (72%) and the number of patients dependent on mechanical ventilation at RICU discharge (10%), most patients were likely weaned from mechanical ventilation by the time they received Step 3. Therefore, it is difficult to identify the additive benefit for patients who remain dependent on mechanical ventilation.

In the second randomized controlled trial, Chiang et al. (2006) tested the effect of a 6-week physical training program in patients on mechanical ventilation for > 14 days (range 23–81 days) who had received no physical therapy prior to enrollment. The program consisted of limb and respiratory muscle training. Limb muscle training progressed in the following order: 1) upper and lower extremity exercise, focusing on passive and active range of motion with light weights while patient was in bed; 2) bedside functional training, focusing on turning and transfer out of the bed, and 3) ambulation, focusing on walking. Respiratory muscle training involved diaphragmatic breathing exercises during spontaneous breathing trials. From baseline to 6 weeks, the intervention group showed significant improvement in respiratory and limb muscle strength, whereas the control group showed a significant decrease in limb muscle function. Ventilator-free hours were significantly improved in the intervention group (from 0 hr to a median of 6 hr at 6 weeks [IQR 3–13 hours]). Significant improvement was reported in the Barthel Index and all subdomains of the functional independence measure (FIM), which includes activities of daily living, sphincter control, mobility and executive function. Importantly, though not statistically significant, the control group showed a decrease in executive function over 6 weeks. At the end of the intervention, if the patient was able to breathe without support from mechanical ventilation for at least an hour, a 2-min walk test was performed with supplemental oxygen and/or a walker. Whereas 53% of patients in the intervention group were able to complete the 2-min walk test at 6 weeks (mean distance = 42.9 ± 12.7 m), all patients in the control group were bedridden at 6 weeks and none were able to ambulate. This study is considered to be the only randomized controlled trial testing the effects of a whole body physical therapy intervention on mobility outcomes in PMV patients that used a no-intervention control group. The reported decrease in limb muscle strength in the control group provides strong evidence of the benefit of whole body physical therapy. While replication in a larger sample would provide stronger evidence, there are ethical issues related to withholding physical therapy, given the marked deterioration in the control group and significant benefit to the intervention group.

U. J. Martin et al. (2005) conducted a retrospective analysis of the effects of whole body physical therapy in consecutive PMV patients transferred to a ventilatory rehabilitation unit. Training focused initially on trunk and posture control and progressed to include resistance bands and upper and lower extremity ergometry. The regimen significantly increased upper and lower muscle strength and FIM subdomains (supine to sit, sit to stand). Ambulation increased from 0 feet at admission to 52 ± 18 feet at the end of rehabilitation period, which varied by subject. Using stepwise regression analysis, the authors found that use of neuromuscular blockade and steroids and upper-limb muscle strength were significant factors affecting the number of days to weaning. The contribution of upper limb muscle strength to decreasing weaning days ($-.59$) was more than twice that of exposure to either neuromuscular blockade (.21) or steroids (.22), both of which actually increased weaning days. This finding is important as it suggests that loss of upper limb motor strength impairs weaning outcome but can be overcome by whole-body rehabilitation techniques. However, because of

methodological limitations (retrospective analysis without a control group), the evidence from this study is weak.

A prospective cohort study by Bailey et al. (2007) focused on the feasibility and safety of an early ambulation intervention in patients on mechanical ventilation for > 4 days who were admitted to a RICU. Early activity began when the patient met neurologic (responds to verbal stimulation), respiratory ($\text{FiO}_2 < 0.6$, $\text{PEEP} < 10\text{cm H}_2\text{O}$) and circulatory (no catecholamine drips) criteria. The goal was to enable patients to walk > 100 feet at RICU discharge. Of 1,499 recorded activity events, over 50% were ambulation. At RICU discharge, patients were able to walk 212 ± 178 feet. Walk distance appeared to influence placement. Patients discharged home from the RICU were able to walk further (337 ± 130 feet) compared to those discharged to skilled nursing facilities and long-term acute care facilities (293 ± 124 feet and 138 ± 13 feet, respectively). This is the only study that provided details on feasibility and safety of initiating mobility intervention in a relatively early stage of critical illness. Importantly, the study reported that the multidisciplinary team was able to conduct the mobility intervention without staffing increases. However, the study did not provide detailed information to determine eligibility to initiate mobility for those patients who couldn't meet initial criteria and it lacked a control group. It is, therefore, premature to determine the benefit from the findings of this pilot feasibility study.

Though few studies are available to evaluate the effects of whole body physical therapy on mobility outcomes in PMV patients, and the studies that have been published, including the randomized controlled trials, had substantial limitations, findings consistently supported the benefits of whole body rehabilitation and risks appeared to be minimal. Additional studies are warranted to enhance understanding of the safety, feasibility and benefits of early whole body physical therapy and the optimal criteria and team composition for initiating such an intervention

Electrical stimulation

The goal of electrical stimulation (ES) is to improve exercise capacity via increasing peripheral muscle strength (Zanotti et al., 2003). With ES, the motor nerves are stimulated using low-voltage electricity to produce muscular contraction (Clini & Ambrosino, 2005). In patients with COPD and heart failure, this intervention has been shown to delay muscle wasting during immobility and promote recovery of muscle strength (Gosselin et al., 2003; Quittan et al., 2001), leading to the recommendation that ES be used as a type of physical training (Clini & Ambrosino, 2005). ES requires minimal cooperation, produces minimal cardiorespiratory stress and requires less staff involvement than conventional whole body physical therapy. Consequently, Clini & Ambrosino (2005) proposed use of this technique in critically ill patients.

We identified one randomized controlled study that tested use of this technique. Zanotti et al. (2003) examined the benefit of adding ES to active limb mobilization in COPD patients who were bed bound and mechanically ventilated for longer than 30 days. Patients who received systemic corticosteroids or neuromuscular blockade for longer than 5 days were excluded in order to control for potential neuromuscular weakness from these medications. The ES was applied when patients were in bed using bilateral surface electrodes placed on the quadriceps femoris and vastus glutei. Once the electrostimulator was on, the physical therapist started active limb mobilization. Therefore, muscle contraction occurred via both ES and limb movement. After 4 weeks, patients who received ES had a greater increase in muscle strength score (2.16 ± 1.02 vs. 1.25 ± 0.75 , $p = .02$) and required fewer days to transfer from bed to chair (10.75 ± 2.41 days vs. 14.33 ± 2.53 days, $p = .001$) than those who received physical therapy alone. The strengths of this study include its objective outcome measures, inclusion of patients with a homogenous diagnosis and exclusion of patients who received steroids or

neuromuscular blockade. However, such stringent eligibility criteria can also be a limitation. Because patients who were prescribed systemic steroids or neuromuscular blockade were excluded, it is unknown if ES can achieve the same benefits in patients who received these commonly prescribed medications. Including another group of patients who were on systemic steroids or neuromuscular blockade would provide stronger evidence.

Thus, evidence of the benefit of ES is promising but limited. Findings suggest that ES can benefit PMV patients while they are still bed bound and thus at an early stage of critical illness. In the above study ES was only applied to the lower limbs, but it might be useful for both upper and lower limb muscles. Because use of systemic steroid or neuromuscular blockade is common in the ICU, it is important to determine if ES can preserve or improve muscle strength in PMV patients who are prescribed such medications. Additional studies are warranted to enhance understanding of the safety and benefits of this intervention in PMV patients.

Arm exercise

Arm exercise consists of two types: 1) supported arm exercise, using arm ergometry, and 2) unsupported arm exercise, using free weights or stretch bands. In patients with COPD, both supported and unsupported arm exercise have been shown to improve arm endurance (Epstein et al., 1997; Epstein et al., 1995; Lake, Henderson, Briffa, Openshaw, & Musk, 1990; Martinez et al., 1993). However, the potential benefits of an arm exercise program in patients on PMV have received limited study.

Three of the reviewed studies include supported arm exercise (U. J. Martin et al., 2005) or unsupported arm exercise (Chiang et al., 2006; Nava, 1998) as a component of whole body physical therapy. Although it is not possible to independently evaluate the contribution of arm exercise, all three studies provide support for benefit. Notably, U. J. Martin et al. (2005) reported that an increase of 1 point in upper extremity motor strength score resulted in ~ 7 days reduction in weaning time.

One randomized controlled study (Porta et al., 2005) independently tested the effects of arm exercise. In this study, patients recently weaned from PMV were randomized to receive a supported arm exercise intervention in addition to physical therapy or physical therapy alone. The exercise intervention involved arm bicycling for a minimum of 20 min while sitting on the bed with the bicycle placed on the bedside table at shoulder level. Study outcome measures included exercise capacity, maximal inspiratory pressure (MIP), and symptoms (dyspnea, muscle fatigue) during exercise. Exercise capacity was measured using a symptom limited incremental test and an endurance test performed at 50% of maximal workload on the incremental test. When overall improvement was compared, the intervention group showed greater improvement in both the incremental (7.3 vs. 2.6 W, $p = .003$) and endurance tests (8 vs. 4 min, $p = .021$). Maximal inspiratory pressure (MIP) improved and dyspnea and muscle fatigue decreased, but the magnitude of change was not different between groups. Stepwise regression analysis showed only baseline MIP as a significant predictor of improvement. However, based upon the odds ratio (1.12, 1.07, respectively), it is difficult to conclude that baseline MIP could explain the improvement in exercise capacity. Moreover, because the intervention was targeting patients who were already weaned from PMV, evidence of benefit to patients who are still on mechanical ventilation is limited.

In summary, the independent benefit of arm exercise is difficult to evaluate, as this exercise program is commonly included in whole body rehabilitation. Because Porta et al. (2005) enrolled patients who had recently (< 90 hrs) weaned from PMV, it is likely that similar benefits could be shown in PMV patients. Arm exercise is attractive because it can be accomplished while patients are in bed, a factor that allows earlier introduction. There is also the potential to utilize leg bicycle exercise as an intervention while patients are in bed.

Inspiratory muscle training

Weakness in the diaphragm and accessory inspiratory muscles, e.g., intercostals, scalene, and sternocleidomastoids, is considered to be the most common contributor to weaning failure (Capdevila et al., 1998; Cluzel et al., 2000). Failure of the respiratory muscle pump may result from an increased load on the muscles and/or decreased neuromuscular capacity (Purro et al., 2000). Common causes of an increase in muscle load include changes in carbon dioxide production, work of breathing, dead space, and/or respiratory drive (Sprague & Hopkins, 2003). Neuromuscular capacity may be compromised due to neuromuscular dysfunction and/or decreased respiratory muscle strength and endurance (Chao & Scheinhorn, 1998).

Benefits from training the inspiratory muscles have been reported for patients with COPD (Larson, Kim, Sharp, & Larson, 1988; Nield, 1999), laryngeal cancer (Sapienza, Brown, Martin, & Davenport, 1999), cystic fibrosis (Sawyer & Clanton, 1993), congestive heart failure (Cahalin, Semigran, & Dec, 1997; Weiner, Waizman, Magadle, Berar-Yanay, & Pelled, 1999), neuromuscular disorders (Koessler et al., 2001), and cervical spinal cord injury (Liaw, Lin, Cheng, Wong, & Tang, 2000). In these studies, researchers used one of the following two types of inspiratory muscle training (IMT) devices. Resistance-training devices require the patient to breathe through an adjustable orifice of progressively decreasing diameter with the goal of increasing load on the respiratory muscles. With such devices, breathing pattern is important: long, slow breaths produce less resistance and, if the patient chooses this pattern, training will not be optimal (Belman, 1993). Threshold-training devices produce a pressure that remains constant over varying flow rates and is altered by adjusting tension on a spring (Larson et al., 1988). Such devices challenge patients to breathe with sufficient force to open a spring-loaded valve and maintain that force during inspiration in order to keep the valve open (A. D. Martin et al., 2002; Sprague & Hopkins, 2003).

Although the potential benefits of IMT were first described in the late 1980s (Aldrich et al., 1989), our search revealed few controlled studies testing the effects of this intervention. The 5 selected studies included 1 randomized controlled trial (Caruso et al., 2005), 3 prospective nonrandomized studies (Aldrich et al., 1989; A. D. Martin et al., 2002; Sprague & Hopkins, 2003), and 1 nonrandomized retrospective analysis that added IMT as a part of whole body physical therapy (U. J. Martin et al., 2005).

Caruso et al. (2005) randomized patients in a surgical ICU to usual care alone or usual care plus IMT accomplished by adjusting the ventilator sensitivity based on MIP. The intervention was well tolerated, with 86% of 167 sessions completed without distress. However, the study demonstrated no benefit in terms of weaning duration or reintubation rate. MIP showed a trend toward a modest increase in the intervention group and a decrease in the control group. Due to the small sample size and limited information regarding the training duration and subject characteristics, it is premature to judge the usefulness of this intervention based on this study.

Aldrich et al. (1989) tested the potential of improving weaning outcomes by adding twice daily inspiratory resistance training sessions to the weaning regimen. Training was accomplished by adding a resistance trainer (Pflex, Respironics, Inc., Murrysville, PA) to a nonrebreathing valve connected to the tracheotomy tube or ventilator circuit. The authors reported a significant increase in MIP and vital capacity and weaning success in 63% of the sample. Due to the small sample size and lack of a control group, it is also premature to determine the potential benefit of this intervention based on this study.

Similar success was reported by A. D. Martin et al. (2002) using a low-repetition, high-intensity IMT regimen accomplished with a threshold device (PEP, HealthScan Products, Cedar Gove, NJ). Although improvement in IMT pressure and a 90% weaning success rate were reported, it is difficult to determine whether the improvement resulted from the effect of IMT, the lengthy

training period (mean 44 days) or from the improvement in patients' underlying illnesses. The small sample size and lack of control group are other major limitations.

Sprague and Hopkins (2003) reported improvement in MIP and weaning success after use of IMT with a threshold device. However, because of the heterogeneous characteristics of the small sample, which varied in range of days on mechanical ventilation, and the lack of a control group, the strength of the evidence from this study is very low.

U. J. Martin et al. (2005) evaluated the benefits of IMT in combination with whole body physical therapy. Training was initiated using a threshold device when patients were able to breathe spontaneously for more than 2 hr. The regimen involved twice daily sessions with resistance set at one-third of the patient's maximum negative inspiratory force (NIF). The maximum NIF improved significantly. Because this study also included outcome measures directly related to limb muscle strength and ambulation, findings suggest a potential link between the benefits of IMT, weaning and mobility outcomes. Stepwise regression did not identify NIF as a significant predictor of weaning. However, the sample size was small ($n = 49$) and a large number of variables were entered into the regression model, which may have made it difficult to examine the independent effect of NIF on weaning success.

In summary, there is no evidence supporting the independent benefit of IMT in improving weaning outcomes. Although several studies have reported a potential contributory effect, none of these included a control group. The one randomized trial conducted using this technique reported no benefit. Given the design limitations and small sample size of prior studies, the potential independent or contributory benefit of IMT remains unknown.

Discussion

Skeletal muscle weakness and decreased functional status are widely recognized problems in individuals undergoing PMV. However, limited attention has been paid to systematically measuring benefits of mobility therapy in such patients. Many areas remain to be investigated before identifying optimal mobility interventions. Major findings of this review are that 1) few studies have objectively examined the outcomes of mobility interventions in patients with PMV, and 2) in particular, studies testing the feasibility and effectiveness of intervention in the early stages of critical illness are few in number.

The 10 studies in this review varied in quality. With the exception of whole body physical therapy, benefits remain uncertain. Only 5 randomized controlled studies were selected and all had limitations, including small sample size, heterogeneity of the sample, duration of intervention, choice of outcome variables and instruments. The duration of the intervention was not fully described in more than a half of the studies (Aldrich et al., 1989; Bailey et al., 2007; Caruso et al., 2005; U. J. Martin et al., 2005; Nava, 1998; Sprague and Hopkins, 2003). Therefore, it was hard to estimate how the duration of the intervention potentially affected mobility outcomes. The duration of the intervention was not fully described in more than a half of the studies (Aldrich et al., 1989; Bailey et al., 2007; Caruso et al., 2005; U. J. Martin et al., 2005; Nava, 1998) or reported in other studies (Chiang et al., 2006; Porta et al., 2005; Zanotti et al., 2003), making it difficult to estimate how the duration of the intervention may have affected mobility outcomes. Nevertheless, these studies provide valuable insights into the potential benefits of mobility interventions in PMV patients. In regard to study design, although randomized controlled trials are considered the gold standard, such trials may not be feasible due to ethical considerations, as they could deprive patients of a potentially beneficial therapy. In the randomized trial by Nava (1998), the authors noted the unequal sample size (3:1) between the intervention and control groups as a study limitation. However, in this study, a 1:1 group allocation was not accepted by the hospital ethics committee due to its potential disadvantage

to those allocated to the control group (Nava, 1998). Similarly, Porta et al. (2005) cited the lack of a no-intervention control group as a limitation. In the study by Chiang et al. (2006), patients who did not receive the intervention showed marked deterioration in muscle strength at 3 weeks, suggesting that use of no-intervention control group is not appropriate due to ethical concerns.

Except for the feasibility study by Bailey et al. (2006), no studies tested the effect of mobility interventions in the early stages of critical illness. In fact, most studies introduced the intervention after transfer to a rehabilitation-focused setting. Despite the observation that rapid loss of skeletal muscle strength occurs early in critical illness (Topp et al., 2002), most studies enrolled patients who had not received mobility interventions in the ICU setting (Chiang et al., 2006; U. J. Martin et al., 2005; Nava, 1998; Porta et al., 2005). According to Eskildsen's (2007) general review of long-term acute care, the main focus of this care is weaning from PMV. In many long-term acute care setting, the ability to tolerate spontaneous breathing trials was used as a marker of ability to tolerate initiation of mobility interventions. For example, U. J. Martin et al. (2005) reported that physical therapy was scheduled separately from weaning trials until patients could tolerate spontaneous breathing for > 4 hr. However, the approach of Bailey et al. (2007) differed from this traditional approach in that physical therapy was given higher priority. The mobility intervention was provided to patients who required a relatively high level of support ($\text{FiO}_2 \leq 0.6$, and $\text{PEEP} \leq 10 \text{ cm H}_2\text{O}$) as long as the investigators determined the patient was able to tolerate the therapy. In this study, adverse events occurred in less than 1 % of patients and were minor, for example, a fall to the knees without injury, systolic pressure < 90mmHg or > 200 mmHg, oxygen desaturation < 80%, and feeding tube removal. None resulted in extubation or additional therapy, costs or length of stay. Based on these findings, early initiation of physical therapy seems feasible and safe. However, this study is the only such report of safety and feasibility issues identified in our search, and the authors did not provide detailed criteria to determine eligibility for intervention initiation. Because of the importance of preventing loss of skeletal muscle strength, it is important to test strategies to provide mobility interventions earlier and to confirm their safety. This approach may require a shift in the current culture of critical care practice. In order to encourage such a shift, pilot studies are necessary to identify physiological criteria that will help to determine patients' readiness to initiate mobility interventions.

In this review, several techniques hold promise as early interventions. However, questions remain to be answered before these interventions can be integrated into standard care. For example, can ES be applied in earlier stages of critical illness? In the study reviewed (Zanotti et al., 2003), participants had been bed bound for at least 30 days prior to enrollment. Given the rapid deterioration in skeletal muscle strength during the first weeks of bed rest (Topp et al., 2002), testing the effect of ES in earlier stages of critical illness may provide valuable insight regarding a preventive intervention. In the case of supportive arm training, testing the feasibility of using an arm bicycle exercise in PMV patients who are not yet weaned from mechanical ventilation would be useful. Bicycle exercise could also be tested for the lower limbs.

Finally, the availability of reliable and valid instruments is the key to isolating the effects of mobility interventions. Many of the instruments used to document changes in physical response in the studies reviewed here were developed for individuals with chronic disorders who are assumed to be at a higher functional level than PMV patients. These instruments, therefore, may have limitations for studying this patient population. Each instrument needs further evaluation and possible modification to insure that it can detect significant clinical changes in PMV patients. The development of more sensitive instruments would be of great benefit to this crucial area of research.

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Table 1

Summary of Studies Testing Mobility Interventions

Study	Design	Sample	Setting	Intervention	Significant Mobility Outcomes
Aldrich et al. (1989)	Prospective nonrandomized study	N = 27 (7 neuromuscular disease; 20 chronic lung disease), on MV 12.8 ± 13.0 weeks	Two ICUs & one rehabilitation unit	<ul style="list-style-type: none">• Content: IMT with inspiratory resistance training when T-piece tolerance was > 2 hr• Frequency: 2–14 sessions per week; increased resistance as tolerated from 8 to 28cm H₂O• Duration of session: up to 30 min• Duration of intervention: unknown	↑ MIP, ↑ VC, 63% weaned
Nava (1998)	Randomized trial	Respiratory failure secondary to COPD exacerbation; n = 60 intervention group, 78% ventilated at entry; n = 20 control group, 70% ventilated at entry	Respiratory ICU	<ul style="list-style-type: none">• Content: 1) passive range of motion, 2) early ambulation, 3) respiratory and lower skeletal muscle training, and 4) complete lower limb training on a treadmill.	↑ 6MWT, ↑ MIP, ↓ Dyspnea VAS
A. D. Martin et al. (2002)	Prospective nonrandomized case study	N = 10, on MV for 34 ± 31 days	Unknown	<ul style="list-style-type: none">• Frequency: twice daily• Duration of session: 30–45 min• Duration of intervention: unknown• Content: IMT with threshold device• Frequency: 6 breaths/set, 3–5 sets/day, 5–7 days/week• Duration of session: 10 min• Duration of intervention: 44 ± 43 days	↑ IMT pressure, ↑ spontaneous breathing time, 9/10 patients weaned from MV

Study	Design	Sample	Setting	Intervention	Significant Mobility Outcomes
Sprague & Hopkins (2003)	Prospective nonrandomized case study	$N = 6$, varied diagnoses, MV for 18–221 days	Surgical ICU	<ul style="list-style-type: none"> Content: IMT with threshold device Frequency: 6–8 breaths/set, 4 sets/day, 5–10 min rest between sets, 6–7 days/week Duration of session: 30–50 min (including resting period) Duration of intervention: unknown 	All weaned from MV after 9–18 days, ↑ IMT pressure (195%), ↑ MIP (140%)
Zanotti et al. (2003)	Randomized trial	COPD, bed bound; $n = 12$ intervention group, ICU 52 ±15 days at entry; $n = 12$ control group, ICU 47 ±19 days at entry	Respiratory high-dependency care unit	<ul style="list-style-type: none"> Content: usual care = physical therapy; intervention = physical therapy + ES for 5 min at 8-Hz pulse width 250 μs, then 25 min at 35-Hz pulse width 350 μs. Frequency: 5 days/week Duration of session: up to 30 min per session depending on tolerance Duration of intervention: 4 weeks Content: IMT by adjusting MV trigger sensitivity Frequency: 2 sessions daily with MV trigger sensitivity set at 20% MIP; increase to 40% if tolerated Duration of session: up to 30 min per session Duration of intervention: unknown Content: progressive physical therapy from trunk control to ambulation, IMT with threshold device 	<p>↑ 5-point motor strength score, ↓ days to transfer bed to chair</p> <p>No effect on MIP, weaning status, or reintubation rate</p> <p>↑ 1 point in upper-extremity motor strength scale resulted in ~ 7 day ↓ in weaning time.</p>
Caruso et al. (2005)	Randomized trial	Varied diagnoses; $n = 12$ intervention group, $n = 13$ control group	Surgical ICU		
U.J.Martin et al. (2005)	Retrospective analysis	$N = 49$, varied diagnoses, MV 18.1 ± 7 days at entry, failed ≥ 2 weaning attempts	Ventilatory rehabilitation unit		

Study	Design	Sample	Setting	Intervention	Significant Mobility Outcomes
Porta et al. (2005)	Randomized trial	Varied diagnoses, weaned < 48–96 hrs., <i>n</i> = 32 intervention group, <i>n</i> = 34 control group	Respiratory intermediate ICU	<ul style="list-style-type: none"> • Frequency: 5 days/week; begin once daily; twice daily when able to tolerate > 45 min per session. • Duration of session: 30–60 min physical therapy, and 15 min IMT • Duration of intervention: unknown • Content: usual care = physical therapy; intervention = physical therapy + supported arm training on arm ergometer • Frequency: daily • Duration of session: 20 min • Duration of intervention: 2 weeks • Content: usual care = no intervention; 	Upper motor strength contribution was greater than those of corticosteroids and paralytics.
Chiang et al. (2006)	Randomized trial	Varied diagnoses; <i>n</i> = 17 intervention group, MV 46 (range 31–81) days, <i>n</i> = 15 control group, MV 52 (range 23–81) days	Respiratory ICU	<ul style="list-style-type: none"> • intervention = upper- and lower-extremity exercise, bedside functional training, ambulation, and diaphragmatic breathing exercise. • Frequency: 5 days per week • Duration of session: not stated • Duration of intervention: 6 weeks 	<p>↑ symptom limited incremental test (W), ↑ endurance test (min), ↓ dyspnea, ↓ muscle fatigue, ↑ MIP</p> <p>↑ limb muscle strength (dynamometer), ↑ MIP, ↑ BI, ↑ FIM; 9 patients in intervention group completed 2MWT at 6 weeks (42.9 ± 12.7 m)</p>
Bailey et al. (2007)	Prospective cohort study	<i>N</i> = 103, varied diagnoses, MV 19 ± 15 days at entry	Respiratory ICU	<ul style="list-style-type: none"> • Content: early activity protocol initiated after evaluation within ≤ 24 hr of RICU admission; progression from trunk 	1,449 activity events: sit on bed (16%), sit in chair (31%), and ambulate (53%); at RICU discharge, 70% were able to walk > 100 ft

Study	Design	Sample	Setting	Intervention	Significant Mobility Outcomes
				control to ambulation as tolerated • Frequency: twice daily • Duration of session: not stated • Duration of intervention: unknown	

Note. 2MWT = 2-min walk test, 6MWT = 6-min walk test, BI = Barthel index, COPD = chronic obstructive pulmonary disease, ES = electrical stimulation, FIM = functional independence measurement, ICU = intensive care unit, IMT = inspiratory muscle training, MEP = maximal expiratory pressure, MIP, maximal inspiratory pressure, MV = mechanical ventilation, VAS, visual analogue scale, VC = vital capacity.