## Effects of Physical Training on Functional Status in Patients With Prolonged Mechanical Ventilation

Background and Purpose. Patients requiring prolonged mechanical ventilation (PMV) are frequently deconditioned because of respiratory failure precipitated by the underlying disease, the adverse effects of medications, and a period of prolonged immobilization. The effects of 6 weeks of physical training on the strength of respiratory and limb muscles, on ventilator-free time, and on functional status in patients requiring PMV were examined. Subjects. Thirty-nine patients with PMV were initially enrolled in the study and were assigned to either a treatment group (n=20) or a control group (n=19). Three subjects in the treatment group and 4 subjects in the control group died during the 6-week intervention period and thus their data were excluded from the final analysis. Methods. Subjects in the treatment group received physical training 5 days a week for 6 weeks. Strength of respiratory and limb muscles, ventilator-free time, and functional status, which was measured by the Barthel Index of Activities of Daily Living (BI) and Functional Independence Measure (FIM), were examined at baseline and at the third and sixth weeks of the study period. Results. Respiratory and limb muscle strength improved significantly at the third and sixth weeks in the treatment group compared with baseline measurements. Total BI and FIM scores increased significantly in the treatment group and remained unchanged in the control group. Effect sizes of the BI and FIM scores were 2.02 and 1.93, respectively, at the sixth week. Discussion and Conclusion. The results show that a 6-week physical training program may improve limb muscle strength and ventilator-free time and thus improve functional outcomes in patients requiring PMV. [Chiang LL, Wang LY, Wu CP, et al. Effects of physical training on functional status in patients with prolonged mechanical ventilation. Phys Ther. 2006;86:1271-1281.]

**Key Words:** Barthel Index of Activities of Daily Living, Functional Independence Measure, Mechanical ventilation, Muscle strength, Respiratory muscles.

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Ithough advances in critical care and mechanical ventilation over the past 2 decades have resulted in the increased survival of patients who are critically ill, some patients develop the need for prolonged mechanical ventilation (PMV). Patients requiring PMV are frequently deconditioned because of respiratory failure precipitated by the underlying disease, the adverse effects of medications, and a period of prolonged immobilization.<sup>1,2</sup> Patients requiring PMV often have substantial weakness of the respiratory and limb muscles that further impairs their functional status and health-related quality of life.<sup>3</sup>

Alternative care settings for patients requiring PMV have been set up in order to wean them off the ventilator. Outcome studies in patients requiring PMV in these care units have focused more on the weaning outcome, disposition, and survival data, whereas only limited information is available on functional status assessed using validated instruments.<sup>4–7</sup> To the best of our knowledge, only one preliminary report has evaluated the functional status of patients requiring PMV using certain items in the Functional Independence Measure (FIM).<sup>8</sup>

The physical and psychological benefits of physical training on a wide range of patient groups are well established. Results of previous case reports and nonrandomized controlled studies have demonstrated that patients who have significantly reduced body functions after weaning from PMV needed a physical training program after their discharge from the hospital.<sup>9–11</sup> Although physical training has been recognized as an important component in the care of patients requiring PMV,<sup>11,12</sup> randomized controlled studies to evaluate the effects of physical training on muscle strength (the force-generating capacity of muscle) and functional status outcomes are lacking.

We hypothesized that a 6-week physical training program could lead to improvements in respiratory and limb muscle strength, ventilator-free time, and functional status of patients requiring PMV. A controlled design was used to test this hypothesis, and the relationships between changes in these parameters also were explored.

### Method

### Subjects

Subjects were recruited from the respiratory care center (RCC, a post-intensive care unit) in a medical center (Tri-Service General Hospital, Taipei, Taiwan) between January and August 2003. Consecutive patients were screened by reviewing their charts and interviewing them. Inclusion criteria required the subjects to be mentally alert, to have acceptable hemodynamic stability (defined as a lack of hypotension or a need for only low-dose pressors<sup>13</sup>), and to be mechanically ventilated for more than 14 days. Patients with comorbid medical conditions (eg, neurological diseases) or who were under any sedative or paralytic agents that would interfere with strength measurements and limb exercises were excluded. Using a sample size calculation program

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#### Table 1.

Characteristics of Subjects in the Control and Treatment Groups<sup>a</sup>

Parameter	Control Group (n=15)	Treatment Group (n=17)	Р
Sex (M/F)	12/3	12/5	.376
Age, y	79 (72.5–82.8)	75 (63.0–80.3)	.457
Ventilator used, d	52 (22.8–80.8)	46 (31.0–80.8)	.569
Albumin, g/dL	3.1 (2.6–3.4)	3.0 (2.9–3.1)	.902
Hemoglobin, g/dL	10.7 (10.1–11.9)	10.5 (9.4–11.8)	.410
Blood urea nitrogen, mg/dL	20 (13.8–35.3)	27 (20–43.8)	.140
Creatinine, mg/dL	0.7 (0.6–1.0)	1.2 (0.7–1.3)	.228
Classification of Gillespie et al, <sup>14</sup> n (%) Previous lung disease Postoperative Multisystem failure Acute lung injury Other medical causes	7 (46.7) 4 (26.7) 2 (13.3) 1 (6.7) 1 (6.7)	8 (47.1) 4 (23.5) 2 (11.8) 2 (11.8) 1 (5.9)	

<sup>a</sup> Data are presented as median values with 25%-75% quartiles in parentheses.

(SigmaStat version 3.0\*)—with a group mean difference of 10 points for the Barthel Index of Activities of Daily Living (BI) (SD=10), an alpha of .05, and a statistical power of 0.8—we calculated that a sample of 17 subjects per group was required.

A total of 39 patients who met the inclusion criteria, agreed to participate, and had signed an informed consent form were initially enrolled in the study and were assigned, using alternate numbers, to either a treatment group (n=20) or a control group (n=19). The examiner was blinded to the group assignments. None of subjects had received any rehabilitation prior to enrollment in the study, and all subjects underwent identical protocol-directed weaning, which was implemented by respiratory therapists under the supervision of the chest or critical care physicians during the study period. The distribution of diagnosis was analyzed by category as described by Gillespie et al.<sup>14</sup>

Three subjects in the treatment group and 4 subjects in the control group died during the 6-week intervention period and thus their data were excluded from the final analysis. Baseline characteristics of the 32 patients who completed the study are outlined in Table 1. The age range of the study sample was 53 to 88 years for the control group and 50 to 87 years for the treatment group. Subjects in both groups received a tracheostomy.

### Physical Training

Supervised training sessions were conducted by an experienced physical therapist 5 times per week for 6 weeks for subjects in the treatment group. Physical training included bedside strengthening exercises for the upper and lower extremities and functional activity retraining. All subjects in the treatment group either continued to receive mechanical ventilator assistance or used an oxygen supplement during training. Exercise intensity was judged based on the Borg Rating of Perceived Exertion Scales (RPE). The rating of perceived exertion was set at 10 to 11 for the first week of training and then progressed to 12 to 13 for the next 5 weeks. Based on subjects' physiological responses to the training, rate of progression was then adjusted by the physical therapist.

Upper-extremity exercises included range-of-motion (ROM) exercises for the wrist; elbow and shoulder flexion

and extension; and shoulder abduction, adduction, and internal and external rotation, with 10 repetitions of each motion per set for 2 sets. Subjects initially performed these exercises against gravity in a supine position and progressed to a sitting position as tolerated. These exercises then were advanced to repetitions against resistance using weights (0-600 g). Lowerextremity exercises included ROM exercises for ankle dorsiflexion and plantar flexion, hip and knee flexion and extension, and straight leg raising, with 10 repetitions of each motion per set for 2 sets in the supine position. Bedside functional retraining included turning from side to side on the bed; transfers to and from the bed, chair, and wheelchair; and coming to a standing position. Ambulation was instituted as early as subjects could tolerate it. Subjects were allowed to rest between training sets, and pulse oxygen saturation (Spo<sub>2</sub>) and any sign or symptom that indicated intolerance were closely monitored throughout the training session.

Diaphragmatic breathing exercises were facilitated during spontaneous breathing hours and practiced in the supine, semi-Fowler (sitting at a 45° angle), and sitting positions. The physical therapist placed one hand over the subjects' abdomen and the other on the upper chest. Subjects then were instructed to observe the increased hand motion over the abdominal area during inspiration while keeping the movement of the upper chest as small as possible. The physical therapist then performed a quick stretch inward and upward in the abdomen area at the end of expiration. Subjects and their primary caregivers were instructed in this technique as a home program, which began with three 10-minute sessions a day and was progressed as tolerated.

<sup>\*</sup> SPSS Inc, 233 S Wacker Dr, Chicago, IL 60606.

Subjects in both groups received standard therapy for the underlying disease and possible complications, nutritional support, and patient care, which included proper positioning and assistance with activities of daily living (ADL), such as bathing and toileting. The promotion of physical mobilization (eg, exercise or ambulation) was usually encouraged verbally but not routinely performed by the nursing or medical staff. Only the subjects in the treatment group had intervention provided by a physical therapist.

#### **Measurements**

Respiratory muscle strength was assessed by measuring maximum pressures through the tracheostomy tube after the morning care. Respiratory tract and oropharyngeal secretions were suctioned prior to the measurements. The balloon cuff pressure was checked for any possible leak. The subjects were tested with the head of the bed elevated to 45 degrees or higher, if possible, and were encouraged to make a maximal effort. Maximum inspiratory pressure (PImax) was measured at residual volume, whereas maximum expiratory pressure (PEmax) was measured at total lung capacity with an aneroid manometer (model  $4103^{\dagger}$ ) attached to the tracheostomy tube.15 The hole in the extension tubing was occluded while the subjects inspired or expired maximally for 1 to 3 seconds. This procedure was repeated 3 to 5 times, and the highest 3 repeatable values were averaged and recorded as the subjects' volitional PImax and PEmax.<sup>16</sup>

Upper- and lower-extremity muscle strength was assessed by using a handheld dynamometer (Commander PowerTrack II<sup>‡</sup>). The intraobserver or interobserver reliability of data obtained during muscle strength testing was done with 5 subjects. The intraclass correlation coefficients (ICCs) were .91 and .83 for intraobserver and interobserver reliability, respectively. The shoulder flexor, elbow flexor, and knee extensor muscle groups were included in the measurements. Standard test positions were modified because most subjects in this study were using a mechanical ventilator and were unable to sit up at initial examination. The shoulder and elbow flexors were tested in the semi-Fowler position. The isometric force of the shoulder flexors was tested with the shoulder flexed 90 degrees and the elbow in extended position. The dynamometer was placed just proximal to the epicondyles of the humerus, and the subjects were stabilized at the axillary region. The isometric force of the elbow flexors was tested with the elbow flexed 90 degrees, the forearm supinated, and the shoulder in neutral position; the dynamometer was placed just proximal to styloid processes of ulna and radius, and the subjects were stabilized at the superior aspect of the arm.  $^{\rm 17}$ 

All subjects in the study received mechanical ventilation through the tracheostomy tube; therefore, the recommended test position (ie, prone position) for the knee extensors was modified. The test position for the knee extensors was modified to the supine position, with the knee slightly flexed at 20 to 30 degrees, a roller behind the knee, the ankle not touching the bed, and the hands resting on the lap.<sup>18</sup> The dynamometer was placed just proximal to the malleoli of the tibia and fibula.<sup>17</sup> The dynamometer shaft was held perpendicular to the tested limb segment, and the tester applied all manual stabilization. All measurements were performed 3 times using isometric "make" tests. The subjects were asked to increase force to a maximum effort over a 2-second period, maintain the maximum effort for approximately 5 seconds, and then stop. This procedure has been shown to yield reliable measurements and to be adequate for measuring maximum isometric strength.<sup>19</sup> The peak force (in pounds) of 3 tests was recorded and converted into kilograms. Two minutes of rest were allowed between repeated readings.

Two instruments, the BI<sup>20</sup> and the FIM,<sup>21</sup> with proven good reliability and validity were used by an experienced physical therapist to assess the subjects' functional status.<sup>22–24</sup> The BI is composed of 10 items with varying weights. Two items (grooming and bathing) were evaluated with a 2-point scale (0 and 5 points); 6 items (feeding, dressing, bowel function, bladder function, toilet use, and stairs) were evaluated with a 3-point scale (0, 5, and 10 points); and 2 items (transferring from bed to chair and back and walking on a level surface) were evaluated with a 4-point scale (0, 5, 10, and 15 points). The BI score was calculated by summing each item score with a range of 0 (completely dependent) to 100 (independent in basic ADL). Higher scores represented a higher degree of independence.

The FIM instrument consists of 18 items that assesses a person's levels of independence. Each item is rated with a score from 1 (total assistance) to 7 (complete independence). The FIM identifies levels of independence in self-care, sphincter control, transfers, locomotion, communication, and social cognitive function. The FIM items were organized into 4 subscales (ie, ADL, sphincter management, mobility, and executive functioning), based on impairment-specific dimensions.<sup>25</sup> The ADL subscale included eating, grooming, bathing, dressing the upper body, dressing the lower body, and toileting. The sphincter management. The mobility subscale included bladder and bowel management. The mobility subscale included bladder shower transfer, walking/wheelchair management, and

<sup>&</sup>lt;sup>†</sup> Boehringer Laboratories Inc, PO Box 870, Norristown, PA 19404.

<sup>&</sup>lt;sup>‡</sup> JTech Medical Industries, 470 Lawndale Dr, Suite G, Salt Lake City, UT 84115.

stair climbing. The executive functioning subscale included comprehension, expression, social interaction, problem solving, and memory.

If a subject could ambulate and tolerate being without the ventilator for at least 1 hour, a 2-minute walk test was performed, with vital signs and  $\text{Spo}_2$  closely monitored. Subjects were asked to walk at their comfortable walking speed. Oxygen supplementation and assistive devices (eg, walker, cane) were used if needed during the test. Subjects were advised that they could rest, by sitting or standing, at any point during the course of walking a 50-m rectangular hallway around the periphery of the RCC unit. The distance walked in 2 minutes was recorded.

In both groups, limb and respiratory muscle strength were measured and the BI and FIM were administered at baseline (first physical therapist visit after study entry) and at the third and sixth weeks of the study. Preadmission functional status was assessed retrospectively using the BI, based on the information provided by the subjects or primary care providers. The time (in hours) that the subjects were free from the mechanical ventilator during the spontaneous breathing trials (ventilatorfree time) also was recorded.

#### Data Analysis

The results are presented as medians with 25%-75% quartiles. The SPSS for Windows statistical package (version 11.0\*) was used for data analysis. A Friedman repeated-measures analysis of variance on ranks was used to determine the differences within groups across baseline and the third and sixth weeks. A Mann-Whitney Utest was used to assess the differences between the 2 groups at baseline and the third and the sixth weeks and the differences among the baseline characteristics of the 2 groups. Spearman correlation coefficients were used to examine the relationship between changes in muscle strength, ventilator-free time, and functional scales after 6 weeks of physical training. To determine the magnitude of differences between the treatment and control groups, effect sizes were calculated as the group mean differences divided by pooled standard deviations. A P of  $\leq .05$  was considered statistically significant.

### Results

Subjects in the control and treatment groups had been mechanically ventilated for a median of 52 and 46 days, respectively. No significant differences in subject characteristics between the control and treatment groups were observed (Tab. 1). The distribution of diagnosis also was not different between the 2 groups; 46.7% and 47.1% of subjects in the control and treatment groups, respectively, had previous lung disease according to the classification of Gillespie et al<sup>14</sup> (Tab. 1).

Table 2 displays the median muscle strength, with 25% to 75% quartile values, of the limb and respiratory muscles for both groups at baseline and the third and sixth weeks of the study. The limb strength increased significantly in the treatment group (P<.001) at the third and sixth weeks compared with baseline. Strength of the 3 tested muscle groups were the same at baseline in both groups. After 3 and 6 weeks of physical training, however, the strength of all 3 muscle groups tested was significantly greater in the treatment group than in the control group. The effect sizes at the third week of intervention were 0.77 (95% confidence interval [CI]=0.03-1.47) for the shoulder flexors, 1.36 (95% CI=0.56-2.10) for the elbow flexors, and 0.94 (95% CI=0.19-1.65) for the knee extensors.

The limb strength increased further in the treatment group (P < .05) from the third week to the sixth week of physical training (Tab. 2). The effect sizes were 1.48 (95% CI=0.66-2.22) for the shoulder flexors, 1.82 (95% CI=0.95-2.59) for the elbow flexors, and 1.26 (95% CI=0.47-1.99) for the knee extensors after 6 weeks of intervention. In contrast, the limb strength in the control group deteriorated significantly at both third and sixth weeks of the study period compared with baseline.

The respiratory muscle strength (ie, PImax and PEmax) was similar in both groups at baseline. At the third and sixth weeks of the study period, PImax and PEmax increased significantly (P < .01) in the treatment group and decreased significantly ( $P \le .001$ ) in the control group compared with baseline. Both PImax and PEmax were significantly greater in the treatment group than in the control group after 6 weeks of physical training. The mean effect sizes were 1.45 (95% CI=0.63-2.18) for PImax and 1.26 (95% CI=0.47–1.99) for PEmax after the 6-week intervention. At the end of the 6-week study period, 8 subjects (47%) in the treatment group and 3 subjects (20%) in the control group were able to be removed from the ventilator for at least 12 hours per day. The ventilator-free time increased an average of 8.9 hours (P < .01) in the treatment group and 4.8 hours (P=.1) in the control group after 6 weeks compared with baseline.

Table 3 displays the medians (and 25%-75% quartile values) for BI and FIM scores of both subject groups. The median BI score decreased significantly (P<.001) compared with the pre-admission score at the first physical therapy visit (ie, baseline) in both groups. The BI scores and FIM total and subscale scores were not different between the 2 groups at baseline. After 3 and 6 weeks of physical training, however, all functional scores were significantly greater in the treatment group than in the control group except executive functioning (which was significant only after 6 weeks). The overall effect

	Baseline		Third Week		Sixth Week	
	Control Group	Treatment Group	Control Group	Treatment Group	<b>Control Group</b>	Treatment Group
Shoulder flexors, kg	2.0 (1.4–4.5)	3.2 (2.2–4.2)	0.9 (0.7–3.1) <sup>6</sup>	4.1 (3.2–5.6) <sup>b,c</sup>	0.9 (0–1.8) <sup>b,d</sup>	4.5 (4.0–5.8) <sup>b,c,d</sup>
Elbow flexors, kg	4.5 (2.1–6.0)	4.3 (3.2–6.0)	1.8 (1.2–3.2) <sup>6</sup>	6.6 (4.5–8.0) <sup>b,c</sup>	1.1 (0.7–3.2) <sup>b</sup>	7.3 (5.4–7.8) <sup>b,c,d</sup>
Knee extensors, kg	4.1 (2.3–6.0)	4.1 (3.1–7.5)	2.0 (1.1–4.5) <sup>b</sup>	6.6 (4.0–8.7) <sup>b,c</sup>	1.8 (0.7–3.0) <sup>b,d</sup>	7.3 (4.4–8.9) <sup>b,c</sup>
PImax, cm $H_2O$	38.0 (29.0–59.3)	46.0 (30.0–60.0)	34.0 (27.0–45.0)	58.0 (35.0–63.5) <sup>b</sup>	30.0 (25.0–42.0) <sup>b</sup>	60.0 (40.5–71.5) <sup>b,c,d</sup>
PEmax, cm $H_2O$	42.0 (30.5–56.5)	45.0 (37.0–64.5)	32.0 (27.0–47.0)	58.0 (45.0–71.0) <sup>b,c</sup>	35.0 (18.0–45.0)	62.0 (49.5–72.0) <sup>b,c,d</sup>
Ventilator-free time, hr	(00) 0	0 (0-0)	0 (0–21) <sup>b</sup>	6 (1–12) <sup>b</sup>	(0-0) 0	6 (3–13) <sup>6</sup>
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**Table 2.** Comparison of Limb and Respiratory Muscle Strength at Baseline at the Third and Sixth Weeks of Rehabilitation Between Control and Treatment Groups<sup>a</sup>

Data are presented as median values with 25%-75% quartiles in parentheses. Pimax=maximum inspiratory pressure, PEmax=maximum expiratory pressure.

P < .05, compared with baseline.

 $^{e}$  P<.05, compared with control group.  $^{d}$  P<.05, compared with third week.

# Table 3.

Values for Functional Status Measures (Barthel Index of Activities of Daily Living [BI] and Functional Independence Measure [FIM]) at Pre-admission, Baseline, and the Third and Sixth Weeks of Physical Training for the Control and Treatment Groups<sup>a</sup>

Control GroupTreatment GroupTreatment GroupTreatment GroupTreatment GroupTreatment GroupTreatment GroupB195.0 [90.0-100.0] 95.0 [53.8-100.0]0.0 [0.0-5.0]5.0 [0.0-10.0]5.0 [0.0-8.8]*200 [15.0-31.3]*d*0.0 [0.0-8.8]*35.0 [20.0-55.0]*d*F1M* $6.0 [6.0-6.0]$ $6.0 [6.0-6.0]$ $6.0 [6.0-6.3]$ $6.0 [6.0-6.8]$ $11.0 [9.0-13.5]^{d,e}$ $6.0 [6.0-6.8]$ $13.0 [10.0-19.0]^{d,e,f}$ F1M* $ADL$ $2.0 [5.0-5.0]$ $5.0 [5.0-5.0]$ $5.0 [5.0-5.0]$ $5.0 [5.0-5.0]^{d,e,f}$ $6.0 [6.0-6.8]$ $5.0 [5.0-5.0]^{d,e,f}$ Sphincter $ADL$ $2.0 [5.0-5.0]$ $5.0 [5.0-5.0]$ $5.0 [5.0-5.0]^{d,e,f}$ $5.0 [5.0-5.0]^{d,e,f}$ $9.0 [7.8-12.5]^{d,e,f}$ MobilityExecutive $2.0 [1.3-22.5]$ $2.0 [16.5-20.3]$ $2.0 [19.0-24.3]^{d,e,f}$ $9.0 [7.8-12.5]^{d,e,f}$ Total score $13.0 [11.3-22.5]$ $2.0 [16.5-20.3]$ $2.0 [19.0-24.3]^{d,e,f}$ $9.0 [7.8-12.5]^{d,e,f}$ Total score $13.0 [24.3-37.0]$ $34.0 [30.3-38.3]$ $28.0 [22.0-53.5]^{d,e,f}$ $49.0 [45.0-66.3]^{d,e,f}$		Pre-admission	Baseline		Third Week		Sixth Week	
95.0 (90.0-100.0) 95.0 (53.8-100.0) 0.0 (0.0-5.0) 5.0 (0.0-10.0) 0.0 (0.0-8.8)° 20.0 (15.0-31.3) <sup>c.d.e</sup> 0.0 (0.0-8.8)°   6.0 (6.0-6.0) 6.0 (6.0-7.3) 6.0 (6.0-6.8) 11.0 (9.0-13.5) <sup>d.e</sup> 6.0 (6.0-6.8)   2.0 (5.0-5.0) 5.0 (5.0-5.0) 5.0 (5.0-5.0) 5.0 (5.0-5.0) 7.0 (6.0-9.0) <sup>d.e</sup> 5.0 (5.0-5.0)   19.0 (11.3-22.5) 20.0 (16.5-20.3) 14.0 (9.3-20.0) 22.0 (19.0-53.3) <sup>d.e</sup> 26.0 (19.5-20.0)   33.0 (24.3-37.0) 34.0 (30.3-38.3) 28.0 (22.0-35.8) 45.0 (40.0-53.5) <sup>d.e</sup> 26.0 (19.5-35.5) <sup>d.e</sup>		Control Group Treatment Group	Control Group	Treatment Group	Control Group	Treatment Group	Control Group	Treatment Group
6.0 ( $6.0-6.0$ ) $6.0$ ( $6.0-5.3$ ) $6.0$ ( $6.0-6.8$ ) $11.0$ ( $9.0-13.5$ ) $6.0$ ( $6.0-6.8$ ) $2.0$ ( $2.0-3.0$ ) $2.0$ ( $2.0-5.3$ ) $2.0$ ( $2.0-4.5$ ) $5.0$ ( $3.5-8.0$ ) $2.0$ ( $5.0-5.3$ ) $5.0$ ( $5.0-5.0$ ) $5.0$ ( $5.0-5.0$ ) $5.0$ ( $5.0-5.0$ ) $7.0$ ( $6.0-9.0$ ) $4.0$ $19.0$ ( $11.3-22.5$ ) $20.0$ ( $16.5-20.3$ ) $14.0$ ( $9.3-20.0$ ) $22.0$ ( $19.0-24.3$ ) $13.0$ ( $6.5-20.0$ ) $33.0$ ( $24.3-37.0$ ) $34.0$ ( $30.3-38.3$ ) $28.0$ ( $22.0-35.8$ ) $45.0$ ( $40.0-53.5$ ) $26.0$ ( $19.5-35.5$ )	BI	95.0 (90.0–100.0) 95.0 (53.8–100.0)	0.0 (0.0–5.0)	5.0 (0.0–10.0)		20.0 (15.0–31.3) <sup>c,d,e</sup>	0.0 (0.0–8.8) <sup>c</sup>	35.0 (20.0–55.0) <sup>c,d,e,f</sup>
$6.0 (6.0-6.0)$ $6.0 (6.0-7.3)$ $6.0 (6.0-6.8)$ $11.0 (9.0-13.5)^{d,a}$ $6.0 (6.0-6.8)$ $2.0 (2.0-3.0)$ $2.0 (2.0-5.3)$ $2.0 (2.0-4.5)$ $5.0 (3.5-8.0)^{d,a}$ $2.0 (2.0-5.3)$ $5.0 (5.0-5.0)$ $5.0 (5.0-5.0)$ $5.0 (5.0-5.0)$ $7.0 (6.0-9.0)^{d,a}$ $5.0 (5.0-5.0)$ $19.0 (11.3-22.5)$ $20.0 (16.5-20.3)$ $14.0 (9.3-20.0)$ $22.0 (19.0-24.3)^d$ $13.0 (6.5-20.0)$ $33.0 (24.3-37.0)$ $34.0 (30.3-38.3)$ $28.0 (22.0-35.8)$ $45.0 (40.0-53.5)^{d,a}$ $26.0 (19.5-35.5)$	FIMb							
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	ADL		6.0 (6.0-6.0)	6.0 (6.0–7.3)	6.0 (6.0-6.8)	11.0 (9.0–13.5) <sup>d,e</sup>	6.0 (6.0-6.8)	13.0 (10.0–19.0) <sup>d,e,f</sup>
5.0 (5.0–5.0) 5.0 (5.0–5.0) 5.0 (5.0–5.0) 5.0 (5.0–5.0) 7.0 (6.0–9.0) $^{d,e}$ 19.0 (11.3–22.5) 20.0 (16.5–20.3) 14.0 (9.3–20.0) 22.0 (19.0–24.3) $^{d}$ 33.0 (24.3–37.0) 34.0 (30.3–38.3) 28.0 (22.0–35.8) 45.0 (40.0–53.5) $^{d,e}$	Sphincter		2.0 (2.0–3.0)	2.0 (2.0–5.3)	2.0 (2.0-4.5)	5.0 (3.5–8.0) <sup>d,e</sup>	2.0 (2.0–5.3)	6.0 (4.8–8.0) <sup>d,e,f</sup>
19.0 (11.3–22.5) 20.0 (16.5–20.3) 14.0 (9.3–20.0) 22.0 (19.0–24.3) <sup>d</sup> 33.0 (24.3–37.0) 34.0 (30.3–38.3) 28.0 (22.0–35.8) 45.0 (40.0–53.5) <sup>d,e</sup>	Mobility		5.0 (5.0-5.0)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	7.0 (6.0–9.0) <sup>d,e</sup>	5.0 (5.0-5.0)	9.0 (7.8–12.5) <sup>d,e,f</sup>
33.0 (24.3–37.0)   34.0 (30.3–38.3)    28.0 (22.0–35.8)   45.0 (40.0–53.5) <sup>d,e</sup>	Executive			20.0 (16.5–20.3)	14.0 (9.3–20.0)	22.0 (19.0–24.3) <sup>d</sup>	13.0 (6.5–20.0)	24.0 (20.8–27.3) <sup>d,e,f</sup>
	Total score		33.0 (24.3–37.0)	34.0 (30.3–38.3)	28.0 (22.0–35.8)	45.0 (40.0–53.5) <sup>d,e</sup>		49.0 (45.0–66.3) <sup>d,e,f</sup>

<sup>b</sup> ADL=cating, grooming, bathing, dressing upper body, dressing lower body, and toileting; Sphincter=bladder management and bowel management; Mobility=bed-to-chair/wheelchair transfer, toilet transfer, tub/ shower transfer, walking/wheelchair management, and stair climbing; Executive=comprehension, expression, social interaction, problem solving, and memory.

P < .05, compared with preadmission.

<sup>4</sup> P<05, compared with baseline. "P<05, compared with control group. P<05, compared with third week.

#### Table 4.

Spearman Correlation Coefficients (r) Between Changes (Sixth Week–Baseline) of Muscle Strength, Ventilator-Free Time, and Functional Scales<sup>a</sup>

	Shoulder Flexors	Elbow Flexors	Knee Extensors	Pımax	PEmax	Ventilator-Free Time
BI	.70 <sup>b</sup>	.83 <sup><i>b</i></sup>	.68 <sup><i>b</i></sup>	.67 <sup>b</sup>	.56 <sup>b</sup>	.65 <sup>b</sup>
FIM		100	100		100	100
ADL	.68 <sup>b</sup>	.72 <sup>b</sup>	.71 <sup>b</sup>	.55 <sup>b</sup>	.50 <sup>b</sup>	.84 <sup>b</sup>
Eating	.10	.12	.05	.13	.21	.22
Grooming	.68 <sup>b</sup>	.80 <sup>b</sup>	.68 <sup>b</sup>	.62 <sup>b</sup>	.49 <sup>b</sup>	.82 <sup>b</sup>
Bathing	.54 <sup>b</sup>	.58 <sup>b</sup>	.55 <sup>b</sup>	.35	.29	.68 <sup>b</sup>
Dressing-upper	.69 <sup>b</sup>	.76 <sup>b</sup>	.76 <sup>b</sup>	.52 <sup>b</sup>	.51 <sup>b</sup>	.82 <sup>b</sup>
Dressing–lower	.77 <sup>b</sup>	.74 <sup>b</sup>	.76 <sup>b</sup>	.61 <sup>b</sup>	.53 <sup>b</sup>	.85 <sup>b</sup>
Toileting	.32	.24	.37	.29	.29	.47 <sup>b</sup>
Sphincter	.46 <sup>b</sup>	.41 <sup>b</sup>	.39	.40 <sup>b</sup>	.35	.48 <sup>b</sup>
Bladder	.29	.28	.30	.30	.36	.39
Bowel	.50 <sup>b</sup>	.44 <sup>b</sup>	.36	.43 <sup>b</sup>	.29	.47 <sup>b</sup>
Mobility	.67 <sup>b</sup>	.61 <sup><i>b</i></sup>	.68 <sup>b</sup>	.56 <sup>b</sup>	.51 <sup>b</sup>	.81 <sup><i>b</i></sup>
Bed, chair, WC	.73 <sup>b</sup>	.72 <sup>b</sup>	.76 <sup>b</sup>	.61 <sup>b</sup>	.58 <sup>b</sup>	.81 <sup><i>b</i></sup>
Toilet	.29	.24	.35	.26	.26	.46 <sup>b</sup>
Tub, shower	.25	.15	.18	.23	.27	.48 <sup>b</sup>
Walk/WC	.67 <sup>b</sup>	.48 <sup>b</sup>	.63 <sup>b</sup>	.45 <sup>b</sup>	.47 <sup>b</sup>	.66 <sup>b</sup>
Stairs	.24	.26	.26	.30	.28	.18
Executive	.61 <sup>b</sup>	.65 <sup>b</sup>	.60 <sup>b</sup>	.50 <sup>b</sup>	.41 <sup>b</sup>	.68 <sup>b</sup>
FIM Total	.62 <sup>b</sup>	.71 <sup>b</sup>	.60 <sup>b</sup>	.64 <sup>b</sup>	.40 <sup>b</sup>	.69 <sup>b</sup>

<sup>a</sup> BI=Barthel Index of Activities of Daily Living, FIM=Functional Independence Measure, ADL=activities of daily living, WC=wheelchair. <sup>b</sup> P<.05.

sizes of the BI were 1.03 (95% CI=0.27-1.74) and 2.02 (95% CI=1.12-2.81) after 3 and 6 weeks of physical training, respectively, between the 2 groups. The overall effect size of the FIM scores after 6 weeks of physical training was 1.93 between the 2 groups.

All subjects scored a 1 on all 3 items in the transfer category and on 2 items in the locomotion category, respectively, at baseline. The median score of FIM mobility subscale in the treatment group increased significantly ( $P \le .001$ ) from baseline by 2 points (40%) after the third week of physical training and 4 points (80%) after the sixth week, respectively, whereas it remained unchanged in the control group. After 6 weeks of physical training, the median score of FIM executive functioning subscale increased (20%) and decreased (32%) significantly from the baseline in the treatment and control groups, respectively. Five patients (29.4%)in the treatment group were able to walk around the bedside with moderate assistance, and 4 patients (23.5%) in the treatment group were able to walk for a minimum of 50 m under supervision or with minimal contact assistance after 3 and 6 weeks of physical training, respectively. At the sixth week of intervention, the average distance walked during the 2-minute walk test was  $42.9\pm12.7$  m (n=9) for the treatment group. In contrast, subjects in the control group remained bedridden, and none were ambulating at the end of the 6-week study period. All functional scores (ie, BI and FIM total and subscale scores) continued to increase in the treatment group ( $P \le .05$ ) from the third week to the sixth week of the training period. All subjects in the treatment group, but only 10% to 15% of the subjects in the control group, demonstrated improvements in all 4 subscales (ADL, sphincter management, mobility, and executive function) of the FIM at the sixth week of training.

Changes in BI scores correlated significantly with changes in both respiratory and limb muscle strength and ventilator-free time (Tab. 4). Changes in ventilatorfree time and the strength of the shoulder and elbow flexors and knee extensors after 6 weeks of physical training correlated significantly with items related to ADL, except for eating and toileting (Tab. 4). Changes in ventilator-free time and the strength of both the respiratory and limb muscles correlated significantly with the mobility dimension of the FIM. There were stronger correlations between changes in the walk/ wheelchair item and changes in strength of the shoulder flexors (r = .67), strength of the knee extensors (r = .63), and ventilator-free time (r=.66) than with changes in respiratory muscle strength. Changes in executive functioning scores and FIM total score correlated significantly with changes in limb muscle strength and ventilator-free time.

#### **Discussion and Conclusion**

The major aim of this study was to examine the effects of physical training in subjects requiring PMV on functional status as assessed by the BI and FIM instruments. The results show that a 6-week physical training program may improve functional status in patients requiring PMV by improving limb muscle strength and ventilator-free time.

Neuromuscular abnormalities acquired in the intensive care unit are common in patients following mechanical ventilation because of many factors.<sup>1</sup> In a study by De Jonghe et al,<sup>2</sup> significant muscle weakness was detected in one fourth of the patients in the intensive care unit after more than a week of mechanical ventilation by a simple bedside muscle strength score. In addition, sensorimotor axonopathy and myopathy confirmed by electrophysiological examination and muscle biopsy often were observed in these patients.<sup>2</sup>

Results of this study show severe reductions in limb muscle strength in patients requiring PMV compared with those values obtained from a community-based, age-matched population (15%, 18%, and 13% of normal values for the shoulder flexors, elbow flexors, and knee extensors, respectively).17 Martin8 reported significant limb muscle weakness in patients who were ventilatordependent, with mean limb strength scores of less than 3 (ie, muscle groups had either visible contraction but no limb movement or active movement but not against gravity) using a 5-point Medical Research Council motor score (0=complete paralysis, 5=normal muscle strength). The magnitude of muscle strength reduction (after being transformed to percentage of normal values) was larger in our subjects, using different methods, than that of Martin.8 This discrepancy might be because the subjects in our study were older  $(72\pm10 \text{ versus } 58\pm14)$ years of age) and had used a ventilator for a longer period  $(61\pm 64 \text{ versus } 17\pm 7 \text{ days}).$ 

It is important to note that, although the improvements in limb muscle strength were relatively small in the treatment group, the effect sizes of the intervention were "large" based on Cohen's definition.<sup>26</sup> The effect sizes of most outcome parameters (eg, strength, FIM subscale scores) increased more at the sixth week compared with the third week of intervention. Most subjects admitted to the RCC were unable to walk because of muscle weakness.

Prolonged bed confinement and deconditioning are other major problems of long-term ventilator use. All subjects at the time of enrollment in our study were unable to walk, but, after 6 weeks of physical training, 53% of the subjects in the treatment group regained their ambulation ability. Nava<sup>11</sup> showed that 87% of patients with chronic obstructive pulmonary disorder (COPD) who were recovering from an episode of acute respiratory failure regained walking autonomy after an average of 7 weeks of rehabilitation. This discrepancy in treatment effect was probably due to the different patient populations studied (various diagnoses versus COPD) and the percentage of patients who were invasively ventilated (100% versus 48%). A comparison of these characteristics shows that our subjects had poorer baseline ability than subjects in the study by Nava.<sup>11</sup>

Reduced respiratory muscle strength is a common feature in patients who are ventilator-dependent<sup>27</sup>; therefore, it is not surprising that patients requiring PMV had marked decreased PImax and PEmax at baseline relative to normal values.<sup>28</sup> Our results show that PImax and PEmax, and thus ventilator-free time, increased after 6 weeks of physical training in patients requiring PMV. Although the underlying mechanisms are not clear, upper-extremity strengthening exercises facilitate the respiratory actions of the pectoralis muscle and other accessory respiratory muscles.29 Weaning from the ventilator support was not the primary goal of physical training in our study; however, increases in ventilatorfree time could improve patient mobility in ADL. In comparison, strength of the limb and respiratory muscles continued to deteriorate in the control group during the 6-week study period, suggesting that immobilization is an important cause of muscle weakness in patients requiring PMV. Our results further suggest that physical training could indeed reverse and prevent the effects of immobilization.

Numerous functional outcome instruments have been developed for various applications and use in specific settings. The BI and FIM are 2 of the most widely used measures of global functional status, but they have not yet been applied to evaluate functional status of patients requiring PMV. Martin<sup>8</sup> reported the use of the FIM to evaluate the functional level of patients who are ventilator-dependent, but provided no details. In the present study, both the BI and FIM were used to evaluate functional ability of patients requiring PMV. Because the FIM has 7-point response items compared with the 2- to 4-point response items in the BI, it could provide more quantitative information about outcomes and psychometrically measure both physical and cognitive disability.<sup>30</sup> Scores on the physical functioning subscale of the 36-Item Short-Form Health Survey (SF-36) have recently been used to measure functional status in patients after discharge from intensive care.9,27,31,32 Patients with tracheostomy for respiratory failure showed poor functional status by low SF-36 physical function scores, which was only 24% of the full domain score at discharge.<sup>31</sup> In our study, the median FIM physical domain score (ADL, sphincter, and mobility) was only 14% of the full domain score at baseline in patients who require PMV. This discrepancy might due to a longer period of mechanical ventilation in our subjects (61 days versus <28 days), to the use of the FIM rather than the SF-36, and to the use of different methods (rated by a physical therapist versus telephone interview) and instruments. Based on the

characteristics of the instruments, the functional content covered by the FIM items is at the lower end of the functional activity continuum, whereas the physical functioning items of SF-36 cover the higher end. It has been shown that the FIM is more precise and relevant for inpatients after acute care than the SF-36 because these patients have a functional status at the lower end of the continuum.<sup>33</sup>

We found that the total BI and FIM scores increased after 6 weeks of physical training in patients requiring PMV. Most of the improvements were in the ADL and mobility dimensions of the FIM after 6 weeks of physical training. It has been demonstrated that patients who are ventilator-dependent exhibited significant improvement in their ability to transfer from the supine position to the sitting position and from the sitting position to the standing position upon discharge from the ventilatory rehabilitation unit.8 Our results, however, showed that improvements in limb muscle strength correlated moderately but significantly to the ADL and mobility subscales of the FIM. This result suggested that general muscle strengthening programs are sufficient to benefit most functional outcomes. Furthermore, it is possible that formulating task-specific training could produce additional gains in the functional outcomes for this patient group. Further studies are warranted to test this speculation. Most importantly, we found highly significant correlations between the ventilator-free time and functional outcomes. This finding suggested that prolonged ventilator use could lead to a substantial impairment in functional performance and, at some point, may reach the threshold of disability. Therefore, the importance of physical training for patients requiring PMV cannot be overemphasized.

The results of this study showed that both BI and FIM scores could identify outcome changes with physical training in patients requiring PMV; however, whether these changes were "clinically significant" remains a concern. Few explicit comments about what constitutes a clinically significant change in BI and FIM scores have been reported. Wade and Collin<sup>34</sup> suggested that a 20-point threshold would certainly indicate an important change in BI scores. Granger et al<sup>35</sup> showed that a 10-point improvement of FIM scores decreases (by 50%) the time required to care for a group of patients with stroke in the community. Our results show that, in the treatment group, 5 (29.4%) and 11 (64.7%) subjects achieved clinically significant changes in BI scores (20 points) at the third and sixth weeks, respectively, and 13 (76.5%) and 17 (100%) subjects achieved clinically significant changes in FIM scores (10 points) at the third and sixth weeks. Although the BI is easy to administer, it is relatively restricted and less responsive, and ceiling and floor effects are commonly seen.36,37 On the other hand, the FIM is more complex and takes longer to administer, but it could detect changes in more subjects, and it correlates more strongly with improvements in muscle strength than the BI in patients requiring PMV. Therefore, the FIM is a more appropriate instrument to measure improvements in functional outcome after physical training in patients requiring PMV.

Measurement of cognitive disability using the FIM in patients requiring PMV has not been reported. The results of our study show that the mean baseline cognitive and physical domain scores of the FIM in all patients requiring PMV were 51% and 17% of the highest possible score, respectively. Prolonged mechanical ventilation appears to have a greater effect on physical function than on cognitive function. After a 6-week training program, the cognitive domain score increased significantly in the treatment group but deteriorated significantly in the control group. These results suggest that physical training could indeed provide both cognitive distraction and depression reduction for patients requiring PMV.38 The relationship between physical training and cognitive function may be explained by the fact that physical training, by keeping the brain vasculature healthy, could preserve or promote its function.<sup>39</sup>

There were several limitations in the present study that need to be acknowledged and addressed. The first limitation was that a wide variety of patients with different diagnoses and etiologies required prolonged mechanical ventilator assistance in the RCC unit. The confounding factors (eg, duration on mechanical ventilator) might exist because the consecutive patient sample used in this study could influence the training or functional status measure. Other limitations were the relatively small sample size and examiner bias. Future studies with larger sample sizes and a randomized study design may allow subgroup analysis to distinguish potential beneficial effects of physical training for different patient populations in RCC units. Finally, although examiners were blinded to group assignments in our study, patients or the primary caregivers might sometimes disclose treatment information.

Disparity between changes recorded by functional measures and those changes reported by patients might exist. Quality of life assessment in this population will help provide more insight regarding the total benefits gained from rehabilitation. In addition, future studies should examine the ideal duration of physical training and how long its effects last.

In conclusion, improvements in muscle strength and ventilator-free time after 6 weeks of physical training in patients requiring PMV may enhance their functional status, including both physical and cognitive dimensions. The FIM appears to be able to detect more functional changes than the BI in patients requiring PMV after physical training. We hope that the results of the current study encourage early referral and active interdisciplinary rehabilitation in appropriate cases when prolonged mechanical ventilation is used.

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