Physical Recovery in Intensive Care Unit Survivors: A Cohort Analysis

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Background Some survivors of critical illness experience poor physical recovery, but which patients experience the most compromise during recovery is unknown.

Objective To identify factors associated with physical recovery by using the 6-minute walk test in adult survivors of critical illness 26 weeks after discharge from the hospital.

Methods A total of 195 adult survivors of a critical illness were enrolled in a multicenter trial of physical rehabilitation after discharge from the hospital. The 6-minute walk test, the 36-Item Short Form Health Survey, and sleep rated on a 5-point scale were completed at weeks 1 and 26. Clinical and demographic data were obtained from patient records.

Results A total of 145 patients completed the 26-week test. Of these, 94 (65%) increased the distance walked in 6 minutes by at least 75 m from the 1-week value and were therefore considered to have improved on the test. Factors associated with improvement included moderate to severe sleeping problems in week 1, moderate to vigorous exercise in week 26, and higher vitality in week 26. Conversely, respiratory problems and higher social functioning in week 1 were associated with less improvement in the distance walked.

Conclusion Multiple factors are associated with physical recovery after critical illness. Interventions to target multidimensional aspects of recovery such as sleep and exercise may result in improved physical function after critical illness. (American Journal of Critical Care. 2015;24:33-40)
Survival after a critical illness that requires admission to an intensive care unit (ICU) is common and occurs in approximately 90% of patients discharged from the hospital in Australia.¹ For some survivors, recovery may be characterized by marked compromise of physical and psychological health after discharge from the hospital. Physical compromise often is manifested as generalized muscle weakness leading to an inability to perform simple activities of daily living. Currently, the muscle deterioration that patients experience during critical illness and the lengthy recovery period that these patients require are widely recognized.²,³

Numerous observational studies⁴-⁶ have indicated the range and extent of physical compromise that patients experience after a critical illness, but exploration of the factors predictive of this compromise has been limited. Physical function can be assessed by using self-report instruments such as the Short-Form 36 (SF-36) or objective measures such as the distance walked in 6 minutes (6MWD).⁴ Concurrently, survivors of critical illness may experience both psychological compromise, in the form of anxiety, depression, and symptoms of posttraumatic stress disorder,⁵,⁶ and cognitive compromise.⁷,⁸

Recognition of compromise after critical illness has prompted a range of small, usually single-center, studies of the factors associated with recovery. Factors identified include age, socioeconomic status, sex, severity of illness, primary diagnosis, and length of ICU stay (including duration of interventions such as mechanical ventilation).⁹,¹⁰ A major limitation of the research to date is that many of the factors associated with recovery cannot be modified. Identification of potentially modifiable factors associated with recovery may allow development of interventions tailored to overcome specific limitations or to address specific factors and may lead to greater improvement in function for survivors of a critical illness. The aim of this substudy analysis was to examine the factors associated with physical recovery by using the 6MWD in adult survivors of critical illness during a period of 26 weeks after hospital discharge.

Methods

Design

Patients in this cohort analysis were enrolled in a multicenter randomized controlled trial that tested the effects of an 8-week home-based rehabilitation program on health-related quality of life and physical function for survivors of critical illness. The study protocol and primary results for the trial have been published previously.¹¹,¹²

Patients and Centers

Patients were recruited from ICUs in 12 hospitals in Sydney, Brisbane, and Perth, Australia (6 teaching, 5 district, and 1 private hospital). Patients were eligible for enrolment if they were 18 years or older; had an ICU length of stay of 48 hours or longer; received mechanical ventilation for 24 hours or longer; were discharged home to self-care or a caregiver (noninstitutional care); resided within the hospitals’ local geographic areas (to enable home visits; approximately 50-km radius); had no neurological, spinal, or skeletal dysfunction preventing participation in physical rehabilitation; were not receiving palliative care; had no organized rehabilitation related to ongoing management of a chronic disease (eg, pulmonary rehabilitation, cardiac rehabilitation); and were cognitively able to complete the self-report
measures and comply with the instructions for physical testing.

The sample size was based on the primary aim of the original trial to determine the effect of a physical rehabilitation program on physical function: a hypothesized effect of a 10-point difference on the physical function domain of the SF-36.16,17

Procedures
After the study was approved by the human research ethics committee of each research site, patients were approached about participating in the study after ICU discharge; informed consent was obtained either at that time or after the patient agreed to be contacted at home after discharge from the hospital. The graded, individualized endurance and strength training that patients received in the primary trial has been described elsewhere.16,17 Blinded assessments in patients' homes at weeks 1, 8, and 26 after hospital discharge included examination of physical functioning, health-related quality of life, and psychological well-being. The 2 groups (control and interventional) did not differ significantly in physical function, 6MWD, or overall health-related quality of life as indicated by scores on the SF-36. Data from both groups were therefore combined for this analysis to identify factors associated with physical recovery in ICU survivors.

Outcome Measures
Primary Outcome. The primary outcome for this analysis was physical function as measured by the 6-minute walk test (6MWT). Specifically, the outcome was the improvement in patients' physical function from week 1 to week 26. Patients whose 6MWD improved by 75 m or more during the 26 weeks of the study were categorized as "improved 6MWD"; this distance was based on 95% CI of the standard error of measurement of the week-1 test. Currently, no agreed-upon minimal clinically important difference for the 6MWD in survivors of a critical illness exists. For patients with chronic obstructive pulmonary disease,19 the estimated minimal clinically important difference is 35 m; therefore, an improvement of 75 m is considered a clinically important improvement in survivors of critical illness.

The 6MWT was performed in the patient's home or environs by trained assessors. The assessors were registered nurses or physiotherapy students who were trained by the physiotherapist investigator (J.A.) to conduct the 6MWT according to the guidelines of the American Thoracic Society.7 The course for the walk test was measured and mapped on paper, and the same course was used for the 1-, 8-, and 26-week tests. The test was performed twice at each assessment, to account for any learning effect, and the best result was recorded for analysis.19 During the 6MWT, patients were directly observed and monitored continuously by the assessor via a portable pulse oximeter (to measure pulse rate and oxygen saturation). Patients' exertion levels were assessed and documented during the test by using the Borg Perceived Exertion Scale.20

Other Measures. Psychological well-being was assessed by using the Depression Anxiety Stress Scales21 and the Impact of Event Scale.22 Quality of sleep was assessed by using an item from the 15D instrument of the health-related quality of life, with a 5-point scale ranging from no problems to severe sleeplessness.23 Clinical and demographic data were obtained from ICU and hospital records. Data on incidental exercise were obtained by telephone interview with patients at each time point; the exercise was categorized as none, mild, moderate, or vigorous. Moderate exercise was exercise that the patients thought caused a moderate increase in heart rate or breathing; vigorous exercise caused a large increase in heart rate or breathing.

Data Analysis
Stata 11 software (StataCorp LP) was used for all analysis of data. Data were cleaned and checked for missing and outlying values. Descriptive characteristics of the population were explored, and the variables were checked for normal distribution.

Baseline variables, including demographic details (age, sex); hospital details (diagnosis, duration of mechanical ventilation, ICU and hospital length of stay, scores on the Acute Physiology and Chronic Health Evaluation II); and week-1 scores for the SF-36, Depression Anxiety and Stress Scales, the Impact of Event Scale, and sleeping instruments; and the amount of incidental exercise were assessed by using univariate analysis to determine if relationships with the outcome existed. Multiple logistic regression modeling included all variables significant at the .10 level on univariate analysis when the backward elimination method was used. After removal of each nonsignificant variable, the model was assessed by using likelihood-ratio tests and Wald statistics. The fit of the final logistic model was assessed by using the Pearson goodness-of-fit statistic and the area under the receiver operating curve.
Results

Flow of Patients

In total 5980 patients were screened, and 195 were enrolled between 2005 and 2008 (see Figure). Patients were a mixed medical and surgical group of ICU patients with an mean age of 57 years; 30% were female (Table 1). A total of 145 patients (74%) completed the 6MWT at 26 weeks. Those who completed the test at 26 weeks did not differ significantly in age, sex, diagnosis, and length of stay in the ICU and the hospital from patients who did not complete the 6MWT.

Prediction of 6MWD

Of those patients who completed the 26-week 6MWT, 94 (65%) increased their distance walked by at least 75 m from the 1-week test and were therefore categorized as improved 6MWD. The mean distance at week 1 after hospital discharge was 307 m (SD, 137 m); this value increased to 435 m (SD, 156 m) for patients who completed the test at week 26, an increase of 42%. For those 143 patients who completed both the week-1 and week-26 6MWT, the mean difference was 121 m (SD, 20 m).

Table 1
Characteristics of the 195 participants in the study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>6-min walk distance</th>
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<tbody>
<tr>
<td></td>
<td>Improved (n = 94)</td>
<td>Not improved (n = 51)</td>
<td>Did not complete test (n = 50)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>56 (16.4)</td>
<td>59 (15.2)</td>
<td>57 (16.2)</td>
</tr>
<tr>
<td>Female sex, No. (%)</td>
<td>34 (36)</td>
<td>23 (45)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Day 1 APACHE II score, mean (SD)</td>
<td>20.6 (12.4)</td>
<td>18.0 (5.7)</td>
<td>17.77 (6.6)</td>
</tr>
<tr>
<td>6-min walk distance, mean (SD), m</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 1</td>
<td>302 (121)</td>
<td>340 (130)</td>
<td></td>
</tr>
<tr>
<td>Week 26</td>
<td>482 (141)</td>
<td>349 (146)</td>
<td></td>
</tr>
<tr>
<td>Operative admissions, No. (%)</td>
<td>47 (50)</td>
<td>21 (41)</td>
<td>18 (36)</td>
</tr>
<tr>
<td>ICU admission diagnosis, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>20 (21)</td>
<td>10 (20)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>11 (12)</td>
<td>19 (37)</td>
<td>16 (32)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>30 (32)</td>
<td>14 (27)</td>
<td>13 (26)</td>
</tr>
<tr>
<td>Other</td>
<td>31 (33)</td>
<td>8 (16)</td>
<td>13 (26)</td>
</tr>
<tr>
<td>Duration of mechanical ventilation, median (IQR), h</td>
<td>92 (46-223)</td>
<td>75 (45-145)</td>
<td>72 (47-139)</td>
</tr>
<tr>
<td>Days in ICU, median (IQR), d</td>
<td>5 (4-10)</td>
<td>6 (4-12)</td>
<td>6 (4-10)</td>
</tr>
<tr>
<td>Days in hospital, median (IQR), d</td>
<td>20 (12-31)</td>
<td>14 (11-30)</td>
<td>18 (11-25)</td>
</tr>
</tbody>
</table>

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; ICU, intensive care unit; IQR, interquartile range.

6 A Admission diagnosis based on APACHE III diagnostic codes.
Univariate relationships (P<.10) existed between an improved 6MWD and several factors: diagnostic group; quality of sleep; scores on the SF-36 domains of social role functioning, vitality, physical function, role–physical and physical component summary at week 1; score on the stress subscale of the Depression Anxiety Stress Scales at week 1; scores on the SF-36 domains of vitality, physical function, role–physical and physical component summary at week 26; and amount of incidental exercise at week 26.

After backward stepwise removal of factors that were not significant in the multivariable model, logistic regression (Table 2) indicated that moderate to severe sleeping problems in week 1 (log odds coefficient, 0.80; 95% CI, 0.11-1.48), moderate to vigorous exercise at week 26 (log odds coefficient, 2.44; 95% CI, 1.04-5.84), and higher vitality at week 26 (log odds coefficient, 0.06; 95% CI, 0.02-0.09) were associated with an improved 6MWD. Conversely, respiratory diagnosis (log odds coefficient, -2.24; 95% CI, -4.06 to -0.41), higher scores on the SF-36 social functioning domain at week 1 (log odds coefficient, -0.03; 95% CI, -0.05 to -0.01), and greater 6MWD at week 1 (log odds coefficient, -0.01; 95% CI, 0.01-0.00) were associated with no improvement in the 6MWD. The final model was an excellent predictor of improvement in 6MWD, with an area under the curve of 0.88 and a Pearson χ² of 82.7, P=.95.

Discussion

In this study, we sought to identify factors independently associated with improvement in physical function during a 26-week period in survivors of critical illness treated in an ICU who returned home. Patients were considered to have improved physical function if they increased their distance walked on the 6MWT from 1 week to 26 weeks after hospital discharge by 75 m or more. Two-thirds of patients had an increase in their 6MWD; the mean distance increased by more than 40%.

Improvement in 6MWD by 75 m or more was independently associated with moderate to severe sleeping difficulties at week 1 and moderate to vigorous incidental exercise and higher vitality at week 26. A lack of improvement in physical function was independently associated with admission to the ICU because of a respiratory diagnosis, higher social functioning, and greater 6MWD in the first week after hospital discharge.

Physical function, as reflected by the 6MWD, has rarely been measured in cohorts of ICU survivors. Herridge and colleagues followed up 109 survivors of acute respiratory distress syndrome for 5 years. A total of 83 patients walked approximately 280 m 3 months after hospital discharge, 400 m at 6 months, 420 m at 12 months, and 440 m at 5 years. Similar improvements were noted by Wright et al in 31 patients with pancreatitis, who walked approximately 350 m at 3 months and 420 m at 12 months. In a study by McWilliams et al, general ICU patients walked approximately 280 m at 1 week and 440 m 6 weeks later. We found no other reports of factors associated with improved 6MWD. Thus, our results are only the second description of factors associated with improved walking distance in the general ICU population, and our sample had markedly more patients than did the only previous report.

In our cohort of ICU survivors, moderate to severe sleeping difficulties 1 week after hospital discharge were associated with greater improvement in physical function. Poor sleep quality in the ICU is well recognized, but examination of whether compromised sleep continues after hospital discharge has been limited. In our study, 50% of patients reported moderate to severe problems sleeping at week 1, and the percentage remained greater than 30% at weeks 8 and 26. These findings are consistent with those of a study in which 50% of 40 ICU patients with acute lung injury reported insomnia 6 months after discharge and with the results of study in which 7 of 109 survivors of acute respiratory distress syndrome who reported persistent changes in sleep quality had abnormal sleep architecture on polysomnography 6 months or more after hospital discharge. A similar relationship

### Table 2
Multivariate regression with improvement in 6-minute walk distance as the dependent outcome

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Log odds coefficient (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidental exercise</td>
<td>2.44 (1.04-3.84)</td>
<td>.001</td>
</tr>
<tr>
<td>Social functioning (SF-36) in week 1</td>
<td>-0.03 (-0.05 to -0.01)</td>
<td>.004</td>
</tr>
<tr>
<td>Diagnostic group (cardiac)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>-2.24 (-4.06 to -0.41)</td>
<td>.02</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>0.57 (-1.05 to 2.18)</td>
<td>.49</td>
</tr>
<tr>
<td>Other</td>
<td>-0.27 (-1.79 to 1.24)</td>
<td>.72</td>
</tr>
<tr>
<td>Sleep in week 1</td>
<td>0.80 (0.11-1.48)</td>
<td>.02</td>
</tr>
<tr>
<td>Vitality (SF-36) in week 26</td>
<td>0.06 (0.02-0.09)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6-minute walk distance in week 1</td>
<td>-0.01 (0.01-0.00)</td>
<td>.004</td>
</tr>
</tbody>
</table>

Abbreviation: SF-36, 36-Item Short Form Survey.

- Model: Area under receiver operating curve = 0.88; Pearson χ² goodness-of-fit test: χ² = 82.7, P=.95.
- Exercise is moderate/vigorous compared with mild or none.
- Sleep codes 3, 4 and 5 (moderate/great/severe problems) compared with codes 1 and 2 (normal/slight problems).
between sleep problems after hospital discharge, physical function, and quality of life was also found in former ICU patients.\(^1\)

The meaning of such relationships is unclear. Possible explanations include that as the patients’ sleep improved, their physical function also improved, or that the physiological aspects that resulted in a short 6MWD at week 1 also affected sleep quality and quantity. The latter explanation is consistent with our finding that patients who improved their distance walked in 6 minutes had a lower mean 6MWD at week 1 than did patients whose 6MWD did not improve. Regardless, this finding suggests that strategies to improve sleep may also improve other aspects of recovery after critical illness.

Not unexpectedly, moderate to vigorous incidental exercise independent of the study intervention and higher self-reports of vitality were associated with longer 6MWDs. Moderate to vigorous incidental exercise was exertion that patients thought caused a moderate or large increase in their heart rate or breathing. However, the direction of the relationships between incidental exercise, self-reported vitality, the study intervention, and the 6MWD are not clear. Incidental exercise may have resulted in improved 6MWD, or alternatively the study intervention may have contributed to the patients’ ability to undertake moderate to vigorous incidental exercise. Similarly, the higher sense of vitality may have led patients to feel capable of pushing themselves to walk farther on the 6MWT, or alternatively the longer 6MWD may have contributed to a high sense of vitality. Regardless of the direction of these relationships, moderate to vigorous incidental exercise and a high self-rating of vitality appear to assist physical function. In the context of this finding, and because the study intervention was not associated with improvement in 6MWD, possibly a more intense or prolonged exercise intervention would be required to elicit improvements in the 6MWD. Such an intervention might commence earlier in recovery, last for longer than 8 weeks, or consist of more frequent or intense episodes of exercise. Since the current study intervention was designed, several studies have been done to test the feasibility and efficacy of early exercise interventions, both within the ICU\(^1\) and after ICU discharge but before discharge from the hospital,\(^1\) and to determine the effectiveness of a more intense home-based exercise intervention.\(^2\)

Patients with a primary respiratory diagnosis experienced less improvement in the 6MWD than did patients with other diagnoses. Herridge et al\(^1\) reported minimal increase in 6MWD after 6 months in patients with acute respiratory distress syndrome; the patients’ mean 6MWD was only 440 m 5 years after hospitalization. This finding may indicate that ongoing pathological damage to the lungs resulting in limited physical function may require more intense rehabilitation, such as provided in pulmonary rehabilitation programs.\(^3\)

The role of social functioning in recovery is unclear. Higher social functioning soon after discharge was associated with less improvement in physical function. Possibly patients who felt their social functioning was adequate were not motivated to increase physical activity to interact with friends and family, although the rationale for such an association is not obvious.

**Strengths and Limitations**

This analysis incorporated results from a multisite study of 195 survivors of critical illness, representing a larger cohort than any other examination of 6MWD in this population of patients. Control for a wide range of factors that might affect improvement in physical function was incorporated in the study design.

Limitations include the low number of patients, only 195 of the almost 6000 patients screened, who were enrolled in the study, raising questions about the representativeness of this cohort when the wider ICU population is considered. Further, 143 of the 195 patients enrolled completed the 6MWT at both 1 and 6 months, but the baseline characteristics of those who completed the test were similar to those of patients who did not complete the assessment.

In conclusion, various factors affected recovery after critical illness. These factors probably did not occur in isolation; most likely an interaction occurred between physical, psychological, and cognitive health.\(^1\) Exploration of the effects interventions designed to improve recovery have on all of these elements is essential. Further, the most effective interventions may target more than one aspect of recovery.

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REFERENCES


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