Rehabilitation of Patients Admitted to a Respiratory Intensive Care Unit

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Objective: Pulmonary rehabilitation has been shown to be of benefit to clinically stable patients with chronic obstructive pulmonary disease (COPD). This study examined the effect of pulmonary rehabilitation on some physiologic variables in COPD patients recovering from an episode of acute respiratory failure.

Design: A prospective, randomized study.

Setting: A respiratory intensive care unit (RICU).

Patients: Eighty COPD patients recovering from an episode of acute respiratory failure were randomized in a 3:1 fashion to receive stepwise pulmonary rehabilitation (group A, n = 60 patients) or standard medical therapy (group B, n = 20 patients).

Main Outcome Measures: Improvements in exercise tolerance, sense of breathlessness, respiratory muscle function, and pulmonary function test values were measured, respectively, by exercise capacity (6-minute walking distance [6MWD]), dyspnea score (Visual Analog Scale [VAS]), maximal inspiratory pressure (MIP), forced expiratory volume in 1 second (FEV1), and forced vital capacity (FVC).

Interventions: Group A received pulmonary rehabilitation that consisted of passive mobilization (step I), early deambulation (step II), respiratory and lower skeletal muscle training (step III), and if the patients were able, complete lower extremity training on a treadmill (step IV). Group B received standard medical therapy plus a basic deambulation program.

Results: Sixty-one of 80 patients were mechanically ventilated at admission to the unit and most of them were bedridden. Twelve of the 60 group A patients and 4 of the 20 group B patients died during their RICU stay, and 9 patients required invasive mechanical ventilation at home after their discharge. The total length of RICU stay was 38 ± 14 days for patients in group A versus 33.2 ± 11 days for those in group B. Most patients from both groups regained the ability to walk, either unaided or aided. At discharge, 6 MWD results were significantly improved (p < .001 in Group A only. MIP improved in Group A only (p < .05), while VAS scores improved in both groups, but the improvement was more marked in group A (p < .05). In group B (p < .05).

Conclusions: COPD patients who were admitted to a RICU in critical condition after an episode of acute respiratory failure and who, in most cases, required mechanical ventilation benefited from comprehensive early pulmonary rehabilitation, compared with patients who received standard medical therapy and progressive ambulation.

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The potential benefit of a rehabilitation program for both inpatients and outpatients with chronic obstructive pulmonary disease (COPD) or other chronic lung disease has been well documented.1,2 These studies, however, were performed either long after the patients' episodes of acute respiratory failure or in subjects who were clinically stable. It is surprising that no controlled studies have assessed the role of a rehabilitation program in patients recovering from severe ventilatory insufficiency, who often require mechanical ventilation. Respiratory and skeletal muscle weakness and prolonged inactivity lead to severe curtailment of even the simplest daily activities.3-5

Make and associates6 found that only 5 of 16 ventilator-dependent patients did not benefit from a rehabilitation program started after their admission to an intensive care unit (ICU), while Foster and coworkers,7 in an uncontrolled study, found improvement in exercise tolerance, pulmonary function, and arterial blood gas values in a subset of COPD patients with severe hypoxemia, some of whom were transferred directly from an ICU. These data suggest that for patients recovering from an episode of acute exacerbation, early institution of a rehabilitation program may be useful in improving the outcome.

The development of the respiratory intensive care unit (RICU) enables medical staff to work in a specialized environment in which medical and paramedical teams are familiar with and well trained in the care and management of severely ill respiratory patients, including treatment with invasive and noninvasive mechanical ventilation.8 In this prospective, controlled, and randomized study, we compared the effects of early stepwise comprehensive rehabilitation plus standard therapy with the effects of standard therapy and progressive ambulation only, on exercise tolerance and dyspnea in two groups of patients with COPD affected by respiratory insufficiency.

MATERIALS AND METHODS

Subjects

Eighty consecutive COPD patients admitted to a rehabilitation center's RICU between June 1995 and June 1997 were studied. The study was approved by the local Ethics Committee. Oral informed consent was given by each patient. The American Thoracic Society (ATS) criteria were used to define COPD.9

The patients had been admitted to the RICU because of an episode of acute respiratory failure and were transferred from the Department of Pneumology or one of the ICUs connected to the Rehabilitation Center. Patients with severe lung disease who had poor functional status were referred to this hospital by

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pulmonary and intensive care physicians from a large geographic area. Most of these patients were recovering from an episode of acute respiratory failure and were too impaired to participate in an outpatient rehabilitation program. A comprehensive rehabilitation program is usually begun shortly after admission to the RICU. For the purposes of this randomized study, however, a proposal was made to the Ethics Committee that only 1 of 3 patients would undergo standard therapy plus progressive ambulation (see below), so that 60 patients would participate in a comprehensive rehabilitation program (group A) and 20 patients would undergo standard therapy plus progressive ambulation (group B). Randomization was performed using a computer program.

Clinically stable patients were enrolled in the study 3 to 5 days after admission to the RICU. Clinical stability was defined as (1) the absence of hyperthermia, (2) stable hemodynamics (mean arterial blood pressure not varying by more than 10mmHg in the preceding 3 days, with systolic pressure of >90 and <170mmHg), (3) a conscious and cooperative state, and (4) no use of respiratory-depressant drugs. Patients were excluded if they had systemic neurologic diseases, severe orthopedic problems, cardiovascular instability, or severe arrhythmia.

At admission 47 of 60 (78%) of group A patients were ventilated (29 invasively and 18 noninvasively), versus 14 of 20 (70%) of group B patients (9 invasively and 5 noninvasively). The time from intubation (usually performed in one of the five ICUs connected with the institution) to admission to the RICU varied between 5 and 19 days, while in the case of patients who required noninvasive ventilatory support and who had been transferred from the Pneumology Department, mechanical ventilation was started in the RICU. All patients ventilated invasively required at least 12 hours of ventilation on admission, previous weaning attempts with T piece of pressure-supported ventilation (PSV) having been unsuccessful. Thirty-one of 38 patients invasively ventilated were tracheostomized. Table 1 shows some characteristics of the two groups of patients on admission to the RICU. Arterial blood gases were recorded while the patients breathed spontaneously for a short time (5 to 10 min) in either room air or oxygen to achieve an oxygen saturation of >90%.

Instruments

Arterial blood gases from the radial artery were analyzed using a blood gas analyser. Pulmonary function tests were recorded using a Wright's spirometer. In invasively ventilated patients the measurements were performed during spontaneous breathing with supplemental oxygen and the cuff of the endotracheal cannula or tube inflated. These tests were also repeated at discharge from the RICU.

Maximal inspiratory pressure (MIP) against an occluded airway was recorded by a differential pressure transducer, using a one-way valve with a tube-type piece with a small hole. The maneuvers were performed at residual volume and patients were encouraged to make a maximal expiration and a short apnea before the maximal inspiratory effort. The MIP maneuvers were performed a minimum of five times, with at least a 1-minute interval between efforts, until two acceptable values, not differing from each other by more than 5%, were obtained.

Procedures

As soon as patients were able to walk on their own, subjective evaluation of dyspnea was recorded at rest and after a mild effort (50m at 1.5km/h) walking on a treadmill, using a visual analog scale (VAS), described by Woodcock and colleagues. The VAS consists of a horizontal line labelled "not at all breathless" at one end and "very breathless" at the other. When asked, the subject records the intensity of breathlessness on the VAS by means of finger controls and the information is stored in the computer.

At this stage exercise performance was also assessed by the 6-minute walking distance (6MWD) test, described by McAspin and coworkers. Verbal encouragement was given continuously to patients during the test, although they were free to stop when they wanted. Three practice attempts were performed on 2 consecutive days, and the best attempt was considered as the baseline value. Results are expressed as the actual distance walked in meters. Oxygen was supplemented during the test to achieve an SaO2 of >88%; a portable device for oxygen was carried by a respiratory therapist.

Interventions

The comprehensive rehabilitation program consisted of two daily sessions of 30 to 45 minutes each. This program consisted of four different steps of increasing difficulty. Steps I and II were considered progressive ambulation training and were common to both groups of patients.

As soon as each patient's clinical condition allowed, step I was started. If a patient's clinical status worsened and the patient could not perform certain tasks, then the program did not proceed to the next step. The grading of this program was as follows.

**Step I** was started soon after admission to the RICU (usually 24 hours) and consisted of maintaining optimal postural position, for instance, sitting upright in bed or in a chair. The patients also underwent sessions aimed at passively and actively training the lower extremities, such as lifting light weights or pushing against a resistance. When needed, postural drainage and cough education were performed. As soon as they regained walking autonomy, patients passed to step II. Any patient able to walk at admission to the RICU started directly at step II, while also receiving passive training of the lower extremities.

**Step II** consisted of progressive walking retraining. The rolling platform walker was used in the first stage. Whenever they were able, patients were free to walk alone or with the therapist's assistance. As soon as patients regained independence in walking, they performed the 6MWD test and the VAS assessment. During step II the patients' SaO2 and heart rate were continuously monitored and supplemental oxygen was given to

<table>
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<tr>
<th>Table 1: Arterial Blood Gas Values and Functional Characteristics of the Two Groups of Patients at Admission to the RICU</th>
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<tbody>
<tr>
<td>Age (yrs)</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Group A (n = 60)</td>
</tr>
<tr>
<td>p Value</td>
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<td>Group B (n = 20)</td>
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Abbreviations: PaO2, arterial oxygen tension; FiO2, fractional inspiratory oxygen; PacO2, arterial carbon dioxide tension; FEV1%, forced expiratory volume in 1 second % of predicted; FVC%, forced vital capacity % of predicted.
maintain an $\mathrm{SaO}_2$ of $>88\%$. When a patient could not be weaned from the ventilator, a portable respirator was used to decrease the work of breathing during walking.

*Step III* included two kinds of exercise. The first consisted of specific respiratory muscle training. A threshold device was used and patients were asked to breathe twice a day for 10 minutes at a target pressure of 50% of MIP. The second exercise consisted of specific lower extremity training. In the morning the patients cycled for about 20 minutes at a speed they could maintain without provoking severe dyspnea ($<6$ on the Borg scale) with a workload of 15 watts, while in the afternoon they were asked to climb a flight of 25 stairs at least five times. $\mathrm{SaO}_2$ and heart rate were again continuously monitored.

In *step IV*, patients who successfully regained complete autonomy and could perform the *step III* tasks without severe oxygen desaturation ($\mathrm{SaO}_2$ of $>88\%$ in oxygen) participated in a complete lower extremity rehabilitation program that consisted of 3 weeks of twice-daily 30-minute sessions of continuous treadmill walking at $70\%$ of the load achieved on the incremental pre-exercise test carried out at enrollment. The 6MWD test and VAS assessment were repeated using the above-described modalities at the end of the training program.

During this rehabilitation program the patients also received the same comprehensive treatment as the control group.

Group B patients received medical therapy for the underlying disease and possible complications, nutritional support, and progressive ambulation program (steps I and II) during their stay in hospital. In the subgroup of ventilated patients, weaning attempts were performed using PSV by gradually decreasing the levels of inspiratory assistance. Weaning success was defined as complete autonomy from the ventilator for at least 48 hours with oxygen saturation (breathing room air or oxygen) above $90\%$ and absence of a fatiguing breathing pattern. The patients enrolled in this group also performed pulmonary function tests and the MIP maneuver at the same times as the rehabilitation group, while the 6MWD test and the VAS assessment were done as soon as the patients regained the ability to walk either aided or unaided.

**Data Analysis**

Statistical analysis was performed using Student's $t$ test for paired data to analyze differences in the two groups at enrollment and at discharge, in arterial blood gases, functional characteristics, MIP, VAS, and 6MWD. One-way analysis of variance (ANOVA) was used to compare, within each single group, the changes in the above-mentioned variables before and after treatment. A $p$ value $<.05$ was considered statistically significant.

**RESULTS**

**Length of RICU stay and clinical outcome.** The total length of RICU stay was 33.2 (standard deviation [SD], 11.7) days for the control group versus 38.1 (SD, 14.3) days for the rehabilitation group (not significant [NS]), while the mean duration of hospital stay was longer because patients were transferred to the Division of Pneumology when their clinical condition allowed. Twelve of 60 (20%) group A patients and 4 of the 20 group B patients (20%) died while in hospital (NS), with a mean survival of 18.1 (SD, 7.2) days and 12.4 (SD, 11.1), respectively (NS). Table 2 shows the number and causes of deaths in the two groups. In 6 of the patients death occurred while still on mechanical ventilation. None of the patients died while performing a rehabilitative task.

At discharge 6 patients from group A who had been ventilated invasively could not achieve autonomy from the machine, while only 2 of the 18 subjects receiving noninvasive ventilation needed home ventilatory support. In group B, 3 patients were discharged as ventilator-dependent. At admission to the RICU all the patients were bed-ridden and none had undergone a rehabilitation program before entering the RICU.

**Feasibility of the rehabilitation program.** In group A, 52 of the 60 patients (87%) regained walking autonomy, unassisted (42 patients) or assisted (10 patients), after the rehabilitation program, and therefore, they achieved at least in part some autonomy in daily living activities. The causes of dropout, other than death, were the following complications: pulmonary embolism in 2 patients, pneumothorax in 1, severe arrhythmia in 1, myocardial infarction in 2, and acute muscular injury in 1. Table 3 lists the number of group A patients enrolled in each rehabilitation step, the number of patients who died at each stage of the program, the number of dropouts, and the duration of the rehabilitation program. It can be seen that most patients performed step III, but only 18 reached a sufficient degree of fitness to be enrolled into step IV.

In group B, 14 of the 20 (70%) patients completed step II and regained walking autonomy, unassisted (10 patients) or assisted (4 patients).

**Pulmonary function tests and arterial blood gases.** Table 4 lists arterial blood gas and pulmonary function test values of the survivors at admission to the RICU and at discharge. In both groups there was a significant difference in $\mathrm{Paco}_2$ recorded at discharge, while improvement in dynamic lung volumes was not statistically significant.

**Exercise tolerance.** Figure 1 shows the individual and mean changes in the distance walked in 6 minutes when the patients were able to walk and at discharge from the hospital. Patients from the rehabilitation group showed a dramatic, significant improvement ($p < .0001$), whereas in the control group there was a small improvement that was not statistically significant. The percentage degree of improvement was also statistically higher in the rehabilitation group ($p < .001$).

The heart rate at rest and after the 6MWD test was significantly lower in patients who completed the rehabilitation.
program: 91 (SD, 12) beats/min at rest at the start of the rehabilitation program versus 80 (SD, 9) beats/min at rest at the end of the program (p < .05), and 128 (SD, 21) beats/min after the 6MWD test at the beginning of the rehabilitation program versus 100 (SD, 19) beats/min after the 6MWD test at the end of the program (p < .05), and 128 (SD, 21) beats/min after the 6MWD test at the end of the program (p < .05), and 128 (SD, 21) beats/min after the 6MWD test at the end of the program (p < .05).

Dyspnea score. Figure 2 depicts the changes in the patients' sense of dyspnea, as assessed on the VAS, at enrollment and at discharge in both groups (p < .001 for group A and p < .05 for group B); the percentage rate of decrease was significantly different in the two groups (p < .01). In group B the heart rate at rest was also significantly lower at discharge: 95 (SD, 13) beats/min at admission versus 82 (SD, 9) beats/min at discharge (p < .05), although no significant improvement was recorded after the walking test.

Inspiratory muscle function. MIP improved significantly in the rehabilitation group undergoing specific training, from 45 (SD, 12) cmH2O to 61 (SD, 14) cmH2O (p < .05).

DISCUSSION

There is clear evidence that pulmonary rehabilitation benefits patients with mild to moderate symptomatic COPD and other lung diseases if they are clinically stable. This is the first prospective randomized study concerning the efficacy of a rehabilitation program in COPD patients recovering from a severe episode of acute respiratory failure who were admitted to a RICU. Despite the fact that several book chapters and position papers have pointed out the importance of specific rehabilitation in an intensive environment for severely ill patients affected by different pathologies, only three investigations have commented on the possible utility of a rehabilitation program in the outcome of their patients. Unfortunately no data were reported for these studies. We had, however, already suggested that a comprehensive rehabilitation program, consisting of leg and arm mobilization, chest physiotherapy, respiratory muscle training, postural drainage, and counselling, may enhance the weaning ability of ventilated patients.

A retrospective study of ventilator-dependent patients by

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Table 4: Admission Versus Discharge Pulmonary Function Test and Arterial Blood Gas Values in the Patients Who Survived in Both Groups

<table>
<thead>
<tr>
<th></th>
<th>Pao2/Fio2</th>
<th>pH</th>
<th>Paco2 (mmHg)</th>
<th>FEV1 % Predicted</th>
<th>FVC % Predicted</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Admission</td>
<td>Discharge</td>
<td>Admission</td>
<td>Discharge</td>
<td>Admission</td>
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<tr>
<td>Group A</td>
<td>238 ± 10</td>
<td>219 ± 8</td>
<td>7.37 ± .06</td>
<td>7.38 ± .05</td>
<td>54.1 ± 5.8</td>
</tr>
<tr>
<td>p Value</td>
<td>.44</td>
<td>.57</td>
<td>.91</td>
<td>.88</td>
<td>.43</td>
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<tr>
<td></td>
<td>253 ± 12</td>
<td>245 ± 10</td>
<td>7.37 ± .06</td>
<td>7.38 ± .07</td>
<td>55.2 ± 8.0</td>
</tr>
</tbody>
</table>

Abbreviations as for table 1.
Make and colleagues,\(^5\) demonstrated the feasibility of training these individual to be independent and to participate in home activities. The rehabilitation program, however, was initiated long after the acute episode that had necessitated mechanical ventilation (mean, 148 days in COPD patients and 43 in the restrictive group). Despite the fact that only one of these patients could be weaned totally from ventilatory support, most of the others were allowed to go home and had some time (about 8h/d) free from the ventilator. Patient mobility and independence were greatly enhanced during this period, and patients were even allowed trips outside the home. These data strongly suggested that pulmonary rehabilitation may also be useful in patients considered too sick or too deconditioned to derive any advantage from a training program.

Another interesting study by Foster and colleagues\(^7\) investigated a group of COPD patients with hypercapnia that, in some cases, was quite severe (34 patients with a PaCO\(_2\) of $>55$mmHg). Despite having severe ventilatory impairment and weak respiratory muscle, the group benefited significantly from an intensive inpatient rehabilitation program. This uncontrolled and unrandomized study had been performed in very sick patients, with an exercise tolerance similar to our patients, but who were not recovering from an episode of acute respiratory failure.

In classical ICUs these rehabilitation programs are usually difficult to perform because the patients, if ventilated, are often paralyzed or sedated, at least during the first 24 to 48 hours after admission. Also, these patients are discharged from ICUs as soon as they start to recover because of the lack of beds. Indeed, an "open setting" such as a RICU is more suited for organizing rehabilitation programs than is a "closed setting" like an ICU.\(^2\)

The present study clearly demonstrates that most patients undergoing pulmonary rehabilitation can dramatically improve their capacity for exercise, much more so than that described for stable COPD patients, and therefore regain autonomy in activities of daily living. A consistent number of control patients also showed improvement in exercise tolerance, but the rate of improvement in 6MWD test and sense of dyspnea was much lower than in the group treated with a rehabilitation program.

One of the main problems in these patients is the effect of prolonged confinement to bed and deconditioning. In fact, most patients admitted to our RICU were unable to walk because they were too weak or because they wanted to avoid the dyspnea sensation that activity elicited. Most of these patients experienced dyspnea during or after mild physical exertion such as washing or dressing. As a result, the patients frequently became debilitated secondary to a continuous cycle of anxiety attributed to dyspnea and avoidance of any activity that might produce breathlessness, resulting in cardiorespiratory and skeletal muscle atrophy due to inactivity. The effects of deconditioning are well known: changes in skeletal muscle composition lead to a decrease in the potential of muscle to perform exercise aerobically. The cardiovascular response is also dramatically altered, while bone mineralization, protein wasting, and a decrease in total body water can also occur.\(^3,5\) Indeed, the central nervous system, endocrine functions, and blood composition may also be altered by prolonged (longer than 10 days) inactivity. Steroid myopathy and drug effects may also reduce skeletal and respiratory muscle function.\(^2\) Also, there are often medical problems secondary to COPD that result in an added loss of functional capability. These problems may include congestive heart failure, chronic hypoxia, hypercapnia, malnutrition, altered respiratory mechanics, and an increase in secretions that the patient may be unable to expectorate. These complications may influence the patient's ability to concentrate on an apparently simple task. At step II, when the patients regained walking autonomy, their degree of breathlessness, as assessed by the VAS, was severe, and exercise tolerance was severely impaired since most patients could not reach 80m in the 6MWD test. Inspiratory muscle force was also markedly reduced. In the first two stages of our program retraining of the lower extremities was nonspecific and common to both groups. This was because progressive ambulation is considered to be part of the standard therapy and not part of a comprehensive rehabilitation program that includes specific tasks such as cycling, stair climbing, respiratory muscle training, and incremental exercise on the treadmill (steps III and IV).

The mechanisms by which lower extremity exercise improves endurance and breathlessness are still controversial. Our study confirms the lack of changes in functional respiratory function already reported\(^14-16\) and therefore seems to exclude a mechanical explanation for the phenomenon. Support for a true training effect was provided by Casaburi and coworkers,\(^2\) who showed a reduction in lactic acidosis and ventilation that was proportional to the training intensity after completion of an exercise program. Indeed, a recent study by Malais and colleagues\(^25\) documented other evidence for this effect. In this latter study, muscle biopsies of trained patients, but not those of control subjects, showed significant increases in citrate synthase and 3-hydroxyacyl-CoA dehydrogenase (HADH), both oxidative enzymes. In contrast, there was no increase in the three glycolytic enzymes such as lactate dehydrogenase, hexokinase, and phosphofructokinase. The degree of increase in exercise tolerance recorded after step III was much higher than that generally reported after rehabilitative programs in COPD patients.\(^2\) One can speculate that the severely ill patients, who are bedridden for longer periods of time and almost completely deconditioned, may show a more impressive improvement than would stable patients. ZuWallack and associates\(^26\) found a greater improvement in exercise performance in patients who showed poorer initial performance.

The control group also showed an improvement in the sensation of dyspnea not accompanied by an increase in exercise tolerance. It is well known that the mechanisms of dyspnea are complex and that they are not necessarily linked to the effort performed.

Inspiratory muscle function, as assessed by MIP, was also impaired at admission to the RICU. At discharge the increase in MIP in group A was 30% to 35%, which was statistically significant. These data are in agreement with most of the studies that have sought to assess the role of specific inspiratory muscle training.\(^22,28\) Many factors, however, may have influenced the results of the respiratory muscle strength test. Motivation and learning may affect measurements, and anemia, malnutrition, disuse atrophy caused by prolonged mechanical ventilation, steroid-induced myopathy,\(^23\) and the degree of hyperinflation may impair respiratory muscle force. Therefore, the improvement in MIP may not depend solely on the training program, but may depend also on the simultaneous correction of the abnormalities described above. However, no significant changes in MIP were observed in the control group.

The main limitation of the present study is that the two groups of patients were composed of different numbers of subjects, even though randomized, and this was for ethical reasons, since a real 1:1 randomization was not considered acceptable by our hospital Ethics Committee because the primary task of our hospital is rehabilitation. Nevertheless, although there was no significant difference in the two groups—the rehabilitation program unfortunately had no influence on survival or pulmonary function tests—autonomy...
and exercise performance were dramatically improved in the comprehensive rehabilitation group.

In conclusion, we showed that an early, stepwise, comprehensive rehabilitation program may be useful in COPD patients admitted to a RICU recovering from acute respiratory failure as compared with a control group of patients receiving standard medical therapy plus progressive ambulation only. About 80% of the survivors, who were bedridden at admission, recovered satisfactory functional improvement so that they could be discharged in autonomy. A good percentage of these patients showed dramatic improvement, gaining an improved exercise capacity and a reduced sensation of dyspnea not achieved with standard medical therapy. A comprehensive rehabilitation program should thus be started early in every COPD patient admitted to an intensive care environment.

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References