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Effectiveness of early rehabilitation on patients with chronic obstructive lung disease and acute respiratory failure in intensive care units: A case–control study

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Abstract

The effect of early rehabilitation on the outcome of patients with chronic obstructive pulmonary disease (COPD) and acute respiratory failure (ARF) in intensive care units (ICUs) remains unclear. We examined the effect of early rehabilitation on the outcomes of COPD patients requiring mechanical ventilation (MV) in the ICU. This retrospective, observational, case–control study was conducted in a medical center with a 19-bed ICU. The records of all 105 ICU patients with COPD and ARF who required MV from January to December 2011 were examined. The outcomes (MV duration, rates of successful weaning and survival, lengths of ICU and hospital stays, and medical costs) were recorded and analyzed. During the study period, 35 patients with COPD underwent early rehabilitation in the ICU and 70 demographically and clinically matched patients with similar COPD stage, cause of intubation, type of respiratory failure, and levels of disease severity who had not undergone early rehabilitation in the ICU were selected as comparative controls. Multiple regression analysis showed that early rehabilitation was significantly negatively associated with MV duration. Early rehabilitation for COPD patients in the ICU with ARF shortened the duration of their MV.

Keywords

Early rehabilitation, mechanical ventilation, intensive care unit, chronic obstructive pulmonary disease

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by progressive airway limitation, which can cause dyspnea, chronic cough, sputum production, wheezing, fatigue, and hypoxemia. Acute exacerbation, a common complication of COPD, sometimes requires mechanical ventilation (MV) in an intensive care unit (ICU). Pulmonary rehabilitation as a nonpharmacological therapy has recently been added to the standard of care for COPD patients[1,2] because accumulating evidence supports its effectiveness.[3–5] Several studies[1–3,5–7] have reported that pulmonary rehabilitation therapy reduced dyspnea, improved exercise capacity, improved quality of life (QoL), and reduced the lengths of hospital stays. Even for patients with a recent exacerbation of COPD,[4,8–10] pulmonary rehabilitation has been proved an effective and safe intervention that reduced hospital admissions and mortality and improved health-related quality of life (HRQoL). All these studies focus on patients with the most severe form of COPD.[8–11] We previously reported[12] that the early mobilization of MV patients in the ICU shortened MV durations and ICU stays. However, early pulmonary rehabilitation for patients with acute exacerbations COPD, which causes respiratory failure and requires invasive MV in the ICU, is rare. Therefore, we evaluated the effects of this early rehabilitation on the outcomes of COPD patients with acute respiratory failure (ARF) that required MV in the ICU. We collected data on MV duration, rates of successful weaning and survival, lengths of ICU and hospital stays, and medical costs as outcome measurements and analyzed them.

Methods

Setting and patients

The study was done in a medical center with a 19-bed medical ICU. We retrospectively reviewed the medical records of all COPD patients who required an invasive MV using an endotracheal tube for 48 hours and who had been prepared for a scheduled extubation between January 1 and December 31, 2011. Each patient was assessed for their readiness for extubation using the following criteria: hemodynamic stability and recovery from the precipitating illness; and respiratory criteria. Respiratory therapists evaluated patients daily using these criteria for weaning. The intensivists in charge decided whether to extubate.

A multidisciplinary team—a critical care nurse, a nursing assistant, a respiratory therapist, and a physical therapist—was set up to initiate the rehabilitation program within 72 hours of MV in hemodynamically and respiratory stable patients, that is, they did not need a vasopressor, or else they had been using <60% FiO_2 since early 2011. The pulmonary rehabilitation therapy component included dyspnea-relieving strategies, muscle training for upper and lower extremities and inspiratory muscles, and sputum clearance techniques. The rehabilitation protocol included two stages: stage I: passive extremity movement for unconscious patients; and stage II: active extremity movement and interaction with the physical therapist for conscious patients who were able to respond to simple commands in a sitting position on the bed. Physiotherapy was provided twice daily 5 days per week. During the study period, rehabilitation was at the discretion of an attending physician, and rehabilitation was initiated only after physicians had consulted the physical therapist. Therefore, the patients who had not been treated with invasive MV using an endotracheal tube for 48 hours did not undergo additional physiotherapy.

Data collection

Demographic and clinical information of all included patients was collected. The COPD stage was classified using the outcome of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) (http://goldcopd.org/) of each patient's pulmonary function test 3 months before this admission. Outcomes—duration of MV, lengths of ICU and hospital stays, and medical costs—were recorded. The data were retrospectively collected and then analyzed; therefore, informed consent was specifically waived and the study was approved by the Institutional Review Board of Chi Mei Medical Center (IRB #: 10603-009).

Definitions of causes of respiratory failure and successful extubation

Causes of respiratory failure were classified as the pulmonary system (upper airway obstruction, acute respiratory distress syndrome, COPD, pneumonia, malignant effusion, lobar collapse, asthma attack), cardiovascular system (congestive heart failure, pericarditis, cardiomyopathy, acute myocardial infarction, endocarditis), neurological system (status

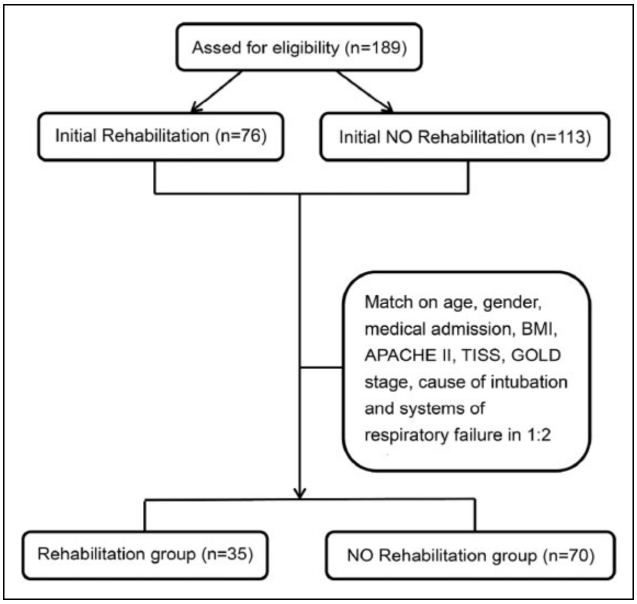

Figure 1. Study algorithm.

epilepticus, stroke), renal system (acute renal failure), gastrointestinal system, and others, as previously described.[12] Successful extubation was defined as not reintubated within 48 hours after extubation.

Statistical analysis

The medical records of 189 COPD patients with respiratory failure were initially reviewed. They were assigned to one of two groups: patients who had undergone rehabilitation therapy (n = 76) and patients who had not (n = 113) (Figure 1). To decrease selection bias, we matched age, gender, medical admission; body mass index (BMI), Acute Physiology and Chronic Health Evaluation (APACHE) II, Therapeutic Intervention Scoring System (TISS), and GOLD stage scores; cause of intubation and systems of respiratory failure in a 1:2 ratio (35 rehabilitation patients and 70 nonrehabilitation patients). Descriptive and inferential statistics were then analyzed and presented as mean ± standard deviation (SD) for continuous variables and as frequencies (%) for categorical variables for the two groups. The differences in demographic, clinical, and laboratory characteristics between the groups were examined using independent samples t tests. The associations between the variables and patient characteristics were analyzed using chi-square or Fisher exact test. Finally, to examine the association between the rehabilitation therapy and clinical outcomes (MV, lengths of ICU and hospital stays, and medical costs), we used multiple regression analysis and adjusted for the confounding effects of demographic, clinical, and laboratory variables significantly related to outcomes. SPSS 19.0 for Windows was used for all statistical analyses.

Results

Demographic characteristics of patients

We matched—based on age, gender, medical admission, BMI, APACHE II, TISS, GOLD stage, cause of intubation, and systems of respiratory failure (Table 1)—35 patients who had undergone early rehabilitation with 70 controls who had not. Most patients (101 (96.2%)) came from Internal Medicine; mean BMI was 22.1 ± 5.3 kg/m^2; mean APACHE II scores were 19.2 ± 6.2; GOLD stages were: 1 (n = 3 (2.9%)), 2 (n = 24 (22.9%)), 3 (n = 50 (47.6%)), and 4 (n = 28 (26.7%)). The mean number of comorbidities was 0.9 ± 0.8. Diabetes was the most common, cancer was the second, and coronary artery disease was the third. The largest number of patients (n = 51 (48.6%)) was postoperatively put on MV (intubated), and the second largest was intubated because of pneumonia (n = 28 (26.7%)). The respiratory system was the most common cause of respiratory failure, and the cardiovascular system was the second most common. The mean MV duration was 152.5 ± 129.3 hours, and the mean lengths of stay were 8.1 ± 7.8 days in the ICU and 22.9 ± 21.5 days in the hospital.

Patients who had undergone early rehabilitation had more comorbidities (1.3 ± 0.9 vs. 0.8 ± 0.7, p = 0.002) and a higher mean hemoglobin level (12.0 ± 2.2 vs. 11.0 ± 2.0, p = 0.018) than did patients who had not undergone rehabilitation therapy (Tables 1 and 2). Most of their laboratory findings and respiratory parameters were not significantly different.

Outcome analyses

Outcome analyses showed that the early rehabilitation group had a higher survival rate and a higher successful extubation rate, a shorter MV duration, shorter ICU and hospital stays, and lower medical costs (Table 3). Moreover, a multiple regression model controlled for age, sex, APACHE II and TISS, COPD stage, hemoglobin and albumin levels, comorbidities, and pulmonary system-induced respiratory failure showed that early mobilization was significantly negatively associated with MV duration, but not

Table 1. Baseline characteristics of planned extubation in COPD patients with respiratory failure.[a]

Groups: Variables	Total (n = 105)	Rehabilitation (n = 35)	No rehabilitation (n = 70)	p
Age (years)	74.8 ± 0.6	74.9 ± 10.5	74.7 ± 10.7	0.912
Age ≥ 65 years	88 (83.8)	30 (85.7)	58 (82.9)	0.708
Male	81 (77.01)	28 (80.0)	53 (75.7)	0.622
Medical admission	101 (96.2)	34 (97.1)	67 (95.7)	1.000
BMI	221 ± 5.3	21.4 ± 4.5	22.4 ± 5.6	0.325
APACHE II	19.2 ± 6.2	17.6 ± 5.6	20.0 ± 6.4	0.061
TISS scale	23.9 ± 6.5	23.1 ± 6.6	24.4 ± 6.4	0.361
COPD stage				
GOLD 1	3 (2.9)	1 (2.9)	2 (2.9)	1.000
GOLD 2	24 (22.9)	7 (20.0)	17 (24.3)	0.622
GOLD 3	50 (47.6)	17 (48.6)	33 (47.1)	0.890
GOLD 4	28 (26.7)	10 (28.6)	18 (25.7)	0.755
Comorbidity	0.9 ± 0.8	1.3 ± 0.9	0.8 ± 0.7	0.002
Coronary artery disease	24 (22.9)	11 (31.4)	13 (18.6)	0.139
Uremia	2 (1.9)	0 (0)	2 (2.9)	0.551
Liver cirrhosis	2 (1.9)	0 (0)	2 (2.9)	0.551
Diabetes	26 (24.8)	14 (40.0)	12 (17.1)	0.011
Stroke	19 (18.1)	8 (22.9)	11 (15.7)	0.370
Cancer	24 (22.9)	11 (31.4)	13 (18.6)	0.139
Cause of intubation				
Hypoventilation	3 (2.9)	1 (2.9)	2 (2.9)	1.000
Upper airway obstruction	5 (4.8)	2 (5.7)	3 (4.3)	1.000
Pneumonia	28 (26.7)	7 (20.0)	21 (30.0)	0.275
Cardiogenic edema	7 (6.7)	2 (5.7)	5 (7.1)	1.000
Extrapulmonary shock	11 (10.5)	4 (11.4)	7 (10.0)	1.000
Postoperative	51 (48.6)	19 (54.3)	32 (45.7)	0.407
Systems of respiratory failure				
Pulmonary	81 (77.1)	25 (71.4)	56 (80.0)	0.324
Cardiovascular	9 (8.6)	4 (11.4)	5 (7.1)	0.477
Neurogenic	3 (2.9)	2 (5.7)	1 (1.4)	0.257
Renal	4 (3.8)	1 (2.9)	3 (4.3)	1.000
Gastrointestinal	4 (3.8)	2 (5.7)	2 (2.9)	0.599
Others[b]	4 (3.8)	1 (2.9)	3 (4.3)	1.000

COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease; BMI: body mass index; APACHE: Acute Physiology and Chronic Health Evaluation; TISS: Therapeutic Intervention Scoring System.
[a]Continuous variables: mean ± standard deviation; nominal variables: number (%); COPD stage using the GOLD (http://goldcopd.org/) classification from each patient's pulmonary function test 3 months before this admission
[b]Bone fracture, oral surgery, and nasopharyngeal surgery.

significantly associated with lengths of ICU and hospital stays, or with medical costs (Table 4).

Discussion

In this 1-year study, we examined the effect of early rehabilitation, with which COPD patients with ARF were treated in a medical ICU within the first 3 days of MV. We found that the duration of MV was significantly shorter in patients treated with early rehabilitation than in matched controls who were not. In one randomized controlled study,[8] airflow obstruction and dyspnea were attenuated and exercise capacity increased in patients who had been admitted with exacerbated COPD and had undergone early rehabilitation therapy compared with patients who had not undergone early rehabilitation therapy. Puhan et al.[10] reported that rehabilitation therapy had moderate-to-large positive effects on HRQoL and exercise capacity in patients with ARF. Therefore, our findings are consistent with those of other studies[3,8,10] and indicate that early rehabilitation for COPD patients with ARF is beneficial. However, our findings are different from one recent RCT,[11] which reported that early rehabilitation during hospital admission for ARF did not reduce the risk of readmission or improve patients'

Table 2. Vital signs and laboratory data before and after planned extubation in COPD patients with respiratory failure.

Groups: Variables	Total ($n = 105$)	Rehabilitation ($n = 35$)	No rehabilitation ($n = 70$)	p
Hemoglobin (g/dL)	11.3 ± 2.1	12.0 ± 2.2	11.0 ± 2.0	0.018
Hematocrit (%)	35.1 ± 7.8	37.4 ± 7.3	33.9 ± 7.8	0.029
Blood urea nitrogen (mg/dL)	28.3 ± 26.9	31.2 ± 36.1	26.9 ± 21.1	0.450
Creatinine (mg/dL)	1.8 ± 1.9	1.8 ± 1.9	1.8 ± 2.0	0.881
Sodium (mmol/L)	137.5 ± 7.6	137.4 ± 7.5	137.6 ± 7.7	0.913
Potassium (mmol/L)	3.9 ± 0.5	3.9 ± 0.6	3.9 ± 0.5	0.788
Calcium (mg/dL)	7.9 ± 0.7	8.0 ± 0.5	7.9 ± 0.8	0.447
Phosphate (mg/dL)	3.51 ± 0.87	3.6 ± 0.8	3.5 ± 0.9	0.569
Albumin (g/dL)	2.72 ± 0.42	2.83 ± 0.49	2.7 ± 0.37	0.058
Heart rate change	−0.1 ± 0.3	−0.1 ± 0.3	−0.1 ± 0.2	0.432
Before extubation	110.0 ± 24.0	107.6 ± 25.0	111.2 ± 23.6	0.477
After extubation	101.8 ± 21.7	97.7 ± 21.7	103.9 ± 21.5	0.167
Mean artery pressure change (%)	−0.2 ± 0.3	−0.2 ± 0.3	−0.2 ± 0.3	0.739
Before extubation	103.1 ± 23.4	106.5 ± 21.8	101.4 ± 24.2	0.292
After extubation	88.3 ± 17.5	92.6 ± 17.2	86.2 ± 17.3	0.075
Respiratory rate change (%)	−0.4 ± 0.5	−0.3 ± 0.6	−0.4 ± 0.5	0.745
Before extubation	24.6 ± 6.5	23.5 ± 5.7	25.2 ± 6.8	0.196
After extubation	19.4 ± 5.7	19.0 ± 5.0	19.5 ± 6.0	0.664
PH change (%)	0.01 ± 0.02	0.01 ± 0.01	0.01 ± 0.02	0.066
Before extubation	7.29 ± 0.14	7.31 ± 0.08	7.29 ± 0.16	0.285
After extubation	7.38 ± 0.09	7.37 ± 0.07	7.39 ± 0.10	0.530
$PaCO_2$ change (%)	−0.4 ± 0.6	−0.2 ± 0.3	−0.4 ± 0.7	0.119
Before extubation	64.1 ± 26.7	61.0 ± 20.0	65.7 ± 29.5	0.396
After extubation	47.8 ± 13.2	50.0 ± 13.4	46.7 ± 13.1	0.233
PaO_2 change (%)	−0.2 ± 1.0	−0.3 ± 0.9	−0.2 ± 1.1	0.679
Before extubation	121.2 ± 76.2	127.4 ± 66.2	118.1 ± 81.0	0.556
After extubation	128.7 ± 83.5	131.4 ± 94.0	127.4 ± 78.4	0.817
PaO_2/FiO_2 change (%)	−0.2 ± 1.1	−0.2 ± 0.7	−0.3 ± 1.2	0.699
Before extubation	244.7 ± 73.5	265.2 ± 62.8	235.9 ± 76.9	0.054
After extubation	260.5 ± 125.8	267.5 ± 101.4	256.9 ± 136.9	0.687

COPD: chronic obstructive pulmonary disease.
[a]Continuous variables: mean ± standard deviation; nominal variables: number (%).

Table 3. Clinical outcomes of the groups.[a]

Groups: Variables	Total ($n = 105$)	Rehabilitation ($n = 35$)	No rehabilitation ($n = 70$)	p
28-Day survival	97 (92.4)	33 (94.3)	64 (91.4)	0.716
Survival at discharge	90 (85.7)	31 (88.6)	59 (84.3)	0.554
Successful extubation	93 (88.6)	33 (94.3)	60 (85.7)	0.329
MV duration (hours)	152.5 ± 129.3	137.3 ± 136.9	160.1 ± 125.7	0.396
ICU stays (days)	8.1 ± 7.8	5.8 ± 6.1	9.2 ± 8.3	0.033
Hospital stays (days)	22.9 ± 21.5	17.9 ± 14.6	25.4 ± 24.0	0.095
Medical costs (×NT$10,000)	20.3 ± 19.7	15.2 ± 13.6	22.9 ± 21.7	0.058

COPD: chronic obstructive pulmonary disease; MV: mechanical ventilation; ICU: intensive care unit; NT$: New Taiwan dollars (US$1 = NT$30).
[a]Continuous variables: mean ± standard deviation; nominal variables: number (%).

recovery of physical function. These differences between our study and this trial might be because of different patients, methods, and outcome measurements. All our patients had ARF, required MV, and underwent early rehabilitation in the ICU, and we focused on short-term outcomes such as MV duration and length of hospital stay. In the cited RCT,[11] not all were COPD patients, the setting was not an ICU, and

Table 4. Multiple regression model: the predictors of MV, ICU stays, hospital stays, and medical costs after planned extubation in COPD patients with respiratory failure.

Variables	Mechanical ventilation (hours)						ICU stays (days)					
	β	*SE*	*t*	*p*	95.0% CI		β	*SE*	*t*	*p*	95.0% CI	
Rehabilitation therapy	−.188	24.327	2.115	**0.037**	−99.754	−3.137	−0.001	1.361	−0.008	0.994	−2.713	2.693
Age	−0.027	1.066	−0.308	0.759	−2.446	1.789	0.090	0.060	1.110	0.270	−0.052	0.185
Gender	−0.088	25.401	−1.064	0.290	−77.465	23.417	−0.033	1.421	−0.422	0.674	−3.422	2.222
APACHE II Score	−0.117	2.360	−1.035	0.304	−7.129	2.245	0.128	0.132	1.222	0.225	−0.101	0.424
TISS	0.062	1.868	0.668	0.506	−2.461	4.959	−0.005	0.105	−0.058	0.954	−0.214	0.202
Hemoglobin	−0.300	5.706	−3.188	**0.002**	−29.522	−6.859	−0.156	0.319	−1.781	0.078	−1.203	0.065
Albumin	−0.089	26.254	−1.047	0.298	−79.629	24.640	−0.033	1.469	−0.411	0.682	−3.521	2.313
Comorbidity	−.198	14.089	−2.294	**0.024**	−60.307	−4.349	−0.076	0.788	−.951	0.344	−2.315	0.816
Pulmonary cause of respiratory failure	0.277	25.561	3.319	**0.001**	34.081	135.598	0.110	1.430	1.413	0.161	−0.819	4.861

Variables	Hospital stays (days)						Medical costs (×NT$10,000)					
	β	*SE*	*t*	*p*	95.0% CI		β	*SE*	*t*	*p*	95.0% CI	
Rehabilitation therapy	−0.058	4.622	−0.568	0.572	−11.802	6.554	−0.041	3.962	−0.429	0.669	−9.568	6.169
Age	−.039	0.203	−.388	0.699	−.481	0.324	0.079	0.174	0.840	0.403	−.199	0.491
Gender	0.038	4.826	0.397	0.692	−7.668	11.498	0.052	4.137	0.582	0.562	−5.808	10.623
APACHE II Score	0.110	0.448	0.854	0.395	−.507	1.273	0.132	0.384	1.092	0.277	−.343	1.183
TISS	0.103	0.355	0.967	0.336	−0.362	1.048	0.137	0.304	1.372	0.174	−.187	1.022
Hemoglobin	−.140	1.084	−1.307	0.194	−3.570	0.736	−.146	0.929	−1.454	0.149	−3.197	0.494
Albumin	−0.026	4.988	−0.266	0.791	−11.232	8.578	−.028	4.276	−.310	0.757	−9.818	7.165
Comorbidity	0.074	2.677	0.750	0.455	−3.309	7.323	−.016	2.295	−.175	0.861	−4.959	4.155
Pulmonary cause of respiratory failure	0.220	4.856	2.308	**0.023**	1.566	20.853	0.113	4.163	1.262	0.210	−3.015	13.520

MV: mechanical ventilation; ICU: intensive care unit; COPD: chronic obstructive pulmonary disease; APACHE: Acute Physiology and Chronic Health Evaluation.

the outcomes of readmission and physical performance were measured, not the outcomes of early rehabilitation. Thus, our findings differ.

In summary, we found that early rehabilitation (within the first 3 days of MV) was beneficial for COPD patients with ARF and in a medical ICU. Although the early rehabilitation therapy programs in our study and others might differ in some details, this kind of intervention can result in better outcomes for COPD patients in the ICU. Most important, as we previously reported,[12] early rehabilitation therapy should be encouraged for critically ill patients with COPD if the health-care facility can afford this treatment.

Several plausible mechanisms support these benefits of early rehabilitation. COPD comorbid with ARF might cause an ICU patient to be physical inactive, and severe physical inactivity reduces muscle protein synthesis, lean mass, and leg muscle strength.[13–15] In addition, ARF is associated with increased systemic inflammation (higher levels of C-reactive protein, interleukin (IL)-6, IL-8, tumor necrosis factor-α, leptin, endothelin-1, and fibrinogen).[16–19] Moreover, systemic inflammation contributes to muscle dysfunction.[20] One randomized trial,[21] however, reported that a quadriceps resistance training program increased isometric quadriceps force by 10% and that muscle biopsies confirmed the benefit of the training on the anabolic–catabolic balance. Two other studies[22,23] also reported that rehabilitation therapy had a positive effect on quadriceps strength and exercise tolerance in patients with COPD comorbid with ARF.

Limitations

This study has some limitations. First, all findings are based on our experience in a single center; thus, they might not be generalizable to all ICUs. Second, we did not assess the safety or feasibility of early rehabilitation therapy, but patient medical records showed no specific adverse effects during or after the rehabilitation therapy. Third, we did not measure changes in physical function before and after rehabilitation therapy to provide more objective evidence to confirm our findings. Fourth, this study was retrospective and could neither be randomized nor blindly evaluated. Some patients did not undergo early rehabilitation because their in-charge physician was unaware of or unwilling to use (or both) the therapy. However, because most patient profiles were as matched as possible between the rehabilitation and no-rehabilitation groups, confounding factors should be minimal in the present study. Prospective clinical trials are required to confirm our findings. Finally, we assessed only the short-term effects in this study, and we did not check the prevalence of ICU-acquired weakness. Post-discharge studies of the long-term effects of early rehabilitation are warranted, especially on the prevalence and recovery from ICU-acquired weakness.

Conclusions

Early rehabilitation for patients in the ICU with COPD comorbid with ARF shortened the duration of their MV.

Declaration of conflicting interests

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