Intensive Care Med (2010) 36:828–835
DOI 10.1007/s00134-010-1842-4

ORIGINAL

**Amal Jubran**
**Gerald Lawm**
**Joanne Kelly**
**Lisa A. Duffner**
**Gokay Gungor**
**Eileen G. Collins**
**Dorothy M. Lanuza**
**Leslie A. Hoffman**
**Martin J. Tobin**

# Depressive disorders during weaning from prolonged mechanical ventilation

Received: 22 June 2009
Accepted: 2 January 2010
Published online: 16 March 2010


**Electronic supplementary material**
The online version of this article (doi:10.1007/s00134-010-1842-4) contains supplementary material, which is available to authorized users.

A. Jubran (✉) · G. Gungor · M. J. Tobin
Division of Pulmonary and Critical Care Medicine, Edward Hines Jr. Veterans Affairs Hospital, Hines IL and Loyola University of Chicago Stritch School of Medicine, Maywood, IL, USA
e-mail: ajubran@lumc.edu

M. J. Tobin
e-mail: mtobin2@lumc.edu

G. Lawm · J. Kelly · L. A. Duffner
RML Specialty Hospital, Hinsdale, IL, USA

E. G. Collins
Center for Management of Complex Chronic Care, Edward Hines Jr. Veterans Affairs Hospital, Hines IL and University of Illinois at Chicago College of Nursing, Chicago, IL, USA

D. M. Lanuza
University of Wisconsin School of Nursing, Madison, WI, USA

L. A. Hoffman
University of Pittsburgh School of Nursing, Pittsburgh, PA, USA

**Abstract** *Purpose:* Patients who require mechanical ventilation are at risk of emotional stress because of total dependence on a machine for breathing. The stress may negatively impact ventilator weaning and survival. The purpose of this study was to determine whether depressive disorders in patients being weaned from prolonged mechanical ventilation are linked to weaning failure and decreased survival. *Methods:* A prospective study of 478 consecutive patients transferred to a long-term acute care hospital for weaning from prolonged ventilation was undertaken. A clinical psychologist conducted a psychiatric interview to assess for the presence of depressive disorders. *Results:* Of the 478 patients, 142 had persistent coma or delirium and were unable to be evaluated for depressive disorders. Of the remaining 336 patients, 142 (42%) were diagnosed with depressive disorders. In multivariate analysis, co-morbidity score [odds ratio (OR), 1.23; $P = 0.007$], functional dependence before the acute illness (OR, 1.70, $P = 0.03$) and history of psychiatric disorders (OR, 3.04, $P = 0.0001$) were independent predictors of depressive disorders. The rate of weaning failure was higher in patients with depressive disorders than in those without such disorders (61 vs. 33%, $P = 0.0001$), as was mortality (24 vs. 10%, $P = 0.0008$). The presence of depressive disorders was independently associated with mortality (OR, 4.3; $P = 0.0002$); age (OR, 1.06; $P = 0.001$) and co-morbidity score (OR, 1.24; $P = 0.02$) also predicted mortality. *Conclusion:* Depressive disorders were diagnosed in 42% of patients who were being weaned from prolonged ventilation. Patients with depressive disorders were more likely to experience weaning failure and death.

**Keywords** Mechanical ventilation · Weaning · Depressive disorders

## Introduction

Critically ill patients who require mechanical ventilation are at risk for mental stress because they know that their ability to breathe depends on assistance from a machine. The presence of an endotracheal (or tracheostomy) tube makes it extremely difficult for most ventilated patients to communicate their physical and emotional needs [1]. Moreover, the inability to talk decreases a patient's sense of control leading to feelings of helplessness, anger and

despair [2]. Coping mechanisms can become overwhelmed, resulting in feelings of "wanting to give up" and a desire to die [3]. As the duration of mechanical ventilation increases, adverse emotional reactions are likely to increase, which may negatively impact a patient's ability to wean from the ventilator.

In some countries, patients who repeatedly fail weaning attempts in the ICU are transferred to a facility that specializes in weaning from prolonged ventilation [4]. These patients typically have several co-morbid conditions—obstructive lung disease, cardiovascular disease and diabetes mellitus—that were present before the onset of acute respiratory failure [5–7]. Depressive disorders have been reported to be prevalent in patients with these chronic illnesses [8, 9]. Accordingly, the presence of co-morbidities together with the emotional stress secondary to acute respiratory failure may be a catalyst for developing depressive disorders in patients who are being weaned from the ventilator. Research on ventilator weaning has primarily focused on physiological variables that predict weaning outcomes [10–12] and the use of different techniques to facilitate weaning [13–15]. In contrast, studies that explore the impact of mental well-being on weaning outcomes and, in particular, the influence of depressive disorders are virtually non-existent.

The aim of the study was to determine whether the presence of depressive disorders is associated with weaning failure and decreased survival in patients who were being weaned from prolonged ventilation at a weaning facility. Specifically, we hypothesized that the presence of a depressive disorder would be associated with an increased likelihood of weaning failure and decreased survival.

## Methods

### Patients

Between August 2005 and November 2006, 478 consecutive patients transferred to RML Hospital (RMLH), a long-term acute care hospital, for weaning from mechanical ventilation were recruited. All patients were tracheotomized before arrival. The study was approved by the Institutional Review Board of RMLH. Informed consent was waived because this non-interventional study posed no added risk to the patient.

### Baseline assessment

Upon arrival at RMLH, the following data were obtained from the medical record: demographics, premorbid characteristics (Charlson CoMorbidity Index, previous history of psychiatric illness), reason for instituting mechanical ventilation (at the transferring hospital) and its duration before transfer to RMLH. Acute Physiology and Chronic Health Evaluation (APACHE II) scores were calculated within 24 h of admission to RMLH to quantify current severity of illness. Functional level before the onset of respiratory failure was assessed using the Zubrod scoring system: 0 = fully active; 1 = restricted in strenuous activity; 2 = ambulatory, capable of self care but not work; 3 = bed-ridden 50% or more of the time, limited self-care; 4 = totally bed-ridden and disabled, no self-care [16]. The scores were obtained by interviewing the patient or family caregiver.

### Psychiatric interview

Within 3 days of admission to RMLH, patients underwent a two-part psychiatric interview conducted by one of our two doctoral-level clinical psychologists. In the first part, the patient's cognitive status was evaluated using the Neurobehavioral Cognitive Status Examination (Cognistat) (see Appendix) [17]. Patients who were unresponsive to verbal or tactile stimuli were classified as comatose; patients who were minimally responsive and had evidence of cognitive impairment were classified as delirious using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for delirium [18]. Patients who were classified as comatose or delirious upon admission to RMLH were reevaluated on a daily basis; if their mental status improved, a complete psychiatric evaluation was then performed.

Patients who had normal cognition underwent the second part of the interview—the psychiatric evaluation. At that time, the psychologist examined the patient for signs and symptoms of depression (see Appendix). Patients were then classified as having *depressive disorders* (major depressive disorder, dysthmic disorder or depressive disorder not otherwise specified) if they met the DSM-IV criteria for depressive disorders.

### Weaning status

Patients underwent daily weaning trials as tolerated, consisting of either pressure-support ventilation or spontaneous breathing trials through a tracheostomy (see Appendix). A patient who was able to breathe spontaneously without mechanical ventilation at discharge from RMLH was considered a weaning success. A patient who was not successfully weaned at discharge or died while at RMLH was considered a weaning failure. Patients were followed daily until hospital discharge.

### Data analysis

Categorical variables are reported as proportions, and continuous variables are reported as medians and

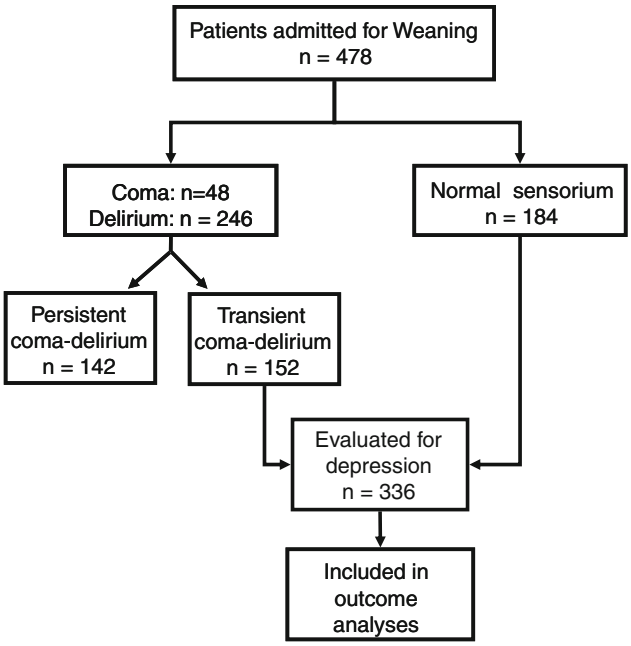


**Fig. 1** Study enrollment

interquartile range. Comparison of continuous variables between two subgroups was performed using Mann-Whitney *U* test and Kruskal–Wallis one-way ANOVA test for multiple subgroups. Comparison between categorical variables was performed using the Pearson chi-square test or Fisher's exact test, as appropriate. Multivariate logistic regression analysis was performed to evaluate the impact of baseline characteristics on the presence of depressive disorders. Multivariate logistic regression analysis was also performed to determine variables independently associated with death. Variables included were clinically relevant baseline characteristics (age, Charlson Comorbidity Index, previous history of psychiatric illness); data related to the previous ICU stay (reason for intubation, days on ventilator before transfer to RMLH); data related to RMLH stay (APACHE II score, presence of transient delirium, presence of depressive disorders, number of days a patient received anxiolytics and anti-depressants).

## Results

Of the 478 patients, 184 (38.5%) were judged to have a normal sensorium and were evaluated for depressive disorders on admission to RMLH (Fig. 1; Table 1).

The remaining 294 could not be evaluated because they were comatose (48 patients) or delirious (246 patients). Of 294 comatose-delirious patients, 142 (29.7%) remained comatose or delirious and were unable to be evaluated for depressive disorders. This cohort was termed the persistent coma-delirium group and not included in the outcome analysis. The other 152 (31.8%) comatose-delirious patients had an improvement in sensorium. This cohort, termed the transient coma-delirium group, was evaluated for depressive disorders when alert and was included in the outcome analysis. The final evaluable cohort consisted of 336 patients (Fig. 1). Compared with the non-evaluable group (persistent comatose-delirium group), the evaluable group (normal sensorium and transient coma-delirium groups) had a lower APACHE score [median 15 (range

**Table 1** Patient characteristics

| Variable | Persistent coma-delirium ($n = 142$) | Transient coma-delirium ($n = 152$) | Normal sensorium ($n = 184$) |
|---|---|---|---|
| Age, median years (IQR)[a] | 73 (58–80) | 72 (63–80) | 68 (57–77)[c] |
| Sex, female/male (% female) | 64/78 (45%) | 75/77 (49%) | 94/90 (51%) |
| APACHE II, median (IQR)[b] | 17 (14–21) | 17 (13–19) | 14 (12–16)[c,d] |
| Reasons for respiratory failure | | | |
| Postoperative (%) | 23 | 32 | 33 |
| Acute lung injury (%) | 20 | 28 | 22 |
| COPD (%) | 4 | 5 | 7 |
| Neuromuscular (%) | 32 | 11 | 15 |
| Others (%) | 21 | 24 | 23 |
| Charlson Comorbidity Index, median (IQR)[b] | 2 (1–3) | 2 (1–4) | 1 (0.8–3)[c] |
| Premorbid functional independence (Zubrod 0–2) (%) | 67 | 57 | 69[e] |
| Duration of mechanical ventilation before transfer, median days (IQR) | 19 (15–27) | 23 (18–30) | 21 (15–31) |

*APACHE* Acute Physiology and Chronic Health Evaluation, *IQR* interquartile range, *COPD* chronic obstructive pulmonary disease

[a] $P < 0.05$ comparing three groups using Kruskal–Wallis one-way ANOVA test

[b] $P < 0.01$ comparing three groups using Kruskal–Wallis one-way ANOVA test

[c] $P < 0.5$ comparing transient coma-delirium group with normal sensorium using Dunn's test

[d] $P < 0.5$ comparing persistent coma-delirium group with normal sensorium using Dunn's test

[e] $P < 0.5$ comparing transient coma-delirium group with normal sensorium using chi-square

**Table 2** Patient characteristics stratified by depressive disorders

| Variable | No depressive disorders ($n = 194$) | Depressive disorders ($n = 142$) | $P$ value |
|---|---|---|---|
| Age, median years (IQR) | 69 (58–77) | 72 (61–78) | 0.17 |
| Sex, female/male (% female) | 99/95 (51%) | 70/72 (49%) | 0.75 |
| APACHE II, median (IQR) | 14 (12–17) | 16 (12–19) | 0.04 |
| Reasons for respiratory failure | | | |
| Postoperative (%) | 31 | 35 | 0.41 |
| Acute lung injury (%) | 22 | 28 | 0.21 |
| COPD (%) | 8 | 4 | 0.11 |
| Neuromuscular (%) | 15 | 11 | 0.33 |
| Others (%) | 24 | 22 | 0.61 |
| Charlson Comorbidity Index, median (IQR) | 1 (0.3–2) | 2 (1–4) | 0.0002 |
| Duration of mechanical ventilation before transfer, median days (IQR) | 20 (15–29) | 23 (18–34) | 0.005 |

*APACHE* Acute Physiology and Chronic Health Evaluation, *IQR* interquartile range, *COPD* chronic obstructive pulmonary disease

12–18) vs. 17 (range 14–21), $P < 0.002$)] and a lower rate of neurological disorder as cause of respiratory failure (13 vs. 32%, $P < 0.0001$).

## Prevalence of delirium (excluding comatose patients)

On arrival to RMLH, delirium was diagnosed in 246 (52%) of the patients. Compared with the normal mentation group, the delirium group was older [73 (64–80) vs. 68 years (57–77), $P < 0.0003$)], had a higher APACHE score [16 (13–19) vs. 14 (12–16), $P < 0.0001$)] and a higher Charlson co-morbidity index [2 (1–3) vs. 1 (0.75 to 3), $P < 0.002$]. The number of days patients received anxiolytics at RLMH was similar in the delirium group and normal mentation group [3 (0–13.25) vs. 7 (0–18) days, $P = 0.26$]. Length of stay at RMLH was higher in the delirium group than in the normal mentation group [35 (26–44) vs. 31 (21–42) days, $P = 0.04$)]. Mortality rate, however, was equivalent in the delirium and normal mentation group: 18 versus 16%, $P = 0.59$.

## Prevalence of depressive disorders

Of the 336 patients evaluated by the psychologist, 142 (42%) were diagnosed with depressive disorders. Of those 142 patients, 17 (12%) were diagnosed with major depression, 6 (4%) with dysthmic disorder and 119 (84%) with depressive disorder not otherwise specified (NOS). In the 142 patients who were diagnosed with a depressive disorder, 90% received antidepressants and psychotherapy, 6% received psychotherapy alone and 4% refused antidepressants but agreed to psychotherapy (see Appendix).

Patients with depressive disorders had a higher APACHE score ($P = 0.04$) and Charlson Co-morbidity Index ($P = 0.0002$), and spent longer on the ventilator before transfer to RMLH ($P = 0.005$) than those without such disorders (Table 2). The percentage of patients who were functionally dependent (Zubrod scores 3–4) before the onset of respiratory failure was greater among patients with depressive disorders than among those without such disorders (47 vs. 29%, $P = 0.0006$) (Fig. 2). Age, gender, and cause of acute respiratory failure were similar among patients with and without depressive disorders. In patients diagnosed with depressive disorders, 35% had a previous history of psychiatric disorders compared with 17% of patients not diagnosed with this condition ($P < 0.0001$). Depressive disorders were more prevalent in patients with transient delirium than in patients with normal mentation (58.6 vs. 28.8%, $P < 0.0001$).

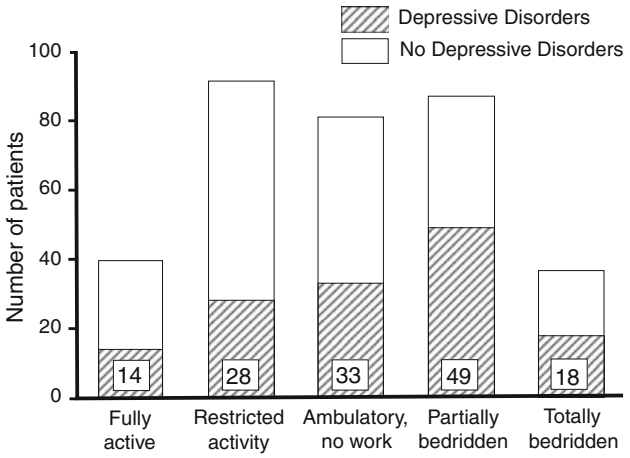


**Fig. 2** Distribution of functional status among enrolled patients the month before onset of respiratory failure. *Hatched area* of each column represents the number of patients diagnosed with depressive disorders at the weaning facility; clear area represents the number of patients without depressive disorders. Functional dependence (partially or totally bedridden) was 1.6 times more frequent among patients with depressive disorders than among those without such disorders ($P = 0.0006$)

Multivariate logistic regression analysis showed that Charlson Co-morbidity Index (odds ratio 1.2), functional dependence before acute illness (odds ratio 1.7) and

**Table 3** Multivariate logistic analysis to determine the relationship between depressive disorders and baseline characteristics

| Variable | Odd ratio | 95% CI | *P* value |
|---|---|---|---|
| Previous psychiatric history | 3.04 | 1.74–5.30 | 0.0001 |
| Premorbid functional dependence (Zubrod >2) (%) | 1.70 | 1.04–2.79 | 0.03 |
| Charlson Comorbidity Index | 1.23 | 1.06–1.44 | 0.007 |
| APACHE II | 1.05 | 0.99–1.12 | 0.11 |
| Etiology of respiratory failure | | | |
| Postoperative | 1.26 | 0.66–2.40 | 0.48 |
| Acute lung injury | 1.28 | 0.65–2.53 | 0.48 |
| COPD | 0.41 | 0.13–1.31 | 0.12 |
| Neuromuscular | 1.47 | 0.64–3.38 | 0.37 |
| Age | 1.00 | 0.98–1.02 | 0.88 |
| Duration of mechanical ventilation before transfer | 1.00 | 0.99–1.01 | 0.36 |
| Female | 0.94 | 0.58–1.53 | 0.80 |

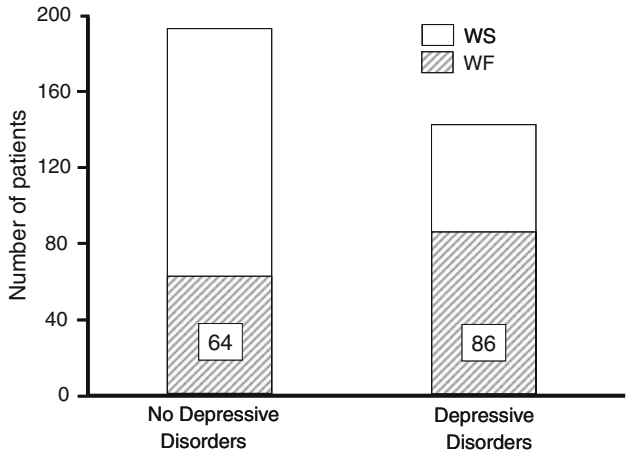


**Fig. 3** Number of patients with and without a depressive disorder. *Hatched area* of each column represents the number of patients who failed weaning, *WF*; clear area represents the number of patients who were successfully weaned, *WS*. Ventilator weaning was less frequent among patients with depressive disorders than among those without such disorders ($P < 0.0001$)

history of psychiatric illness (odds ratio 3.0) were significant predictors of depressive disorders after controlling for age, gender, APACHE score, cause of acute respiratory failure and days on the ventilator before transfer (Table 3).

### Effect of depressive disorders on patient outcome

The number of patients who could not be weaned from the ventilator was greater among patients with depressive disorders than among those without such disorders (Fig. 3). Indeed, patients with depressive disorders were three times more likely to fail weaning as those patients without such disorders (odds ratio 3.1, range 1.9–4.9, $P < 0.0001$). Mortality was 2.4 times higher among patients with depressive disorders than among those without such disorders (Table 4). While the duration of mechanical ventilation at RMLH was twice as long in patients with depressive disorders compared to patients without such disorders, length of stay was equivalent in the two groups (Table 4).

**Table 4** Effect of depressive disorders on patient outcome

| Variable | No depressive disorders ($n = 194$) | Depressive disorders ($n = 142$) | *P* value |
|---|---|---|---|
| Weaning failure (%) | 33.0 | 60.6 | 0.0001 |
| Mortality (%) | 10.3 | 23.9 | 0.0008 |
| Duration of MV at RMLH, days, median (IQR) | 13 (5–38) | 24 (8–41) | 0.007 |
| Length of stay at RMLH, days, median (IQR) | 33 (24–42) | 35 (23–46) | 0.55 |

*IQR* interquartile range

**Table 5** Multivariate logistic regression of variables predicting mortality

| Variable | Odds ratio | 95% CI | *P* value |
|---|---|---|---|
| Depressive disorders | 4.32 | 1.99–9.33 | 0.0002 |
| Charlson Comorbidity Index | 1.24 | 1.03–1.49 | 0.02 |
| Previous psychiatric history | 0.85 | 0.38–1.90 | 0.69 |
| Age | 1.06 | 1.02–1.09 | 0.001 |
| Etiology of respiratory failure | | | |
| Postoperative | 0.58 | 0.23–1.49 | 0.26 |
| Acute lung injury | 1.11 | 0.44–2.80 | 0.82 |
| COPD | 0.89 | 0.19–4.17 | 0.88 |
| Neuromuscular | 0.66 | 0.16–2.63 | 0.55 |
| Duration of mechanical ventilation before transfer | 1.00 | 0.99–1.02 | 0.17 |
| APACHE II | 1.06 | 0.97–1.16 | 0.22 |
| Anxiolytics | 0.99 | 0.96–1.02 | 0.57 |
| Antidepressants | 0.95 | 0.92–0.99 | 0.007 |
| Transient delirium | 0.38 | 0.18–0.83 | 0.02 |

Multivariate logistic regression analysis showed that depressive disorders (odds ratio 4.32, $P = 0.0002$), age (odds ratio 1.06, $P = 0.001$) and Charlson co-morbidity index (odds ratio 1.24, $P = 0.02$) were associated with an increased risk for dying at RMLH (Table 5). Factors associated with a decreased mortality included transient delirium (odds ratio 0.38, $P = 0.02$) and number of days on anti-depressant agents (odds ratio 0.95, $P = 0.007$).

## Discussion

Of patients capable of undergoing a psychiatric interview on arrival to a weaning facility, 42% were diagnosed with depressive disorders. The presence of depressive

disorders appeared to be related to factors present before the onset of acute respiratory failure, namely the co-morbidity index, functional level before acute illness and previous psychiatric illness. The severity of medical illness at the time of arrival to the weaning facility did not contribute to the presence of depressive disorders. The presence of depressive disorders was associated with weaning failure and a higher mortality rate.

## Prevalence of depressive disorders

To our knowledge, this is the first study to prospectively evaluate the prevalence of depressive disorders during weaning from prolonged mechanical ventilation. The prevalence of depression has largely been examined in survivors of critical illness several months after hospital discharge rather than while hospitalized [19–22]. Using the same diagnostic technique that we used (structured interview), Weinert et al. [23] found that 32% of ICU patients who required mechanical ventilation were diagnosed with depressive disorders 2 months after discharge—a rate comparable to ours (42%). Other investigators have reported that when patients requiring mechanical ventilation were surveyed after ICU discharge, the prevalence of depression was 35% at 2 months and 32% at 12 months; that is, depression showed little decrease [6, 24].

In the present study, the presence of depressive disorders was not related to severity of the acute illness (APACHE II score, etiology of respiratory failure, days on ventilator before transfer) (Table 3). Instead, the presence of depressive disorders was related to the patient's previous health status (Charlson Co-morbidity Index, previous psychiatric history and functional dependence). Studies in medical in-patients have revealed that pre-morbid status is a predictor of depressive disorders [25, 26]. These data suggest that ventilated patients with a previous psychiatric history or long-term physical disability may be at risk for developing depressive disorders.

## Delirium

On the basis of a semi-structured interview conducted by an experienced psychologist, patients were considered to have delirium if they met the DSM IV criteria for delirium. Other investigators have used screening tools, such as the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) or Intensive Care Delirium Screening Checklist (ICDSC) to identify delirium in ICU patients [27–30]. Half of our patients had delirium on arrival at RMLH. This incidence of delirium is lower than the incidence of 82% reported by Ely et al. [29] who used the CAM-ICU to define delirium, but higher than the value of 16% reported by Bergeron et al. [31] who used the ICDSC to define delirium.

Although length of hospital stay was greater in our delirium group than in our normal mentation group, mortality was almost identical in the two groups. These findings are in sharp contrast with studies of ICU ventilated patients, where delirium was associated with increased in-hospital mortality [27, 30] and increased mortality 6 months later [29]. Several factors may explain the differences. One, our patients were in the recovery stage, whereas ICU patients were in the acute phase of a critical illness. Possibly, it is the acute illness, not delirium per se, which explains the association between delirium and increased mortality in ICU patients. Indeed, in ventilated patients, delirium paralleled shock and APACHE score as a predictor of ICU mortality [30]. Moreover, when ventilated patients were transferred from the ICU to a step-down unit for weaning, delirium was not associated with increased risk of dying [32]. Two, the daily dosage of lorazepam in our patients (median 0.8 mg) is 10% of the median dose reported for ICU-ventilated patients [33]. Several groups have reported that sedatives are associated with the development of delirium [27, 34, 35], longer ventilator duration and longer hospital stay [36]. Third, delirium in our patients was diagnosed by experienced psychologists, whereas screening tools, such as CAM-ICU or ICDSC, were employed to identify delirium in the ICU studies [29, 30].

On post hoc analysis, we identified two delirium groups: patients with persistent and transient delirium. Characteristics of the two groups were similar with the exception that a neurological disorder as the cause of respiratory failure was 2.4 times more frequent in the persistent-delirium group than in the transient-delirium group (26 vs. 10%, $P = 0.003$).

Delirium improved in 62% of patients following admission to RMLH (the transient delirium group). It seems plausible to infer that improved mentation signals an improvement in overall illness, leading to better survival. Although patients with transient delirium were older and had more severe illness than patients with normal mentation (Table 1), mortality was equivalent (16%) in the two groups. When corrected for these and other variables on multivariate logistic regression analysis, patients who experienced an improvement in delirium experienced a decrease in mortality (Table 5).

## Depressive disorders and outcome

Patients with depressive disorders were three times more likely to fail weaning as patients without such disorders. This observation suggests that the presence of depressive disorders contributed to weaning failure. Conversely, inability to wean before transfer to RMLH may have contributed to depression. Persistent discomfort from a critical illness, prolonged bed rest and ventilator

dependency may have caused depression while the patient was in the ICU.

The presence of depressive disorders might also interfere with the pragmatics of weaning. Weakened or deconditioned respiratory muscles are believed to be a major reason that patients repeatedly fail weaning attempts [37]. One approach to reconditioning is the use of daily trials of spontaneous breathing [38]. Initiation of a spontaneous-breathing trial is under the control of the health-care team. Soon after a trial commences, however, many patients in a chronic weaning facility indicate that they wish to be placed back on the ventilator. Although our reasoning is speculative, it is possible that patients with depressive disorders will be more likely to make such a request. Apathy, loss of energy and diminished motivation are commonly seen with depression [8, 39]. As such, depressed patients may not have the energy and motivation necessary to tolerate the challenge of daily spontaneous breathing trials. If so, depressive disorders would contribute to weaning failure.

Patients with depressive disorders experienced a higher mortality than those patients without such disorders. The increased mortality in patients with depressive disorders was still evident after controlling for age and co-morbidity. Moreover, treatment with anti-depressants was associated with a decreased risk for dying (Table 5). The fact that treatment for depressive disorders was associated with a decrease in mortality suggests a link between depressive disorders and mortality. Conceivably, the presence of depressive disorders may add to the distress that patients experience while receiving mechanical ventilation. Under such circumstances, coping mechanisms may become overwhelmed and, thus, a feeling of giving up may have occurred [3].

The association between poor outcome (weaning failure and death) and depression raises another possible explanation: depression may be a reaction to the underlying physical illness before transfer to RMLH, and depression may not be directly linked to mortality. If that is the case, the final cause of death should be related to the pre-existing physical illness that the patient had before admission to RMLH (as opposed to depression). We found, however, that only 53% of the deaths were a consequence of the illness that patients had before transfer to RMLH.

### Study limitations

First, the study was confined to a single center. The cohort, however, consisted of a mixed population of medical and surgical patients with diverse etiologies of acute respiratory failure (Table 1). Second, unmeasured covariates related to the original ICU stay (e.g., exposure to psychoactive medication, number of failed weaning attempts in the ICU) may have contributed to the presence of depressive disorders. If these factors made a significant contribution, one would have expected duration of mechanical ventilation before arrival at RMLH to be a significant contributor to the presence of depressive disorders. This was not the case. On multivariate analysis, duration of mechanical ventilation before transfer was not a significant predictor of depressive disorders (Table 3). Third, the psychologists were blinded to the managing physician's forecasting of weaning outcome when they first assessed the patient, but it was almost impossible to blind the psychologists to the physician's opinion later in the patient's stay.

In conclusion, evidence of depressive disorders was present in almost half the patients being weaned from prolonged ventilation. The presence of depressive disorders was related to factors present before the onset of acute respiratory failure and associated with an increased risk of weaning failure and death.

**Acknowledgment** This paper was supported by funding from the National Institute of Health (RO1 NR008782) and a Merit Review grant from the Veterans Administration Research Service

**Conflict of interest statement** No financial or other potential conflicts of interest exist.

## References

1. Hoit JD, Banzett RB, Brown R (2008) Ventilator-supported speech. In: Tobin MJ (ed) Principles and practice of mechanical ventilation. McGraw Hill, New York, pp 1163–1172
2. Riggio RE, Singer RD, Hartman K, Sneider R (1982) Psychological issues in the care of critically-ill respirator patients: differential perceptions of patients, relatives, and staff. Psychol Rep 51:363–369
3. Engel GL (1968) A life setting conducive to illness. The giving-up–give-up complex. Ann Intern Med 69:293–300
4. Scheinhorn DJ, Hassenpflug MS, Votto JJ, Chao DC, Epstein SK, Doig GS et al (2007) Post-ICU mechanical ventilation at 23 long-term care hospitals: a multicenter outcomes study. Chest 131:85–93
5. Scheinhorn DJ, Hassenpflug MS, Votto JJ, Chao DC, Epstein SK, Doig GS et al (2007) Ventilator-dependent survivors of catastrophic illness transferred to 23 long-term care hospitals for weaning from prolonged mechanical ventilation. Chest 131:76–84
6. Douglas SL, Daly BJ, Gordon N, Brennan PF (2002) Survival and quality of life: short-term versus long-term ventilator patients. Crit Care Med 30:2655–2662

7. Douglas SL, Daly BJ, Kelley CG, O'Toole E, Montenegro H (2007) Chronically critically ill patients: health-related quality of life and resource use after a disease management intervention. Am J Crit Care 16:447–457
8. Koenig HG, Blazer DG (1992) Epidemiology of geriatric affective disorders. Clin Geriatr Med 8:235–251
9. Suchyta MR, Beck CJ, Key CW, Jephson A, Hopkins RO (2008) Substance dependence and psychiatric disorders are related to outcomes in a mixed ICU population. Intensive Care Med 34:2264–2267
10. Yang K, Tobin MJ (1991) A prospective study of indexes predicting outcome of trials of weaning from mechanical ventilation. N Engl J Med 324:1445–1450
11. Tobin MJ, Jubran A (2006) Variable performance of weaning-predictor tests: role of Bayes' theorem and spectrum and test-referral bias. Intensive Care Med 32:2002–2012
12. Jubran A, Grant BJ, Laghi F, Parthasarathy S, Tobin MJ (2005) Weaning prediction: esophageal pressure monitoring complements readiness testing. Am J Respir Crit Care Med 171:1252–1259
13. Esteban A, Frutos F, Tobin MJ, Alia I, Solsona JF, Valverdu I et al (1995) A comparison of four methods of weaning patients from mechanical ventilation. N Engl J Med 332:345–350
14. Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rekik N et al (1994) Comparison of three methods of gradual withdrawing from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 150:896–903
15. Vitacca M, Vianello A, Colombo D, Clini E, Porta R, Bianchi L et al (2001) Comparison of two methods for weaning patients with chronic obstructive pulmonary disease requiring mechanical ventilation for more than 15 days. Am J Respir Crit Care Med 164:225–230
16. Zubrod C, Schneiderman M, Frei E, Brindley C, Gold G et al (1960) Appraisal of methods for the study of chemotherapy of cancer in man: comparative therapeutic trial of nitrogen mustard and triethylene fluophosphonate. J Chronic Dis 11:7–33
17. Kiernan RJ, Mueller J, Langston JW, Van Dyke C (1987) The Neurobehavioral Cognitive Status Examination: a brief but quantitative approach to cognitive assessment. Ann Intern Med 107:481–485
18. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, 4th edn. American Psychiatric Association, Washington DC
19. Jones C, Skirrow P, Griffiths RD, Humphris GH, Ingleby S, Eddleston J et al (2003) Rehabilitation after critical illness: a randomized, controlled trial. Crit Care Med 31:2456–2461
20. Jackson JC, Hart RP, Gordon SM, Shintani A, Truman B, May L et al (2003) Six-month neuropsychological outcome of medical intensive care unit patients. Crit Care Med 31:1226–1234
21. Hopkins RO, Weaver LK, Collingridge D, Parkinson RB, Chan KJ, Orme JF Jr (2005) Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. Am J Respir Crit Care Med 171:340–347
22. Kress JP, Gehlbach B, Lacy M, Pliskin N, Pohlman AS, Hall JB (2003) The long-term psychological effects of daily sedative interruption on critically ill patients. Am J Respir Crit Care Med 168:1457–1461
23. Weinert C, Meller W (2006) Epidemiology of depression and antidepressant therapy after acute respiratory failure. Psychosomatics 47:399–407
24. Chelluri L, Im KA, Belle SH, Schulz R, Rotondi AJ, Donahoe MP et al (2004) Long-term mortality and quality of life after prolonged mechanical ventilation. Crit Care Med 32:61–69
25. McCusker J, Cole M, Dufouil C, Dendukuri N, Latimer E, Windholz S et al (2005) The prevalence and correlates of major and minor depression in older medical inpatients. J Am Geriatr Soc 53:1344–1353
26. Koenig HG, Meador KG, Shelp F, Goli V, Cohen HJ, Blazer DG (1991) Major depressive disorder in hospitalized medically ill patients: an examination of young and elderly male veterans. J Am Geriatr Soc 39:881–890
27. Ouimet S, Kavanagh BP, Gottfried SB, Skrobik Y (2007) Incidence, risk factors and consequences of ICU delirium. Intensive Care Med 33:66–73
28. Plaschke K, von Haken R, Scholz M, Engelhardt R, Brobeil A, Martin E et al (2008) Comparison of the confusion assessment method for the intensive care unit (CAM-ICU) with the Intensive Care Delirium Screening Checklist (ICDSC) for delirium in critical care patients gives high agreement rate(s). Intensive Care Med 34:431–436
29. Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell FE Jr et al (2004) Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA 291:1753–1762
30. Lin SM, Liu CY, Wang CH, Lin HC, Huang CD, Huang PY et al (2004) The impact of delirium on the survival of mechanically ventilated patients. Crit Care Med 32:2254–2259
31. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y (2001) Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. Intensive Care Med 27:859–864
32. Nelson JE, Tandon N, Mercado AF, Camhi SL, Ely EW, Morrison RS (2006) Brain dysfunction: another burden for the chronically critically ill. Arch Intern Med 166:1993–1999
33. Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT et al (2008) Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (awakening and breathing controlled trial): a randomised controlled trial. Lancet 371:126–134
34. Dubois MJ, Bergeron N, Dumont M, Dial S, Skrobik Y (2001) Delirium in an intensive care unit: a study of risk factors. Intensive Care Med 27:1297–1304
35. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS et al (2006) Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology 104:21–26
36. Kress JP, Pohlman AS, O'Connor MF, Hall JB (2000) Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 342:1471–1477
37. Cattapan SE, Laghi F, Tobin MJ (2003) Can diaphragmatic contractility be assessed by airway twitch pressure in mechanically ventilated patients? Thorax 58:58–62
38. Laghi F, Tobin MJ (2003) Disorders of the respiratory muscles. Am J Respir Crit Care Med 168:10–48
39. Stoudemire A, Thompson TL (1983) Medication noncompliance: systematic approaches to evaluation and intervention. Gen Hosp Psychiatry 5:233–239