Self-Reported Symptoms of Depression and Memory Dysfunction in Survivors of ARDS

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Abstract

Background—Survivors of ARDS have well documented physical limitations, but psychological effects are less clear. We determined the prevalence of self-reported depression and memory dysfunction in ARDS survivors.

Methods—Six to 48 (median 22) months after ICU discharge, we administered instruments assessing depression symptoms (Beck Depression Inventory-II [BDI-II]) and memory dysfunction (Memory Assessment Clinics Self-Rating Scale [MAC-S]) to 82 ARDS patients who were enrolled in a prospective cohort study in four university-affiliated ICUs.

Results—Sixty-one (74%), 64 (78%), and 61 (74%) patients fully completed the BDI-II, MAC-S (Ability subscale), and MAC-S (Frequency of Occurrence subscale) instruments. Responders (similar to nonresponders) were young (median 42 years, interquartile range [IQR] 35 to 56), with high admission illness severity and organ dysfunction. The median BDI-II score was 12 (IQR 5 to 25). Twenty-five (41%) patients reported moderate-severe depression symptoms and were less likely to return to work than those with minimal-mild symptoms (8/25 [32%] vs 25/36 [69%]; $p = 0.005$). Median MAC-S (Ability) and MAC-S (Frequency of Occurrence) scores were 76 (IQR 61 to 93) and 91 (IQR 77 to 102), respectively; 8%, 16%, and 20% scored > 2 , > 1.5 , and > 1 SD(s), respectively, below age-adjusted population norms for each subscale. BDI-II and MAC-S scores were negatively correlated (Spearman coefficient -0.58 and -0.50 for Ability and Frequency of

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Occurrence subscales, respectively; $p < 0.0001$). Univariable analyses showed no demographic or illness-severity predictors of BDI-II (including the Cognitive subscale) or MAC-S (both subscales); results were similar when restricted to patients whose primary language was English.

Conclusions—ARDS survivors report a high prevalence of depression symptoms and a lower prevalence of memory dysfunction 6 to 48 months after ICU discharge. Depression symptoms may hinder the return to work, or patients may report these symptoms because of inability to re-enter the workforce.

Keywords

cross-sectional; depression; memory disorders; outcomes survey; respiratory distress syndrome; adult

Patients with acute lung injury have acute hypoxemic respiratory failure with bilateral pulmonary infiltrates not due to left atrial hypertension.¹ This disorder, including the more hypoxemic subgroup of ARDS, is associated with pulmonary and nonpulmonary risk factors and has an estimated incidence of nearly 200,000 cases/year in the United States,² with a case-fatality rate of 25% to 50%.^{3–8} Given the large number of patients with acute lung injury surviving their ICU and hospital stay, interest in long-term outcomes is growing. Current evidence suggests that survivors have persistent generalized weakness⁹ and reduced quality of life^{9–13} compared to age-matched population controls, but relatively preserved pulmonary function.^{9,11,14,15} Long-term outcomes include significant cognitive impairment and emotional distress,^{11,16} but the prevalence of these findings, their pathophysiology, and their functional consequences remain unclear.

We followed ARDS survivors enrolled in a 5-year prospective cohort study after hospital discharge⁹ and observed that some patients reported symptoms of depression and memory loss; others were unable to return to work. In light of these accruing observations, we decided to more formally evaluate the prevalence of depression symptoms and self-reported memory deficits in ARDS survivors and to determine the relationship between depression symptoms and return to work. We have previously reported some results in abstract form.¹⁷

Materials and Methods

Patients

The patients in this study had participated in a previously reported prospective cohort study of ARDS survivors enrolled from ICUs at four University of Toronto teaching hospital, between May 1998 and May 2001.^{9,11,18} Eligible patients were at least 16 years old and had a P_{aO_2} /inspired fraction of oxygen ratio of 200 or less while receiving mechanical ventilation with a positive end-expiratory pressure of at least 5 cm H₂O, airspace changes in all four quadrants on chest radiography, and an identifiable risk factor for ARDS. Patients were excluded if they were immobile prior to ICU admission, had a history of lung resection, or had a neurologic disease or psychiatric disorder documented in their chart. We obtained informed consent for questionnaire completion. The University Health Network Research Ethics Board approved this study.

Survey Administration and Outcomes

We mailed patients a questionnaire containing two self-administered instruments: the Beck Depression Inventory II (BDI-II)¹⁹ and Memory Assessment Clinics Self-Rating Scale (MAC-S).^{20–22} We followed up nonresponders with two telephone calls. Study personnel or family members helped administer the instruments for those who needed assistance (eg, translation for non-English readers), according to patient preference. Patients returned the questionnaires in person at a follow-up visit or by mail. Because we designed this study while follow-up of patients enrolled in the prospective cohort was underway, questionnaires were administered over a broad range of times after ICU discharge.

The BDI-II instrument consists of 21 questions and screens for depression using criteria consistent with the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition. Higher scores (range, 0 to 63) indicate more depression symptoms. This scale consists of two subscales measuring cognitive (9 items) and somatic-affective (12 items) symptoms,¹⁹ a factor structure which has been validated in medical patients.^{23,24} Based on testing in psychiatric outpatients, depression symptom severity is classified as minimal (score 0 to 13), mild (14 to 19), moderate (20 to 28), and severe (29 to 63).¹⁹ Psychometric properties of the BDI-II instrument include high internal consistency, high content validity, validity in differentiating between depressed and nondepressed persons, and sensitivity to change.²⁵

The MAC-S instrument measures self-reported performance in daily memory tasks, divided into two subscales. Ability (21 items) probes the ability to remember specific types of information, and Frequency of Occurrence (24 items) asks about the frequency of particular memory problems. Higher scores (range for Ability, 21 to 105; range for Frequency of Occurrence, 24 to 120) indicate better performance. Investigators have confirmed the high test-retest reliability of this scale.²⁶

Statistical Analysis

We summarized non-normally distributed continuous data using medians (interquartile range [IQR]) and compared groups using Wilcoxon rank-sum tests. Categorical data were summarized as proportions and compared using χ^2 tests or Fisher exact tests. Correlation between instruments was measured using Spearman correlation. We excluded questionnaires with any missing items, which constituted 10% of questionnaires for BDI-II and MAC-S (Ability subscale) and 14% for MAC-S (Frequency of Occurrence subscale), from all primary analyses. However, we included all responses when describing baseline demographic characteristics. We examined the influence of time of questionnaire return on instrument scores using linear regression, and planned to analyze all surveys together in subsequent analyses in the absence of any association.

We were interested in hypothesis-generating analyses of predictors of BDI-II and MAC-S scores, including *a priori* selected baseline variables (age, sex, acute physiology and chronic health evaluation [APACHE] II score²⁷) and ICU variables (multiple organ dysfunction score [MODS, slope and maximum]²⁸; lung injury score [LIS, slope and maximum]²⁹; use of steroids, muscle relaxants, or high frequency ventilation; days of mechanical ventilation and ICU stay). We tested associations in univariable linear regression analyses. For the BDI-

II regression, we log-transformed the outcome variable and two predictor variables, days of mechanical ventilation and ICU stay, to ensure normally distributed residuals. Residuals for the MAC-S regressions were normally distributed using the untransformed outcome variables, but we log-transformed the same two predictor variables because their distributions were skewed.

We conducted four secondary analyses to explore effects of missing data, English fluency, and exclusion of somatic items from the BDI-II instrument, and the association between depression symptoms and return to work. First, we included questionnaires with < 50% missing items by calculating an adjusted score based on items answered as (total possible score for all items) $\times$ (score for items answered)/(maximum possible score for items answered). Second, we restricted the regression analyses to patients whose primary language was English. Third, we separately tested associations between BDI-II Cognitive and Somatic-affective subscales and the same predictor variables. Because these outcome variables were not normally distributed regardless of transformations, we used Spearman correlations to test continuous predictors and Wilcoxon rank-sum tests for discrete predictors. Finally, for patients with complete BDI-II data, we examined the association between depression symptoms (using total BDI-II score and the Cognitive subscale separately) and return to work at the time of questionnaire completion, and separately adjusted for time since ICU discharge to questionnaire completion. We used patients' definitions of work, which included both paid and unpaid work inside or outside the home. All statistical tests were two-sided; we interpreted $p < 0.05$ as statistically significant. Analyses were conducted using statistical software (SAS, version 8; SAS Institute; Cary, NC).

Results

Study Participants

We enrolled 109 ARDS survivors in the cohort, of whom 13 had died and 14 had withdrawn from the study at the time of questionnaire mailing. We sent questionnaires to all remaining 82 patients in the cohort; they were returned at a median of 22 (IQR 12 to 29; range 6 to 48) months post-ICU discharge (Fig 1). Sixty-eight (83%) patients returned the BDI-II and 71 (87%) patients returned the MAC-S questionnaires. Responders were similar to nonresponders (Table 1); they were young (42 [IQR 35 to 56] years), and the majority was male (54%), spoke English as a first language (65%), and had some post-secondary education (57%). Responders had high illness severity at presentation (as measured by APACHE II score²⁷) and substantial organ dysfunction during the ICU course (as measured by maximum MODS²⁸ and maximum LIS²⁹). Responders had a longer ICU stays than nonresponders (median, 27 vs 17 days) of borderline statistical significance ($p = 0.06$), and they had a moderately limited 6-min walk distance (67% [IQR 54% to 82%] of predicted) at the clinic visit closest in time to when the questionnaires were returned.

Instrument Scores

Complete questionnaires (zero missing items) for BDI-II, MAC-S (Ability), and MAC-S (Frequency of Occurrence) were available from 61/68 (90%), 64/71 (90%), and 61/71 (86%)

respondents, respectively; the number of items missing per questionnaire was generally < 10% (Table 2 and Fig 2). Linear regression analyses of instrument scores by time after ICU discharge to questionnaire completion showed no significant associations (Fig 3).

The median BDI-II score was 12 (IQR 5 to 25). Using BDI-II-defined depression symptom severity categories, 36 (59%) respondents reported minimal or mild depression symptoms and 25 (41%) reported moderate or severe symptoms. Cognitive and Somatic-affective subscale scores were highly correlated (Spearman correlation coefficient 0.78, $p < 0.001$). Scores on the MAC-S instrument were 76 (IQR 61 to 93) for Ability and 91 (IQR 77 to 102) for Frequency of Occurrence. Relative to a US community-based sample,^{20,21} 8% of respondents in each sub-scale scored > 2 SDs below age-adjusted norms; the proportion increased to 16% and 20% with cutoff points of 1.5 and 1 SD respectively (Table 2). BDI-II scores were moderately negatively correlated with MAC-S scores (Spearman correlation coefficient -0.58 and -0.50 for Ability and Frequency of Occurrence subscales, respectively; $p < 0.0001$), implying an association between symptoms of depression and memory loss.

Univariable analyses (Tables 3, 4) did not demonstrate any consistent demographic or illness severity associations with BDI-II or MAC-S scores. Secondary analyses of subgroups again showed no statistically significant associations; these subgroups were (1) patients with questionnaires with < 50% missing items (BDI-II, $n = 67$; MAC-S, $n = 71$ for both subscales) and (2) patients with English as a primary language and questionnaires with no missing items (BDI-II, $n = 40$; MAC-S Ability, $n = 41$; MAC-S Frequency of Occurrence, $n = 40$). When BDI-II Cognitive and Somatic-affective subscales were analyzed separately, the only statistically significant finding was a positive association between the slope of the LIS and BDI-II Cognitive subscale ($p = 0.041$).

Eight of 25 patients (32%) with moderate-to-severe depression symptoms had returned to work, compared to 25/36 (69%) patients with minimal-mild depression symptoms (odds ratio [OR], 0.21; 95% confidence interval [CI], 0.07 to 0.62; $p = 0.005$). The association remained significant when adjusted for time from ICU discharge to questionnaire completion (OR, 0.20; 95% CI, 0.06 to 0.62; $p = 0.006$); patients returning to work completed questionnaires later than those not returning to work (26 [IQR 17 to 31] vs 17 [11 to 25] months; $p = 0.02$). These associations were also significant when only cognitive symptoms of depression were considered (OR per 1-U increase in BDI-II Cognitive subscale, 0.87; 95% CI, 0.79 to 0.97; $p = 0.009$; adjusted OR, 0.88; 95% CI, 0.79 to 0.97; $p = 0.01$). All associations were similar when analyses included questionnaires with < 50% missing items ($n = 67$).

Discussion

In this study, critically ill patients who survived an episode of ARDS completed validated instruments assessing self-reported symptoms of depression and memory dysfunction between 6 and 48 months after ICU discharge. These patients had high initial illness severity and no documented psychiatric comorbidity. Our main findings were a high prevalence (41%) of moderate-severe depression symptoms and a lower prevalence (8 to 20%, depending on the definition used) of self-reported memory deficits. We did not identify any

demographic or clinical predictors of these abnormalities, possibly because the study lacked statistical power or because unmeasured variables were more important determinants of outcome. A novel finding was that survivors with moderate-severe depression symptoms were less likely to have returned to work than those with less severe symptoms. However, our data are insufficient to draw conclusions regarding the direction of the causal relationship, if any, between depression symptoms and work status. Although we did not assess these patients for a clinical diagnosis of depression, our findings are consistent with other studies highlighting the potential importance of depression symptoms in survivors of critical illness.^{30,31}

Other investigators have evaluated neurocognitive function (using validated formal tests) and psychiatric symptoms in patients with ARDS,^{32–39} prolonged mechanical ventilation,^{40,41} and general critical illness.^{39,42,43} Hopkins and Jackson¹⁶ reviewed these studies and reported a prevalence of neurocognitive impairment of 28% to 75% in patients evaluated 2 months to > 6 years following hospital discharge. Studies noted some improvements in the first year after discharge but residual persistent deficits. Affected neurocognitive domains included mental processing speed, memory, attention, problem-solving (executive function), intellectual function, and visual-spatial ability. Using a validated self-reported symptom scale, we found that the prevalence of memory dysfunction depended on the definition: for each subscale, 8% of patients had scores of > 2SD below age-adjusted norms (potentially reflecting moderately severe memory impairment), whereas 20% of patients had scores > 1SD below age-adjusted norms (potentially including patients with mild memory impairment). Other investigators have performed formal memory testing rather than measuring self-reported symptoms and found a higher prevalence of dysfunction,^{32,33,35–37,40–42} raising the possibility that our patients may have had more severe objective memory impairment than they perceived and/or reported. Alternatively, self-reported symptoms of memory dysfunction may be poorly correlated with objective testing in ARDS survivors, a finding described in other patient populations.^{44–53}

Interpretation of literature regarding memory dysfunction is challenging because of the variability in instruments administered and specific diagnostic criteria. These criteria have included a certain number of test scores > 1, 1.5, or 2 SD below a population mean or have used other definitions.^{32–43} Using objective testing, Suchyta et al³⁸ reported a low prevalence (2.9%) of severe memory impairment, defined as at least two test scores > 2 SD below population-based norms, in 30 ARDS survivors at a mean of 6 years after ICU discharge. Although their finding is similar to ours, the low prevalence may be underestimated by the prolonged time from ICU discharge, retrospective data collection, and limitations of memory tests administered by telephone (R. Hopkins; personal communication; January 1, 2007). Similar to our study, others have found no consistent associations between baseline clinical variables, illness severity, and subsequent neurocognitive dysfunction.¹⁶

There are fewer data on depression after critical illness.⁵⁴ A recent systematic review³¹ of psychiatric morbidity in ARDS survivors included three cohorts (169 patients)^{13–34,36} of ARDS patients with self-rated questionnaire-ascertained depression that reported the prevalence of “clinically significant” depression symptoms. One cohort was examined 1

year³⁶ and 2 years³² after hospital discharge. The median prevalence of clinically significant depression symptoms (using questionnaire-determined cutoff scores) in the four studies^{13–32,34–36} was 28% (range, 17% to 43%)³¹ 12 to 28 months after hospital discharge. Our finding that 41% of ARDS survivors had moderate-severe depression symptoms is similar, but it is higher than reported in studies that used the original BDI instrument (~20%).^{32,36} Potential explanations may include differences in illness severity (median APACHE II score of 23 in the current study vs mean APACHE II score of 18 in the previous studies)^{32,36} or the processes of care during and after ICU admission. One small study (n = 24)⁵⁵ found that days of ICU care, days of mechanical ventilation, and days that any sedatives were given were all positively correlated with depression symptoms as measured by the Center for Epidemiologic Studies-Depression scale.⁵⁶

Our data are also consistent with outcomes in other ICU survivors. For example, in patients approximately 1 year after acute respiratory failure⁵⁷ or mechanical ventilation for > 48 h,⁵⁸ the prevalence of moderate-severe depression symptoms⁵⁷ or questionnaire-ascertained depression⁵⁸ was 32% to 34%. In contrast, depression prevalence varies more in noncritically ill patients: 1.6% to 50% in 27 studies of post-myocardial-infarction depression (median 31% in 7 studies using the original BDI instrument)⁵⁹ and 5% to 63% in 49 studies of post-stroke depression.⁶⁰ In the critically ill, there are few studies of objectively ascertained depression. Kapfhammer et al reported that 2 of 46 patients (4%) examined at a median of 8 years (range, 3 to 13 years) after ICU discharge had major depression as determined by standardized psychiatric interviews.⁶¹ In another study assessing 164 patients 2 months after acute respiratory failure, Weinert and Meller³⁰ conducted standardized psychiatric interviews and found a high combined prevalence of major depressive episode (16%) and depressive disorder not otherwise specified (16%); the estimated combined incidence was 25% to 28% in patients without baseline depression. Of the 109 patients not taking an antidepressant before ICU admission, 28% were taking them during the post-ICU period.³⁰

Symptoms of depression and memory loss were moderately correlated in this study, but we did not use standardized interviews to diagnose major depression. Complex relationships between subjective cognitive and memory complaints, objective evidence of such dysfunction, and depression and personality have been documented across various populations.^{44–53,62,63} Many studies have reported a poor correlation between self-rated and observed cognitive dysfunction, including memory loss, and a much stronger positive relationship between subjective complaints and depression.^{44–53} However, some studies using rigorous methods, including community sampling, longitudinal design, and statistical adjustment for depression and level of education, indicate that subjective complaints have moderate construct validity with respect to correlations with objective tests⁶² and prediction of later dementia in older adults.⁶³ Furthermore, studies demonstrate a direct relationship between major depression (not merely depression symptoms) and objective memory deficits,⁶⁴ and emerging data suggests reduced hippocampal neurogenesis as the common biological basis for these findings.^{65,66} The precise relationship between mood and cognitive function, including memory, remains to be established in ARDS, and inconsistencies in research findings are likely to continue as the particular modulatory factors are further explored.

Strengths of this study include the large size and detailed description of the cohort, with little loss to follow-up and a high response rate. To our knowledge, we are the second group after Hopkins et al^{32,36} to examine depression symptoms in ARDS patients using a prospective cohort design, and our 61 patients add 36% to the sample size (n = 169) of three cohorts in whom the prevalence of questionnaire-ascertained clinically significant depression has been reported. As far as we are aware, this study is the first to report an inverse association between more severe depression symptoms and return to work. Another unique feature is our assessment of self-reported memory dysfunction in ARDS survivors, which complements the existing literature that has focused on objective neurocognitive testing. The prospective design permitted analyses of potential predictors of symptoms of depression and memory loss based on detailed and reliably ascertained baseline and ICU care variables.

Nevertheless, our study has several important limitations. It is possible that nonresponders or those who withdrew from the initial cohort had already returned to work. Similar to previous investigators, we did not collect data on other possible determinants of subjective cognitive and affective outcomes, such as medications (*eg*, sedation, analgesia, antipsychotics), hypoxemia,^{32,35,36} and environmental issues (*eg*, sleep, noise, sensory deprivation) in the ICU. Our data set is likely underpowered to detect associations between ICU variables and outcomes. Similarly, we did not collect data on any potentially confounding events occurring between the index hospitalization and administration of the instruments. We did not administer the instruments at ICU discharge, preventing insights into the evolution of these symptoms prior to our study. Although we did not detect temporal variation in instrument scores, the time from ICU discharge to questionnaire completion was highly variable in our study, and it is possible that such temporal variation will be found in an ongoing larger study.⁶⁷ We excluded patients with documented psychiatric disorders in their medical chart, but it is possible that some post-acute-illness symptoms were preexisting rather than new; we did not perform any post hoc tests of premorbid cognitive function or affect. We did not administer a broad range of mental health instruments to screen for other diagnoses such as generalized anxiety disorder, post-traumatic stress disorder, delirium, or dementia, nor did we conduct standardized psychiatric interviews. Finally, although we used instruments validated in other populations, their relationship to formal neurocognitive testing and clinical outcomes in the critically ill is unclear. In particular, we cannot determine the prevalence of major depressive disorder in our cohort. The measurement properties of psychiatric screening instruments should be investigated to determine if they are reliable surrogates for clinical disorders in ICU survivors.

In summary, we found a high prevalence of moderate-severe depression symptoms and a substantially lower prevalence of extreme self-reported memory deficits in a cohort of ARDS survivors 6 to 48 months after ICU discharge. An important functional association was that survivors with moderate-severe depression symptoms were less likely to have returned to work than those with less severe symptoms. Further investigations into the clinical and economic burden of these symptoms and methods of mitigating them, including patient screening and referral to appropriate mental health services, are warranted.

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Abbreviations

APACHE	acute physiology and chronic health evaluation
BDI-II	Beck Depression Inventory-II
CI	confidence interval
IQR	interquartile range
LIS	lung injury score
MAC-S	Memory Assessment Clinics Self-Rating Scale
MODS	multiple organ dysfunction score
OR	odds ratio

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Figure 1.
Flow through the study.

Figure 2. Histograms of BDI-II ($n = 61$), MAC-S Ability subscale ($n = 64$), and MAC-S Frequency of Occurrence subscale ($n = 61$). Categories represent 10-point bins and only include questionnaires with no missing items.

Figure 3.

Instrument scores vs time of completion in months after ICU discharge, for the BDI-II, BDI-II Somatic-affective subscale, BDI-II Cognitive subscale, MAC-S Ability subscale, and MAC-S Frequency of Occurrence subscale. *p* Values for the 3-coefficient of the straight regression lines (not plotted) are 0.26, 0.33, 0.53, 0.70, and 0.35, respectively.

Table 1Characteristics of ARDS Survivors^{*}

Variables	Responders (n = 71)	Nonresponders (n = 11)	p Value
Age, yr	42 (35–56)	48 (44–65)	0.21
Female gender	33 (46)	4 (36)	0.76
Primary language English	46 (65)	6 (55)	0.52
Education [†]			0.67
High school or less	30 (43)	6 (55)	
Some college	21 (30)	2 (18)	
University degree	19 (27)	3 (27)	
APACHE II score	23 (15–27)	26 (21–31)	0.13
Maximum LIS during ICU admission [‡]	3.7 (3–4)	3.3 (2.7–4.0)	0.19
Maximum MODS during ICU admission	11 (10–13)	10 (7–12)	0.19
ICU length of stay, d	27 (16–51)	17 (10–25)	0.06
Time since ICU discharge, mo	22 (12–29)	Not applicable	
6-min walk distance at the clinic visit closest in time to return of questionnaire, m; % predicted (n = 67) [§]	425 (289–504); 67 (54–82)	Not available	

^{*}Data are presented as median (interquartile range) or No. (%). The 71 responders returned the MAC-S. Three of these respondents did not return the BDI-II questionnaire.

[†]Information is missing for one patient in the responders group.

[‡]The LIS included the sum of the chest radiography, hypoxemia, and positive end-expiratory pressure scores, while excluding measures of static compliance.

[§]Four patients did not complete the 6-min walk test or the visit was missed. Nonresponders missed follow-up clinic visits and thus did not complete a 6-min walk test.

Table 2**Depression Symptoms and Memory Function in ARDS Survivors ***

Variables	Data
BDI-II (n = 61) [†]	12 (5–25)
Depression symptom severity category (BDI-II score), n = 61 [‡]	
Minimal (0–13)	33(54)
Mild (14–19)	3(5)
Moderate (20–28)	14 (23)
Severe (29–63)	11(18)
MAC-S	
Ability (n = 64) [§]	76 (61–93)
Frequency of Occurrence (n = 61)	91(77–102)
MAC-S, comparison to normative sample [¶]	
Ability (n = 64)	
<2SDs	5(8)
< 1.5 SDs	10(16)
<1SD	13 (20)
Frequency of occurrence (n = 61)	
< 2 SDs	5(8)
< 1.5 SDs	11 (18)
<1SD	11 (18)

* Data are presented as median (interquartile range) or No. (%). Percentages may not sum to 100% because of rounding.

[†] Of 68 BDI-II questionnaires (21 items), 61 had no missing items, 4 had 1 missing item, 2 had 3 missing items, and 1 had 11 missing items.

[‡] Depression categories are from the BDI-II scale.

[§] Of the 71 questionnaires with MAC-S ability responses (21 items), 64 had no missing items, 5 had 1 missing item, and 2 had 2 missing items.

^{||} Of the 71 questionnaires with MAC-S Frequency of Occurrence responses (24 items), 61 had no missing items, 6 had 1 missing item, and 1 each had 2, 3, 4, and 6 missing items.

[¶] Proportion of sample below 2, 1.5, or 1 SD below age-adjusted US sample mean (66, SD 13 for ability; 81, SD 15 for Frequency of Occurrence).

Table 3Univariable Analyses of Predictors of the Logarithm of Total BDI-II Score^{*}

Variables	β -Coefficient (SE)	p Value
APACHE II at ICU admission	0.026 (0.020)	0.22
Female gender	0.30 (0.31)	0.33
Age	– 0.012 (0.01)	0.27
Maximum MODS during ICU admission	– 0.011 (0.051)	0.82
Slope of MODS [†]	0.061 (0.23)	0.79
Maximum LIS during ICU admission	– 0.15 (0.33)	0.66
Slope of LIS [‡]	0.21 (0.19)	0.26
Steroid use in ICU	– 0.011 (0.33)	0.97
ICU days [§]	0.11 (0.19)	0.56
Mechanical ventilation days [§]	0.12 (0.18)	0.53
Any muscle relaxants	0.024 (0.32)	0.94
High-frequency ventilation	0.045 (0.33)	0.89

^{*} Analyses included 61 patients whose questionnaires had no missing items. For three patients with a score of zero, we added 0.5 to their score before taking the logarithm. Positive (negative) β -coefficients imply that the predictor is associated with higher (lower) log-transformed BDI-II scores.

[†] The change in MODS over time during ICU admission is expressed as the slope of the score.

[‡] The change in LIS over time during ICU admission is expressed as the slope of the score.

[§] The logarithm of this variable was used because the untransformed variable had a skewed distribution.

Table 4

Univariable Analyses of Predictors of Memory Assessment Clinics Self-Rating Scale Scores *

Variables	Ability		Frequency of Occurrence	
	β -Coefficient (SE)	p Value	β -Coefficient (SE)	p Value
APACHE II at ICU admission	- 0.02 (0.35)	0.96	0.001 (0.35)	0.99
Female gender	-7.09(5.19)	0.18	- 8.05 (5.26)	0.13
Age	- 0.13 (0.18)	0.49	- 0.25 (0.18)	0.17
Maximum MODS during ICU admission	0.91 (0.85)	0.29	1.51 (0.93)	0.11
Slope of MODS [†]	- 1.14 (3.51)	0.75	- 2.73 (3.92)	0.49
Maximum LIS during ICU admission	3.48 (5.40)	0.52	- 1.19 (5.63)	0.84
Slope of LIS [‡]	- 2.20 (2.89)	0.45	- 3.14 (3.24)	0.34
Steroid use in ICU	2.63 (5.47)	0.63	0.77 (5.51)	0.89
ICU days [§]	0.32 (3.14)	0.92	0.38 (3.29)	0.91
Mechanical ventilation days [§]	0.52 (2.95)	0.86	0.11 (3.11)	0.97
Any muscle relaxants	0.39 (5.30)	0.94	-0.17(5.47)	0.98
High-frequency ventilation	2.03 (5.59)	0.72	1.97 (5.56)	0.72

* Ability and Frequency of Occurrence refer to subscales of the MAC-S. Analyses included 64 patients (ability) and 61 patients (Frequency of Occurrence) whose questionnaires had no missing items. Positive (negative) β -coefficients imply that the predictor is associated with higher (lower) scores.

[†]The change in MODS over time during ICU admission is expressed as the slope of the score.

[‡]The change in LIS over time during ICU admission is expressed as the slope of the score.

[§]The logarithm of this variable was used because the untransformed variable had a skewed distribution.