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Post-Traumatic Stress Disorder after Weaning from Prolonged Mechanical Ventilation

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Abstract

Purpose—Weaning from prolonged mechanical ventilation may be associated with mental discomfort. It is not known whether such discomfort is linked with the development of post-traumatic stress disorder (PTSD). Accordingly, we investigated whether PTSD occurs in patients after weaning from prolonged ventilation. We also determined whether administering a questionnaire would identify patients at risk for developing PTSD.

Methods—A prospective longitudinal study of patients transferred to a long-term acute-care hospital for weaning from prolonged ventilation was undertaken: 72 patients were studied one week after weaning and 41 patients were studied again three months later. An experienced psychologist conducted a structured clinical interview three months after weaning to establish a diagnosis of PTSD. To assess for the presence of PTSD-related symptoms, the Post Traumatic Stress Syndrome (PTSS-10) questionnaire was administered one week after weaning and three months later.

Results—The psychologist diagnosed PTSD in 12% of patients three months after ventilator weaning. Patients who developed PTSD were more likely to have a previous history of psychiatric disorders ($p < 0.02$). A PTSS-10 score greater than 20 one week after weaning reliably identified patients who were diagnosed with PTSD three months later: sensitivity, 1.0; specificity, 0.76; area under receiver-operating characteristic curve, 0.91.

Conclusion—PTSD was diagnosed in 12% of patients who were weaned from prolonged ventilation. A PTSS-10 score greater than 20 one week after weaning identified patients diagnosed with PTSD three months later. This finding suggests that a simple questionnaire administered before hospital discharge can identify patients at risk for developing PTSD.

Descriptor—Mechanical Ventilation: weaning

Index Words

Mechanical ventilation; post-traumatic stress disorder; anxiety

INTRODUCTION

Admission to an ICU is stressful and many who survive subsequently experience psychological problems [1–4]. Previous investigators have suggested that the severity of such problems may be sufficient to meet the criteria for post-traumatic stress disorder (PTSD) [5–11]. PTSD is triggered by events that pose a serious threat to a person's well-being. The patient's reaction is one of intense fear, horror, or helplessness. Survivors of a life-threatening illness who develop PTSD have persistent symptoms that fall into three groups: reliving (or intrusion) symptoms; avoidance and numbing symptoms; and increased arousal symptoms. To satisfy the diagnosis of PTSD, the symptoms must be present for one month or longer [7].

Patients with PTSD are more likely to develop mood, anxiety and substance abuse disorders than patients without PTSD [12]. In addition, patients with PTSD are six times more likely than matched controls to attempt suicide [12]. Accordingly, the earliest possible identification of patients at increased risk for PTSD might permit the implementation of preventive measures [12,13].

Across studies in ICU survivors who required short-term mechanical ventilation (average duration, 6 days), the prevalence of PTSD or PTSD-related symptoms ranged from 8 to 51% [3,14–19]. These prevalence studies, however, have relied mostly on screening questionnaires to detect PTSD and did not focus on patients requiring prolonged ventilation. Critically-ill patients who require prolonged mechanical ventilation may be at an increased risk for developing PTSD. First, the presence of an endotracheal tube makes it difficult for patients to communicate their needs. Second, the use of restraints, lines, devices, sedative agents and neuromuscular blocking agents limit patient movement [15,16,20,21]. Third, ventilator weaning can be particularly stressful; patients commonly experience increased respiratory work, gas-exchange abnormalities, and cardiovascular derangements [22–26]. Some patients panic as soon as they perceive active withdrawal of a life-preserving therapy [27], fearing they will be unable to sustain ventilation on their own. In a recent study, we found that depressive disorders were present in 42% of patients who were being weaned from prolonged ventilation [28].

The prevalence of PTSD in patients who require prolonged mechanical ventilation is largely unknown. Moreover, no studies have attempted to determine whether patients who are at increased risk for developing subsequent PTSD can be identified soon after weaning from prolonged ventilation. Accordingly, we undertook a study to determine whether PTSD develops in patients after weaning from prolonged ventilation. We also determined whether administering a screening questionnaire one week after weaning would identify those patients who will go on to meet the criteria for PTSD three months later.

METHODS

Patients

Patients transferred to RML Specialty Hospital (RMLSH), a long-term acute care (LTAC) hospital, for weaning from mechanical ventilation were recruited for the study. All patients were tracheotomized before transfer. Patients were eligible if they received mechanical ventilation for at least 21 days and had been weaned from the ventilator at RMLSH for at least 3 days (median=7, range 4 to 11). Patients who were not alert, cognitively impaired, non-English speakers and with sensory deficits limiting their ability to communicate were excluded. Of 136 patients approached, 72 (53%) agree to participate, 32% declined to participate and 15% did not meet the inclusion criteria. The study was approved by the Institutional Review Board of RMLSH and informed consent was obtained.

Measurements

Demographic and clinical data—Upon arrival to RMLSH, the following data were obtained from the medical record: demographics, previous history of psychiatric illness (depression, anxiety or substance abuse), reason for instituting mechanical ventilation (at the transferring hospital) and its duration before transfer to RMLSH. Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were calculated within 24 hours of admission to RMLSH to quantify the severity of illness. In addition, the presence of anxiety on arrival to RMLSH, and the weaning time and sedation while at RMLSH were recorded. [See appendix].

Patient recollection of stressful memories during weaning was assessed using the questionnaire of Stoll et al [29] one week and three months after weaning [See Appendix]. Patients were asked to recall whether they experienced any of the following symptoms: breathing difficulty, panic or anxiety, pain, or nightmares during ventilator weaning at RMLSH. Patients were asked to answer each of the four questions with yes or no, independent of the number of occasions the stressful experience occurred [8,16,29].

Diagnosis of PTSD—To establish the diagnosis of PTSD, an experienced psychologist conducted a structured clinical interview (by telephone) [30,31]. This interview is considered the reference standard for diagnosing PTSD [7,31]. To ensure that symptoms were related to PTSD rather than to an acute stress disorder, the interview was conducted at least one month after weaning [32]. Patients were diagnosed with PTSD if they fulfilled the entire Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for PTSD [7]. Patients considered by the psychologist to have PTSD were advised to contact a psychologist or a psychiatrist for further care.

Post-Traumatic Symptom Scale (PTSS)-10—The PTSS-10 questionnaire is a widely used self-reported tool assessing ten symptoms related to PTSD [8,16,29,33,34]. The symptoms included in the PTSS-10 questionnaire are sleep disturbance, nightmares, depression, jumpiness, wishing to withdraw from others, generalized irritability, frequent changes in mood, guilt, fear of places and situations that remind the patient of the time of weaning, and increased muscle tension. Each symptom is rated from 1 (never) to 7 (always); the total score ranges from 10 to 70 points [See Appendix].

Protocol

At enrollment, patients were asked to complete the PTSS-10 questionnaire and the four-item questionnaire regarding stressful memories [See Appendix]. At least one month after weaning (a median of three months), patients were contacted by telephone and asked to complete the same questionnaires. After completion, patients were interviewed by the staff psychologist to determine whether they met clinical criteria for PTSD. The psychologist was blinded to the results of the PTSS-10 questionnaire. The patients were also blinded to the purpose of the interview and the questionnaire.

Data Analysis

Continuous variables are reported as medians and interquartile range, and categorical variables as proportions. Comparison of continuous variables between the two subgroups was performed using Mann-Whitney U test. Comparison between categorical variables was performed using the Pearson chi-square test or Fisher's exact test, as appropriate.

One goal of the study was to determine whether the PTSS-10 questionnaire could be used as a screening test for subsequent development of PTSD (See Appendix) [35–37]. Such a test should have a low number of false-negative results (thus, a high sensitivity). A high false-

positive rate is acceptable (low specificity). To determine whether the PTSS-10 questionnaire is reliable as an early screen for PTSD, PTSS-10 scores at enrollment were compared with the psychologist's diagnosis of PTSD obtained three months after study enrollment. The optimal cut-off point was defined as the threshold value of the PTSS-10 questionnaire that produced the highest sensitivity – the highest number of true-positives with the least number of false-negatives. Sensitivity, specificity, positive-predictive value, and negative-predictive value of the PTSS-10 questionnaire were then calculated at the identified threshold value. Receiver operator characteristic (ROC) curve was generated to determine the accuracy of the PTSS-10 questionnaire in predicting the development of PTSD.

Multivariate regression analysis was performed to determine patient characteristics associated with the presence of PTSD symptoms reported one week after weaning in the 72 enrolled patients [See Appendix for variables included in the analysis].

RESULTS

Of the 72 enrolled patients, 41 (57%) completed the three-month follow-up interview. Reasons for failing to complete the interview were death (n=13), lost to follow-up (n=12), inability to conduct an interview because mechanical ventilation had been reinstituted (n=4) or hospitalization in a psychiatric hospital (n=1); one patient refused to participate. Compared with patients who completed the follow-up interview, patients who did not complete the three-month interview had a lower rate of acute lung injury as a cause of respiratory failure ($p=0.05$); the other patient characteristics were similar in the two groups (Table 1).

PTSD symptoms

Figure 1 shows the distribution of the PTSS-10 scores at one week and three months after weaning in the 41 patients who participated in both evaluations. One week after weaning, the median PTSS-10 score was 20 (range, 13–26). Three months later, the median PTSS-10 score was 19 (range, 13–23). The proportion of patients who reported sleep disturbances was greater at the initial evaluation compared to the three-month evaluation (76% versus. 55%, $p < 0.05$); in contrast, nightmares tended to be more common among patients at three months than in the first week (25% versus 12%, $p = 0.11$).

Diagnosis of PTSD by psychologist

Of patients who underwent a structured interview by the psychologist, 12% met the diagnostic criteria for PTSD. Of patients diagnosed with PTSD, the median PTSS-10 score at the three-month evaluation was 45 (range 38 to 51); the respective median PTSS-10 score for patients not diagnosed with PTSD was 15 (range, 11 to 20, $p < 0.001$). Of the ten PTSD symptoms, sleep disturbance, nightmares, jumpiness, wishing to withdraw from others, frequent changes in mood, guilt, fear of places and situations that reminded the patient of the time of weaning, and increased muscle tension were reported more in patients with PTSD than in patients without PTSD ($p < 0.02$); depression and generalized irritability were reported equally by both groups. As expected, severity of each of the symptoms on the PTSS-10 questionnaire was greater in patients with PTSD than in patients without PTSD ($p < 0.01$ in each instance) (Figure 2).

All patients diagnosed with PTSD had a previous history of a psychiatric disorder compared to 31% of patients not diagnosed with PTSD (Fisher's exact, $p < 0.02$). Age, gender, APACHE II scores, cause of respiratory failure, presence of anxiety on admission to RMLSH, sedation received (number of days and median daily dosage) while at RMLSH, and total duration of mechanical ventilation were not different between patients with PTSD and patients without PTSD (data not shown).

Stressful memories associated with weaning

The number of stressful memories during weaning at RMLSH was similar at the initial evaluation and at follow-up (1 [0–2] versus 1 [0–2], $p=0.35$). In patients who were later diagnosed with PTSD, the number of stressful memories was higher than in patients without PTSD (3 [2.7 to 3] versus 1 [0 to 2], $p=0.01$). At the initial evaluation, dyspnea and anxiety were more commonly remembered by patients than either pain or nightmares; at follow-up, these symptoms were recalled equally (Table 2). Anxiety was recalled more in patients who were later diagnosed with PTSD than in patients who were not diagnosed with PTSD (100% versus 32%, $p<0.02$). Dyspnea, pain and nightmares were recalled equally by both groups.

Use of early screening to predict subsequent PTSD

At the initial evaluation, PTSS-10 scores were higher in patients who were later diagnosed with PTSD than in patients who did not develop PTSD: median, 31 (range 27 to 38) versus 17 (13 to 20, $p < 0.01$). Comparison of PTSS-10 scores at enrollment with the psychologist's diagnosis of PTSD (three months after weaning) revealed an area under the ROC curve of 0.91. The threshold PTSS-10 score that resulted in highest sensitivity (lowest number of false-negative results) in predicting the future development of PTSD was 20. Its sensitivity was 1.0, specificity 0.76 (95% C.I., 0.56 to 0.89), positive predictive value 0.36 (95% C.I., 0.08 to 0.65), negative predictive value 1.0, and likelihood ratio 4.1 (95% C.I., 1.5 to 7.5).

The relationship between baseline clinical characteristics and PTSS-10 scores in 72 patients obtained one week after ventilator weaning is shown in Table 3. Patients with a previous history of psychiatric disorders had PTSS-10 scores that were 6.2 points (beta coefficient) higher than patients without such a history (95% C.I. 1.8 to 10.6, $p < 0.007$). Age, gender, APACHE scores, and duration of mechanical ventilation were not associated with PTSD symptoms.

DISCUSSION

To our knowledge, this is the first study to assess the presence of PTSD after weaning from prolonged mechanical ventilation. The study has three main findings. First, 12% of patients who survived weaning from prolonged ventilation at a LTAC hospital were diagnosed as having PTSD three months later by a psychologist who conducted a standardized clinical interview. Second, the development of PTSD was not related to the severity of the patient's recent critical illness (APACHE II, duration of mechanical ventilation) but was related to the presence of a previous history of psychiatric disorders. Third, a PTSS-10 score greater than 20 (on the PTSS-10 questionnaire) obtained one week after ventilator weaning identified patients who were at risk of being diagnosed by the psychologist as having PTSD three months later.

The prevalence of PTSD in our patients (12%) was comparable to the only two studies conducted in ventilated patients where investigators employed the structured clinical interview for diagnosis of PTSD [15,33]. In these two studies, patients required mechanical ventilation for an average of 8 days [15,33]. In contrast, our patients had failed repeated weaning attempts and required mechanical ventilation for an average of 42 days. Thus, one might expect a higher rate of PTSD compared to patients who had been successfully weaned and more quickly discharged from the ICU [15]. Yet, the prevalence of PTSD was equivalent in the two groups. Why? First, gender. Community-based studies and studies in ICU survivors suggest that PTSD is more common in women [16,17,38,39]; and only a third of our patients were women (Table 1). Second, age. Studies in ICU survivors suggest that PTSD symptoms are more likely in young patients [1,16,19], with symptoms declining after age of 50 [16]; the median age of our patients was 66 years.

Ventilator duration and severity of illness might be expected to increase the risk of PTSD. We found no such association: ventilator duration was similar in patients who did and did not develop PTSD, as was severity of illness (quantified by APACHE II). The lack of such an association has been also reported in ICU survivors [2–4,8,16]

The development of PTSD was related to previous psychiatric illness. Indeed, a history of depression, anxiety or alcohol abuse before the onset of acute illness was present in all patients with PTSD compared with only one-third of patients without PTSD. After controlling for age, gender, and severity of critical illness, multivariate analysis revealed that a previous psychiatric history was a strong predictor of PTSD symptoms reported one week after ventilator weaning (Table 3).

Screening for PTSD

Because of the high rates of psychiatric comorbidities and suicide attempts among patients with PTSD, early identification of risk is desirable [12]. This is especially important because treatment of the acute phase of PTSD (1–3) months after exposure to a stressor) can decrease the occurrence of chronic PTSD [13].

In patients with acute respiratory distress syndrome (ARDS), a PTSS-10 score of 35 or more has been proposed as the cut-off for identifying patients who have a high likelihood of developing PTSD five years after ICU discharge [29]. Using a PTSS-10 score of 35 as a criterion of severe PTSD symptoms in patients weaning from prolonged ventilation is problematic. First, this threshold was proposed for a specific subgroup, patients with ARDS [29], and not in patients who required prolonged ventilation for various causes of respiratory failure. Second, the comparison of the PTSS-10 questionnaires against a structured interview by a psychiatrist was performed five years after ICU discharge. Using the threshold of 35 at the time our patients were discharged would have missed 75% of the patients who subsequently developed PTSD.

In the present study, we found that a PTSS-10 score greater than 20 obtained one week after ventilator weaning identified all patients who were later diagnosed by the psychologist as having PTSD (sensitivity, 1.0). To our knowledge, this is the first study that suggests it may be possible to identify patients at risk of developing PTSD following prolonged ventilation at a point before hospital discharge. It is important to note that every patient who scores greater than 20 on the PTSS-10 questionnaire will not necessarily require psychological intervention; some patients will come to terms with their symptoms on their own and will not need further intervention. Our study suggests that patients who score 20 or higher on the PTSS-10 questionnaire should be reevaluated at three months to determine if they do have PTSD so that proper treatment can be initiated.

Study Limitations

The study was confined to a single center which can limit the generalizability of our findings. The use of a single center, however, ensured that the care of these complicated patients was uniform. Second, factors related to the original ICU stay (e.g., exposure to sedatives, number of failed weaning attempts in the ICU) that may have contributed to PTSD were unavailable. Determination of risk factors for PTSD, however, was not the primary goal of our study. Third, the PTSS-10 questionnaire employed in this study is based on the DSM-III (rather than the DSM-IV) criteria for PTSD. Moreover, the questionnaire was administered at two time-points (one week and three months after weaning). Conceivably, administration of the PTSS-10 questionnaire at an intermediate time-point, such as one to two months after weaning, might have greater accuracy in identifying patients at risk for developing PTSD, as suggested in a recent study performed in ICU survivors [40]. Finally, 43% of the patients did not complete

the follow-up assessment primarily because of death, severe illness or refusal for further participation; only 17% of the cohort was lost to follow-up. Baseline characteristics of the patients lost to follow-up and patients evaluated at 3 three months were similar. This does not rule out the possibility of selection bias. Of note, the drop-out rate is lower in this study than in the two studies (67%, 70%) that employed the same methodology to diagnose PTSD in ICU survivors [15,33]. The high drop-out rates in these studies highlight the challenge in studying the long-term consequences of elderly patients who have survived a critical illness.

In summary, 12% of patients requiring prolonged ventilation met the diagnostic criteria for PTSD three months after weaning at a specialized facility. The development of PTSD was related to the presence of previous mental difficulties rather than the severity of the underlying critical illness. A PTSS-10 greater than 20 obtained one week after weaning accurately identified patients who went on to develop PTSD. Our findings suggest it is possible to identify patients at risk of developing PTSD before hospital discharge using a simple screening questionnaire.

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Figure 1.
Distribution of PTSS-10 scores at enrollment (top panel) and three months later (bottom panel).

Figure 2.

Box plots showing median and interquartile ranges of the scores for each of the 10 symptoms on the PTSS-10 questionnaire obtained three months after ventilator weaning in patients diagnosed with PTSD (gray columns) and in patients not diagnosed with PTSD (white columns).

Severity of each symptom on the PTSS-10 questionnaire was greater in patients with PTSD than in patients without PTSD ($p < 0.01$ for each instance).

Table 1

Patient characteristics

Characteristics	Follow-up n = 41	Lost to Follow-up n = 31	p
Age, median years [IQL]	66 [59–72]	69 [62–76]	0.22
Sex, female/male	15/26	11/20	0.56
APACHE II, median [IQL]	15 [12–17]	15 [13–17]	0.52
Duration of mechanical ventilation before transfer, median days [IQL]	24 [18–33]	25 [18–40]	0.88
Reason for respiratory failure			
Post-operative (%)	54 (22/41)	32 (10/31)	0.06
Acute lung injury (%)	29 (12/41)	52 (16/31)	0.05
COPD (%)	7 (3/41)	10 (3/31)	0.52
Neuromuscular (%)	10 (4/41)	6 (2/31)	0.48
Previous psychiatric history (%)	39 (16/41)	20(9/31)	0.27
Anxiety* on admission, %	32 (13/41)	52(16/31)	0.09
Sedation at RMLSH]			
Daily Lorazepam dose(mg), median [IQL]	0.50 [0.05–0.75]	0.50 [0.50–0.88]	0.94
Sedation days median [IQL]	7 [1–27]	7 [1–41]	0.80
Weaning time at RMLSH, median days [IQL]	6 [3–12]	6 [4–21]	0.29
PTSS-10, median [IQL]	20[13–26]	21 [16–27]	0.40

APACHE = Acute Physiology and Chronic Health Evaluation; IQR = interquartile range; COPD = chronic obstructive pulmonary disease

* Assessed by the staff psychologist

Table 2

Memories of dysphoria during ventilator weaning

	Initial Evaluation (n = 41)	Follow-up Evaluation (n = 41)
Dyspnea	18 (44%)	16 (41%)
Anxiety or panic	16 (39%)	16 (39%)
Pain	5 (12%) ^{a,b}	10 (24%)
Nightmares	5 (12%) ^{a,b}	11 (27%)

^a p <0.01 when compared with trouble breathing

^b p <0.01 when compared with anxiety or panic

Table 3

Multivariate Analysis to Determine Relationship between PTSD-Symptoms One Week after Ventilator Weaning and Patients Characteristics (n=72)

Variable	Beta Coefficient	95% C.I.	P value
Age	0.10	−0.08 to 0.28	0.29
Female	−2.72	−7.17 to 1.73	0.23
APACHE II	−0.43	−1.08 to 0.22	0.19
Duration of ventilation	0.06	−0.01 to 0.13	0.09
Previous psychiatric history	6.17	1.75 to 10.59	0.007