

Symptoms experienced by intensive care unit patients at high risk of dying

Kathleen A. Puntillo, RN, DNSc, FAAN; Shoshana Arai, RN, PhD; Neal H. Cohen, MD, MPH, MS; Michael A. Gropper, MD, PhD; John Neuhaus, PhD; Steven M. Paul, PhD; Christine Miaskowski, RN, PhD, FAAN

Objective: To provide a focused, detailed assessment of the symptom experiences of intensive care unit patients at high risk of dying and to evaluate the relationship between delirium and patients' symptom reports.

Design: Prospective, observational study of patients' symptoms.

Setting: Two intensive care units in a tertiary medical center in the western United States.

Patients: One hundred seventy-one intensive care unit patients at high risk of dying.

Interventions: None.

Measurements and Main Results: Patients were interviewed every other day for up to 14 days. Patients rated the presence, intensity (1 = mild; 2 = moderate; 3 = severe), and distress (1 = not very distressing; 2 = moderately distressing; 3 = very distressing) of ten symptoms (that is, pain, tired, short of breath, restless, anxious, sad, hungry, scared, thirsty, confused). The Confusion Assessment Method–Intensive Care Unit was used to ascertain the presence of delirium. A total of 405 symptom assessments were completed by 171 patients. Patients' average age

was 58 ± 15 yrs; 64% were males. Patients were mechanically ventilated during 34% of the 405 assessments, and 22% died in the hospital. Symptom prevalence ranged from 75% (tired) to 27% (confused). Thirst was moderately intense, and shortness of breath, scared, confusion, and pain were moderately distressful. Delirium was found in 34.2% of the 152 patients who could be evaluated. Delirious patients were more acutely ill and received significantly higher doses of opioids. Delirious patients were significantly more likely to report feeling confused (43% vs. 22%, $p = .004$) and sad (46% vs. 31%, $p = .04$) and less likely to report being tired (57% vs. 77%, $p = .006$) than nondelirious patients.

Conclusions: Study findings suggest that unrelieved and distressing symptoms are present for the majority of intensive care unit patients, including those with delirium. Symptom assessment in high-risk intensive care unit patients may lead to more focused interventions to avoid or minimize unnecessary suffering. (Crit Care Med 2010; 38:000–000)

KEY WORDS: critical care; pain; symptoms; symptom assessment; palliative care; delirium

Almost one in five Americans dies in an intensive care unit (ICU) or shortly after an ICU stay (1). Often these patients are unable to communicate their symptoms because they are intubated and mechanically ventilated and receive opioids and sedatives. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) study (2) was one of the first studies to systematically investigate symptoms in seriously ill hospitalized patients. However, the SUPPORT study did not provide detailed information on the

prevalence, severity, and distress associated with the most common symptoms experienced by patients at risk of dying in ICUs. At the same time, it and a number of other studies described persistent unrelieved symptoms in hospitalized patients. In a study that involved 50 ICU patients with current or past cancer diagnoses (3), patients reported numerous symptoms of moderate to severe intensity. Because this study was limited to oncology patients, the generalizability of findings to high-risk ICU patients is limited.

A significant problem in many ICU patients is delirium. In fact, recent studies (4–7) suggest that approximately 28–87% of ICU patients experience one or more episodes of delirium. Delirium might influence clinicians' abilities to understand the prevalence and severity of patients' symptoms.

Because of the paucity of descriptive studies on symptom prevalence or severity, insufficient data exist to develop and test symptom management interventions for patients at high risk of dying in the

ICU. Therefore, as part of a larger study of symptom assessment in communicative and noncommunicative ICU patients at risk of dying, the purposes of this prospective, descriptive study were to provide a focused, detailed assessment of the symptom experiences of ICU patients at high risk of dying and to evaluate relationships between delirium and patients' symptom reports.

MATERIALS AND METHODS

Setting and Participants. This study was conducted in two ICUs in a tertiary medical center in the western United States. Patients ≥ 18 yrs of age who met the following criteria were considered to be at high risk of dying and were eligible for this study: a first 24-hr Acute Physiology and Chronic Health Evaluation (APACHE) II score (8) of ≥ 20 ; in the ICU for ≥ 3 days; and having one or more of the following diagnoses: acute cardiac and/or respiratory failure, chronic liver failure with cirrhosis, multiple organ system dysfunction and sepsis, or any system failure associated with a diagnosis of a malignancy (2). Patients with

From the University of California, San Francisco, CA. This study was supported by a grant from the National Institute for Nursing Research (NR008247).

This study was conducted at the University of California, San Francisco.

The authors have no potential conflicts of interest to disclose.

For information regarding this article, E-mail: kathleen.puntillo@nursing.ucsf.edu

Copyright © 2010 by the Society of Critical Care Medicine and Lippincott Williams & Wilkins

DOI: 10.1097/CCM.0b013e3181f267ee

these diagnoses have hospital death rates that range from 24% to 54% (8–10).

Measures. A ten-item symptom checklist was developed from an extensive review of the literature on symptom assessment instruments. As was true for Nelson and colleagues (3), the basis for this symptom checklist was a modification of the well-validated Edmonton Symptom Assessment Scale (11). The symptoms of tiredness and thirst were added to the Edmonton Symptom Assessment Scale, and 3-point Likert scales were used to rate symptom intensity and distress. Symptoms were chosen that reflected both physical and psychologic symptoms. The checklist had only 10 symptoms (that is, pain, tired, short of breath, restless, anxious, sad, hungry, scared, thirsty, confused) to reduce respondent burden while providing a brief, reliable, and easily administered assessment at the bedside. Patients were asked to rate whether the symptom was present and, if present, its intensity (1 = mild; 2 = moderate; 3 = severe) and distress (1 = not very distressing; 2 = moderately distressing; 3 = very distressing).

This instrument was previously pilot tested on 24 ICU patients by study investigators. Face validity was established in that respondents were able to differentiate among the ten symptoms and chose among the entire range of intensity and distress scores for each symptom. In the current study face, validity of the symptom assessment instrument was established by the fact that both delirious and non-delirious patients were able to differentiate between the presence and absence of various symptoms; were able to differentiate between symptom intensity and distress; and were able to differentiate between the severity of various symptoms. Interrater reliability of the symptom assessment tool was tested in the following manner: two research team members were at the patient's bedside, one member asked the symptom questions, and both members recorded responses independently and then compared responses. Testing took place until each team member achieved 100% interrater reliability.

A modified Motor Activity Assessment Scale (mMAAS) (12) was used to assess a patient's level of sedation before obtaining patient consent or conducting symptom assessments. At the study institution, the MAAS was previously rescored to improve ease of understanding. The middle score, zero, indicates a calm and cooperative state. Three negative scores indicate lesser degrees of responsiveness (−1, −2, and −3), and three positive scores indicate abnormal degrees of responsiveness (for example, agitation) (+1, +2, and +3). Patient consents and symptom assessments were completed when patients had mMAAS scores that ranged from −1 to +1. Over 85% of mMAAS scores were zero; initial mMAAS scores were zero at the beginning of each survey.

Delirium was evaluated at every symptom assessment using the Confusion Assessment Method-ICU instrument (CAM-ICU) (5). The CAM-ICU measures four key cognitive domains: mental status changes, inattention, disorganized thinking, and altered level of consciousness. The CAM-ICU has established criterion (5, 13) and concurrent validity (14) and interrater reliability (15). It has a dichotomous score (that is, delirium present or absent) based on the patient's performance on the four cognitive domains. It has been validated as a measure of delirium in both mechanically ventilated patients who cannot speak and verbal, nonintubated ICU patients (14).

Demographic and treatment-related data included age, gender, ethnicity, diagnosis, and first 24 hrs in ICU APACHE II score (8, 16). Information about specific medications prescribed and administered that could relate to symptoms under study (for example, opioids, benzodiazepines, haloperidol) was obtained from patients' medical records. Calculation of APACHE II scores was done using recommended methods (16). Interrater reliability of chart abstractions was assured by duplicate abstraction of the first 20 charts. Two members of the research team independently abstracted chart data. On completion, they and/or a third member of the team reviewed the abstraction forms to identify discrepancies. If discrepancies were found, two of the three members corrected the discrepancy by rereviewing the chart. These processes were completed 100% of the time with new members of the research team until the interrater agreement was 95–100%. One in every ten charts was abstracted by two team members as an ongoing method to assure accuracy. Data were double-entered into SPSS 14 (SPSS Inc, Chicago, IL) to assure reliability of the data entry process. Files were matched to verify the accuracy of the data, and data were systematically examined for out-of-range values and data inconsistencies.

Procedures. Human subjects approval was obtained from the institution's Institutional Review Board. After screening for eligibility, patients with acceptable mMAAS scores were approached for consent to participate at a time that was convenient for them and agreeable to the patient's nurse. If the patient agreed to participate but was unable to sign the consent because of physical impairment, a family member was asked to provide written witnessed consent for the patient. In some cases, delegated family members gave surrogate consent for patient enrollment if the patient was unable to provide consent on the first study day. Patients were later approached for their own consent if and when they were able to do so.

Research nurses interviewed patients to complete the symptom checklist. After the symptom assessment was completed, a delirium

assessment was performed. Patients were interviewed every other day for up to 14 days for a possible seven interviews. A 14-day cutoff was chosen because the length of ICU stay for mechanically ventilated patients who were expected to be at highest risk for dying ranged from 4 to 14 days in this institution and others (17). Data collection stopped before 14 days if the patient was transferred from the ICU or died.

Statistical Analyses. Fisher's exact tests of proportions and *t* tests of means were used to compare characteristics of patients who were vs. were not able to self-report their symptoms. The prevalence rates for each of the ten symptoms were calculated, and 95% confidence intervals around the percentages were generated using the generalized estimating equation method that takes into account the clustering of assessments by patients (18). That is, the generalized estimating equation method adjusted for the fact that some patients only provided one assessment and other patients provided up to seven assessments (an average of three per patient). The mean intensity and distress ratings with corresponding 95% confidence intervals were generated for each of the ten symptoms using generalized estimating equation. This methodology pays particular attention to the lack of independence in the assessments in calculating the SE. An accurate SE is essential to construct an accurate confidence interval. The relationship between the presence or absence of delirium and the presence of each of the ten symptoms was analyzed separately through simple logistic regression analyses that took into account the clustering of assessments by patients.

RESULTS

Patient Characteristics. A total of 1273 patients were screened, and 245 patients with mean APACHE II scores of 30.4 ± 6.5 during their first 24 hrs in the ICU were enrolled (Fig. 1). Of these 245 patients, 171 (69.8%) were able to respond about the presence or absence of some of the ten symptoms for at least one of the seven assessments. Of the 245 patients enrolled, 32% died in the hospital. Of the 171 who were able to report their symptoms, 22% died in the hospital. The entire 22% died after they were enrolled in the study, an indication of the seriousness of their illnesses. Significantly fewer patients were able to report their symptoms if they were mechanically ventilated (34%) than if they were not mechanically ventilated (66%) ($p = .005$). However, no significant difference was found in first 24-hr APACHE II scores between those who could and could not report symptoms.

The 171 patients (64% male) with an average age of 58 ± 15.1 yrs completed 405 symptom assessments with a mean of

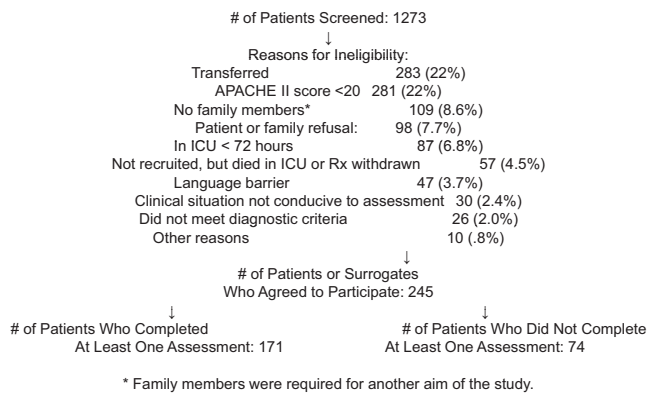


Figure 1. Flow diagram of intensive care unit patients screened and enrolled in the study.

Table 1. Prevalence of symptoms across 405 assessments from 171 patients

Symptom	Percent	SE	95% Confidence Interval
Tired	74.7	2.79	69.2–80.2
Thirsty	70.8	3.13	64.6–76.9
Anxious	57.9	3.17	51.7–64.1
Restless	49.0	3.09	42.9–55.0
Hungry	44.8	3.32	38.3–51.3
Short of breath	43.9	3.37	37.3–50.5
Pain	40.4	3.16	34.2–46.6
Sad	33.9	3.00	28.0–39.7
Scared	32.8	3.42	26.1–39.5
Confused	26.6	2.87	21.0–32.3

Note: SEs and 95% confidence intervals used the robust variance estimate from the generalized estimating equation approach.

Table 2. Mean intensity ratings (mild = 1, moderate = 2, severe = 3) for patients who reported symptom to be present

Symptom Intensity	Mean	SE	95% Confidence Intervals
Tired	1.81	.062	1.69–1.93
Thirsty	2.16	.087	1.99–2.33
Anxious	1.92	.076	1.77–2.06
Restless	1.76	.079	1.61–1.91
Hungry	1.89	.091	1.71–2.07
Short of breath	1.89	.083	1.73–2.05
Pain	1.74	.073	1.60–1.88
Sad	1.85	.107	1.64–2.06
Scared	1.80	.118	1.56–2.03
Confused	1.73	.132	1.47–1.96

Note: SEs and 95% confidence intervals used the robust variance estimate from the generalized estimating equation approach.

3.0 ± 1.8 assessments per patient. Sixty percent of the patients were white; 23% were Asian; 4.5% were black; 0.2% were American Indian/Alaska Natives; and the ethnicity of 12.2% was unknown. Medical diagnoses of these 171 patients included

Table 3. Mean distress ratings (mild = 1, moderate = 2, severe = 3) for patients who reported symptom to be present

Symptom Distress	Mean	SE	95% Confidence Intervals
Tired	1.94	.058	1.83–2.06
Thirsty	1.90	.080	1.74–2.06
Anxious	1.93	.076	1.79–1.79
Restless	1.95	.088	1.78–2.12
Hungry	1.62	.087	1.45–1.79
Short of breath	2.34	.088	2.17–2.52
Pain	2.08	.081	1.92–2.24
Sad	1.97	.114	1.74–2.19
Scared	2.15	.102	1.95–2.35
Confused	2.10	.152	1.80–2.40

Note: SEs and 95% confidence intervals used the robust variance estimate from the generalized estimating equation approach.

respiratory failure (57%), liver disease (19%), multiple organ dysfunction syndrome (21%), heart failure (24%), and any system failure plus malignancy (22%). Some patients had more than one diagnosis.

Table 1 provides a summary of the symptom prevalence data. In >50% of the 405 symptom assessments, patients reported the presence of tiredness, thirst, and anxiety. Tiredness was the most prevalent and confusion was the least prevalent symptom. Table 2 provides a summary of symptom intensity ratings. Thirst was the most intense and confusion was the least intense symptom. Table 3 provides a summary of symptom distress ratings. The four symptoms that were moderately distressful were shortness of breath, scared, confusion, and pain. Linear regression models fitted using generalized estimating equation identified no significant differences in symptom intensity or symptom distress ratings between patients who were or

were not ventilated at the time of an assessment. However, the prevalence of anxiety was significantly higher in patients who were (74.2%) vs. were not (25.8%) mechanically ventilated when they completed the survey ($p = .02$).

Relationship Between Symptoms and Medications Received. Patients who reported their symptoms ($n = 171$) received an average daily dose of 62.4 ± 139.5 mg morphine-equivalent opioids (19) and an average daily dose of 3.6 ± 9.7 mg lorazepam-equivalent benzodiazepines (20). Patients who could not report their symptoms ($n = 74$) received an average daily dose of 347.7 ± 558.1 mg morphine-equivalent opioids and an average daily dose of 23.1 ± 31.9 mg lorazepam-equivalent benzodiazepines. Both differences were statistically significant ($p < .001$). No patients received dexmedetomidine or propofol at the time of symptom assessments.

The amounts of opioids or benzodiazepines that were administered within 3 hrs before symptom assessments were calculated. Patients received an opioid before 83 of the 405 assessments. The average dose of morphine-equivalent opioids was 12.2 ± 15 mg. Patients received a benzodiazepine before only nine of the 405 assessments. The average 3-hr dose of lorazepam-equivalent benzodiazepines was 2.1 ± 3.0 mg.

Relationship Between Symptoms and Delirium. Delirium assessments were completed on 152 of 171 patients. The research team could not complete a delirium assessment on the remaining 19 patients because patients could not or would not respond to the CAM-ICU questions after the symptom assessments. An episode of delirium occurred in 52 (34.2%) of the 152 patients who completed the CAM-ICU assessment after their symptom assessments. No differences were found in gender, age, ethnicity, code status, medical diagnoses, days in the ICU, or hospital mortality between patients who were and were not delirious when clustering of assessments by patients was taken into account. However, delirious patients had higher first 24-hr mean APACHE II scores (31.4 ± 6.3 vs. 29.0 ± 6.1 , $p = .03$); higher assessment day mean APACHE II scores (20.0 ± 5.3 vs. 17.4 ± 4.8 , $p = .001$); and received more opioids (54.5 ± 120.4 mg vs. 18.7 ± 47.7 mg) in a 24-hr period ($p = .04$). Although delirious patients received more lorazepam-equivalent benzodiazepines than nondelirious patients ($3.9 \pm$

Table 4. Differences in prevalence of symptom reports based on delirium status (325 assessments from 152 patients, an average of two per patient)

Symptom	Delirious (n = 61)	Nondelirious (n = 264)	<i>p</i>	Odds Ratio	Confidence Intervals
Confused	43%	22%	.004	1.2	1.1–1.4
Sad	46%	31%	.04	1.2	1.01–1.3
Tired	57%	77%	.006	0.8	0.7–0.9

Note: SES and 95% confidence intervals used the robust variance estimate from the generalized estimating equation approach.

6.3 mg vs. 2.7 ± 10.6 mg) on assessment days, this difference was not statistically significant ($p = .59$). Only nine patients received haloperidol on study days. Delirious patients were more likely to report being sad (odds ratio, 1.2; 95% confidence interval, 1.01–1.3) and confused (odds ratio, 1.2; 95% confidence interval, 1.1–1.4) and were less likely to report being tired (odds ratio, 0.8; 95% confidence interval, 0.7–0.9) than nondelirious patients (Table 4).

DISCUSSION

To our knowledge, this study is the most extensive multisymptom assessment of a heterogeneous group of ICU patients at high risk of dying. Symptom assessments were done at least once on 171 (69%) of 245 patients with an average of three assessments per patient during their ICU stay regardless of whether or not the patient was mechanically ventilated. During 50–75% of the patient assessments, patients reported being anxious, thirsty, and tired.

Anxiety was more common in patients who were mechanically ventilated when providing symptom reports. These higher rates of anxiety may be partially attributable to mechanically ventilated patients' inability to verbally communicate their concerns or to seek information about their condition (21). In fact, in one study (22), 85% of 106 mechanically ventilated patients reported some anxiety, and 69% of the anxiety reports were rated moderate to severe. Taken together, these consistent findings suggest that clinicians need to perform systematic assessments of anxiety, especially in mechanically ventilated patients, and consider using both pharmacologic and nonpharmacologic interventions to decrease this distressing symptom (21).

Thirst was the second most common and the most intense symptom in these patients. Thirst was identified in survey research (23, 24) as one of the greatest

stressors for ICU patients. However, this symptom is not routinely assessed in ICU patients and, when it is, it may be ignored because there is a perception that nothing can be done to address it. In fact, in a recent qualitative study, whereas 20 ICU nurses identified reasons why patients could be thirsty (for example, dehydration, hypernatremia), approximately half of them did not perceive that mechanically ventilated patients could be thirsty (25). Few strategies were recommended by the interviewed nurse to reduce thirst, and none of the nurses reported developing a plan of care to relieve thirst. Given the high prevalence and intensity of thirst in this sample, additional research is warranted on the most effective interventions to prevent or decrease thirst.

The vast majority of patients (75%) reported being tired. This finding is not unexpected because sleep deprivation and abnormal sleep–wake cycles are known to occur in ICU patients (26). However, because sleep was not a focus in this study, the relationship between patients' reports of being tired and their sleep status is unknown. Many other factors associated with their illness such as noise and lights in the ICU environment, frequent awakenings, or medications received could make ICU patients tired (26).

An unexpected finding is that patients reported pain during only 40% of the assessments, and pain was of mild to moderate intensity. This finding is similar to findings from two other recent ICU studies. In an observational study in 44 ICUs in France, up to 51% of 1381 mechanically ventilated patients had substantial nonprocedure-related pain (27). In another study, the incidence of pain in 230 ICU patients when they were at rest was found to be 38% (28). It is possible that patients who responded in our study were receiving the appropriate dose of analgesics, which supports the titration of analgesics to patients' pain reports. At a more general level, this finding may

reflect the increased emphasis given to pain assessment and treatment for ICU patients over the past 10 yrs.

Although pain prevalence in the current study was only 40%, pain distress was moderate to severe. This finding confirms that pain is multidimensional and requires clinicians to attend to both its sensory (that is, intensity) and affective (that is, distress) dimensions. Subsequent treatments could target one or both of these pain dimensions, depending on their severity. Balancing effective pain management with clinical outcomes is important because recent data suggest that patients are discharged from the ICU sooner when sedating medications are interrupted on a daily basis (29). Pain intensity can be treated with judicious use of an analgesic vs. sedative medications. Pain distress may be more amenable to nonpharmacologic interventions such as music, relaxation, and information in conjunction with analgesics, yet these approaches have not been systematically studied in ICU patients.

Consistent with a previous review (30), in approximately 30% of the assessments, patients reported sadness and fear. In fact, being scared was the second most distressful symptom. Similar to the discussion of anxiety, it is not surprising that patients were fearful in an ICU environment and perhaps fearful about their outcomes. In fact, ICU patients have reported fear associated with mechanical ventilation (31), monitors (30), "coming down off all the drugs," and death (22). Findings across these studies suggest that ICU patients should be assessed for the presence and intensity of fear and that appropriate interventions need to be implemented. Anticipation of patients' needs, clear communication practices, and use of caring behaviors can help to alleviate stress and fear. In addition, family members can provide patients with information, explanations, encouragement, and perform relaxation techniques to decrease anxiety and fear (22).

Dyspnea (termed shortness of breath in this study) was the most distressing symptom. Although dyspnea often precipitates the use of mechanical ventilation (32), no differences were found in dyspnea intensity or distress ratings reported by patients who were vs. were not mechanically ventilated. Although previous studies found that patients on mechanical ventilation experienced dyspnea (3, 33, 34), the pathophysiological mechanisms for, and iatrogenic sources of,

dyspnea warrant additional investigation. Given that dyspnea was the most distressful symptom in this sample, clinicians need to perform routine assessments for dyspnea, especially in mechanically ventilated patients. This subjective assessment could be done in conjunction with objective assessments (for example, ventilator settings, arterial blood gases, assessment of mechanics of respiration) that are performed on a routine basis for mechanically ventilated patients. This study did not include documentation of the method of ventilatory support (for example, mandatory ventilation or pressure support ventilation) or its impact on dyspnea. An assessment of the impact of the mode of ventilation might provide important insights into optimal management strategies to address dyspnea.

Delirium was present in approximately 34% of the patients who were able to be assessed, which is consistent with previous studies (4–7, 13, 35, 36). However, some patients could not complete the delirium assessment and, therefore, hypoactive delirium may have been missed. The prevalence of delirium was associated with higher daily dose of opioids, a finding consistent with previous reports (6, 37). However, unlike those reports, this study did not have enough CAM-ICU-tested patients who received benzodiazepines to determine a relationship between delirium and use of benzodiazepines. Attention needs to be paid to the symptom of delirium because of its adverse effect on ICU patient outcomes. Delirium assessments need to be done on a routine basis. However, we were able to perform a delirium assessment after only 80% of the symptom assessments (that is, 325 of 405 assessments) because patients were not able to follow directions or to continue with the delirium assessment after the symptom assessment, most often as a result of fatigue. Every effort should be made to complete delirium assessments using the CAM-ICU or another valid and reliable assessment instrument like the Intensive Care Delirium Screening Checklist (38, 39). If delirium assessment is still impossible, there should be a high index of suspicion that a patient may have delirium. Attention to patients' behaviors and responses, or lack of responses, to questions may help to determine whether delirium is present.

Although research on delirium in ICU patients has increased dramatically in the past 8 yrs (4–7, 13, 35, 36), no studies were found that examined the relationship be-

tween delirium and other symptoms. In this study, a higher number of delirious vs. nondelirious patients reported confusion and sadness, but fewer delirious vs. nondelirious patients reported being tired. Providing patient reassurance, information, and frequent reorientation of the patient to the ICU environment may ameliorate some of the confusion. In some cases, medications may contribute to the delirium. As a result, opioids and benzodiazepines should be used judiciously, titrating their doses to patient need and effect while assessing the potential onset of disturbing symptoms like delirium. At the same time, one must be cautious in balancing the patient's need for analgesics with concerns that the therapy may increase the likelihood of delirium.

Why fewer of the patients in this study with delirium were tired than those without delirium is unknown and inconsistent with previous studies that found a positive association between sleep deprivation and delirium (26). Further studies are needed to confirm these findings and to evaluate the influence of sedatives and analgesics on tiredness. Another finding that warrants further study is the relationship between delirium and sadness. It may be that the patients' delirious thoughts were ones that caused sadness. However, our results cannot be seen as causal and cannot be explained without further investigation. Findings could be the result of confounding factors because patients in the delirious vs. not delirious groups may have differed on other important characteristics.

Several study limitations need to be acknowledged. First, only 10% of the possible 1273 patients screened met eligibility criteria, and only 69% of them (that is, 171) were able to report their symptoms on at least one of seven possible assessments. Furthermore, because some patients who reported their symptoms to be present were unable to rate the symptom's intensity or distress, missing data reduce the generalizability of the findings. Indeed, the presence of missing data reflects the severity of illness of these patients and suggests that clinicians need to assess for at least the presence of symptoms and address symptom intensity and distress whenever possible. Another limitation is that this study assessed symptoms in a subset of ICU patients, which limits the generalizability of the findings to patients with different levels of acuity, different underlying clinical conditions, or different institution, yet given the prevalence rates, intensity,

and distress of symptoms found in these patients, symptom assessments should become a routine part of patient assessments whenever possible.

Of note, only 34% of mechanically ventilated patients responded to the symptom assessments. Hence, it is possible that we could be underreporting the true prevalence of these distressing symptoms in our mechanically ventilated patients, yet the 34% of mechanically ventilated patients completed 138 (out of 405) symptom assessments, providing us with more information about mechanically ventilated patients' symptoms than ever previously reported.

CONCLUSIONS

This study provides evidence that the prevalence, intensity, and distress of particular symptoms were significant for many critically ill patients, including those with delirium. Despite these findings, many patients were unable to report their symptoms at all, especially those who received higher doses of opioids and benzodiazepines. It is not clear whether the medications blunted the symptoms themselves or only the ability of the patients to describe their symptoms. Additional studies are needed to clarify whether more careful titration of opioids and benzodiazepines might improve patient outcomes (29) while allowing more ICU patients to communicate their symptoms. What this study demonstrated is that clinicians must recognize the importance of the assessment process and determine ways to manage patients' symptoms. Greater attention to the symptom assessment of high-risk ICU patients can lead to focused interventions to avoid or minimize unnecessary suffering.

REFERENCES

1. Angus DC, Barnato AE, Linde-Zwirble WT, et al: Use of intensive care at the end of life in the United States: An epidemiologic study. *Crit Care Med* 2004; 32:638–643
2. A controlled trial to improve care for seriously ill hospitalized patients The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT). The SUPPORT Principal Investigators. *JAMA* 1995; 274: 1591–1598
3. Nelson JE, Meier DE, Oei EJ, et al: Self-reported symptom experience of critically ill cancer patients receiving intensive care. *Crit Care Med* 2001; 29:277–282
4. Balas MC, Deutschman CS, Sullivan-Marx EM, et al: Delirium in older patients in surgical intensive care units. *J Nurs Scholarsh* 2007; 39:147–154

5. Ely EW, Margolin R, Francis J, et al: Evaluation of delirium in critically ill patients: Validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med* 2001; 29:1370–1379
6. Pandharipande P, Cotton BA, Shintani A, et al: Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. *J Trauma* 2008; 65:34–41
7. Micek ST, Anand NJ, Laible BR, et al: Delirium as detected by the CAM-ICU predicts restraint use among mechanically ventilated medical patients. *Crit Care Med* 2005; 33: 1260–1265
8. Knaus WA, Draper EA, Wagner DP, et al: APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13: 818–829
9. Groeger JS, Limeshow S, Price K, et al: Multicenter outcome study of cancer patients admitted to the intensive care unit: A probability of mortality model. *J Clin Oncol* 1998; 16:761–770
10. Friedman G, Silva E, Vincent JL: Has the mortality of septic shock changed with time. *Crit Care Med* 1998; 26:2078–2086
11. Chang VT, Hwang SS, Feuerman M: Validation of the Edmonton Symptom Assessment Scale. *Cancer* 2000; 88:2164–2171
12. Devlin JW, Boleski G, Mlynarek M, et al: Motor Activity Assessment Scale: A valid and reliable sedation scale for use with mechanically ventilated patients in an adult surgical intensive care unit. *Crit Care Med* 1999; 27: 1271–1275
13. Ely EW, Gautam S, Margolin R, et al: The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med* 2001; 27:1892–1900
14. Plasmcke K, von Haken R, Scholz M, et al: 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* 2008; 34:431–436
15. Devlin JW, Fong JJ, Schumaker G, et al: Use of a validated delirium assessment tool improves the ability of physicians to identify delirium in medical intensive care unit patients. *Crit Care Med* 2007; 35:2721–2724; quiz 2725
16. Damiano AM, Bergner M, Draper EA, et al: Reliability of a measure of severity of illness: Acute Physiology of Chronic Health Evaluation–II. *J Clin Epidemiol* 1992; 45: 93–101
17. Ely EW, Evans GW, Haponik EF: Mechanical ventilation in a cohort of elderly patients admitted to an intensive care unit. *Ann Intern Med* 1999; 131:96–104
18. Hanley JA, de Gegassa A, Edwards B, et al: Statistical analysis of correlated data using generalized estimating equations: An orientation. *Am J Epidemiol* 2003; 157:364–375
19. Gordon DB, Stevenson KK, Griffe J, et al: Opioid equianalgesic calculations. *J Palliat Med* 1999; 2:209–218
20. Cammarano WB, Pittet JF, Weitz S, et al: Acute withdrawal syndrome related to the administration of analgesic and sedative medications in adult intensive care unit patients. *Crit Care Med* 1998; 26:676–684
21. Chlan L: A review of the evidence for music intervention to manage anxiety in critically ill patients receiving mechanical ventilatory support. *Arch Psychiatr Nurs* 2009; 23: 177–179
22. McKinley S, Nagy S, Stein-Parbury J, et al: Vulnerability and security in seriously ill patients in intensive care. *Intensive Crit Care Nurs* 2002; 18:27–36
23. Ballard KS: Identification of environmental stressors for patients in a surgical intensive care unit. *Issues Ment Health Nurs* 1981; 3:89–108
24. Wilson VS: Identification of stressors related to patients' psychologic responses to the surgical intensive care unit. *Heart Lung* 1987; 16:267–273
25. Landstrom M, Rehn IM, Frisman GH: Perceptions of registered and enrolled nurses on thirst in mechanically ventilated adult patients in intensive care units—A phenomenographic study. *Intensive Crit Care Nurs* 2009; 25:133–139
26. Figueroa-Ramos MI, et al: Sleep and delirium in ICU patients: A review of mechanisms and manifestations. *Intensive Care Med* 2009; 35: 781–795
27. Payen JF, Chanques G, Mantz J, et al: Current practices in sedation and analgesia for mechanically ventilated critically ill patients: A prospective multicenter patient-based study. *Anesthesiology* 2007; 106:687–695; quiz 891–892
28. Chanques G, Sebbane M, Barbotte E, et al: A prospective study of pain at rest: Incidence and characteristics of an unrecognized symptom in surgical and trauma versus medical intensive care unit patients. *Anesthesiology* 2007; 107:858–860
29. Girard TD, Kress JP, Fuchs BD, et al: 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* 2008; 371:126–134
30. Holland C, Cason CL, Prater LR: Patients' recollections of critical care. *Dimens Crit Care Nurs* 1997; 16:132–141
31. Hofhuis JG, Spronk PE, van Stel HF, et al: Experiences of critically ill patients in the ICU. *Intensive Crit Care Nurs* 2008; 24: 300–313
32. Spector N, Connolly MA, Carlson KK: Dyspnea: Applying research to bedside practice. *AACN Adv Crit Care* 2007; 18:45–58; quiz 59–60
33. Nelson JE, Meier DE, Litke A, et al: The symptom burden of chronic critical illness. *Crit Care Med* 2004; 32:1527–1534
34. Connelly B, Gunzerath L, Knebel A: A pilot study exploring mood state and dyspnea in mechanically ventilated patients. *Heart Lung* 2000; 29:173–179
35. Lin SM, Liu CY, Wang CH, et al: The impact of delirium on the survival of mechanically ventilated patients. *Crit Care Med* 2004; 32: 2254–2259
36. Ouimet S, Kavanagh BP, Gottfried SB, et al: Incidence, risk factors and consequences of ICU delirium. *Intensive Care Med* 2007; 33: 66–73
37. Pisani MA, Murphy TE, Araujo KL, et al: Benzodiazepine and opioid use and the duration of intensive care unit delirium in an older population. *Crit Care Med* 2009; 37: 177–183
38. Devlin JW, Fong JJ, Howard EP, et al: Assessment of delirium in the intensive care unit: Nursing practices and perceptions. *Am J Crit Care* 2008; 17:555–565; quiz 566
39. Bergeron N, Dubois MJ, Dumont M, et al: Intensive Care Delirium Screening Checklist: Evaluation of a new screening tool. *Intensive Care Med* 2001; 27:859–864