

Improved Outcomes in Patients With Head and Neck Cancer Using a Standardized Care Protocol for Postoperative Alcohol Withdrawal

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Objective: To show clinical benefit in the main outcome measures by the use of a standardized protocol for identification, characterization, and treatment of alcohol withdrawal syndrome (AWS) in postoperative patients with head and neck cancer.

Design: Prospective cohort study with a retrospective cohort control.

Setting: Tertiary care university.

Patients: A total of 26 consecutive postoperative patients with AWS were selected from among 652 patients with head and neck cancer to be enrolled in the protocol from March 2003 through March 2005. Controls consisted of 14 of 981 consecutive patients with AWS from March 2000 through December 2002.

Intervention: Application of a standardized care protocol.

Main Outcome Measures: Sensitivity and specificity of preoperative screening for AWS risk, predictability of

outcomes, length of stay, transfers to the intensive care unit (ICU), AWS symptoms, postoperative morbidity and mortality, doses of pharmacotherapy required, and charges.

Results: Protocol patients demonstrated significantly fewer AWS-related ICU transfers and less delirium and violence than preprotocol patients. Mortality, wound complications, hospital charges, and doses of benzodiazepines, clonidine, and haloperidol were not significantly different between these 2 groups. Preoperative medical history correlated poorly with AWS outcomes. Screening was 87.5% sensitive and 99.7% specific. Late enrollees to the protocol (false-negative screening results) showed many significantly worse outcomes than immediate enrollees.

Conclusion: Use of the standardized AWS symptom-triggered protocol decreased delirium, violence, and AWS-related ICU transfers without significantly increasing hospital charges.

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THE HIGH PREVALENCE OF heavy alcohol consumption among patients with head and neck squamous cell carcinoma presents their caretakers with a distinct challenge in the postoperative setting. Postoperative alcohol withdrawal management is often a time-consuming process of trial and

error associated with prolonged inpatient stays, frequent use of restraints, high intensive care unit (ICU) requirements, and risk for serious adverse events. The urgency of head and neck cancer treatment usually precludes preoperative detoxifi-

cation, making postoperative alcohol withdrawal management more challenging. Alcohol withdrawal syndrome (AWS) is a significant cause of perioperative morbidity and mortality.¹ Postoperatively, abusers of alcohol have been shown to have morbidity rates and numbers of complications 2 to 3 times higher than patients who drink less than 2 drinks daily. These increased morbidity and complication rates are associated with 50% longer hospital stays, poorer 3-month postoperative outcomes, infections, bleeding, and cardiopulmonary insufficiency.² Early identification of AWS and timely treatment may minimize these negative outcomes. Herein, we describe our experience with an uncomplicated, standardized, symptom-triggered protocol for evaluation, pharmacologic therapy, and nutri-

 CME available online at www.jamaarchivescme.com and questions on page 802

error associated with prolonged inpatient stays, frequent use of restraints, high intensive care unit (ICU) requirements, and risk for serious adverse events. The urgency of head and neck cancer treatment usually precludes preoperative detoxifi-

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AWS TYPE INDICATOR	Check here if yes		Preprinted Nurse Orders Based on Score
Type A Symptoms (CNS Excitation) Does patient appear:			
a. Anxious or nervous		Total Type A Symptoms	If Type A score ≥ 1 , administer lorazepam as ordered q1hr until Type A score = 0 or patient is calm and cooperative. Continue to assess at least q2hr or before each dose of lorazepam. STOP ATIVAN IF STARTING HALDOL
b. Restless			
c. Bothered by bright light?			
d. Bothered by sounds?			
Type B Symptoms (Adrenergic Hyperactivity)			
e. Is nausea or vomiting present?		Total Type B Symptoms	If Type B score ≥ 1 , notify MD to r/o clinical issues such as hypoglycemia, dehydration, electrolyte abnormalities, etc. If all other ruled out, obtain order for clonidine. (Clonidine 0.2 mg po/DHT every 3 hrs prn $\times 2$) Continue to assess at least q2hr and prior to each dose of clonidine. (MD should write order to change BP/pulse parameters when indicated)
f. Is tremor visible with or without arms extended?			
g. Is sweat visible on palms or forehead?			
h. Is SBP > 140 mm Hg?			
i. Is DBP > 90 mm Hg?			
j. Is heart rate > 100?			
k. Are there extra or skipped beats on apical pulse?			
Type C Symptoms (Delirium) Does the patient:			
l. Respond inappropriately to questions?		Total Type C Symptoms	If Type C score ≥ 1 , patient cannot be redirected or reoriented, AND has had previous dose of Ativan, obtain order for baseline 12 lead EKG (check QT interval); and call MD for written order: Haldol 2-5 mg IV every 2 hours prn $\times 2$. If Type C score ≥ 6 AND pt. is still agitated call for further orders. (Haldol max. dose is 0.5 mg/kg/24 hrs) STOP benzodiazepines once Haldol started
m. Report hearing noises that are not there?			
n. Report seeing something that is not there?			
o. Not knowing their name?			
p. Not knowing where they are?			
q. Not knowing how long they have been hospitalized?			
r. Not know the year?			
s. Not know the month?			
t. Not know the day of the week?			

Figure 1. A validated diagnostic scale used by nursing staff every 2 hours to identify symptoms of alcohol withdrawal syndrome (AWS): the AWS Type Indicator³ (adapted with permission). BP indicates blood pressure; CNS, central nervous system; DBP, diastolic BP; DHT, Dobhoff tube; EKG, electrocardiogram; IV, intravenous; max., maximum; po, by mouth; prn, as needed; pt., patient; q, every; r/o, rule out; SBP, systolic BP.

tional support in the treatment of AWS in postoperative inpatients.

Three distinct clusters of symptoms characterize AWS. Type A symptoms represent central nervous system (CNS) excitation and include anxiety, dysphoria, enhanced reaction to abrupt stimuli, insomnia, mood lability, motor activity, and a sense of foreboding. Type B symptoms relate to adrenergic hyperactivity, which manifest as fever, chills, diaphoresis, hypertension, tachycardia, tremors, piloerection, mydriasis, nausea, and palpitations. Type C symptoms include attention deficit, disorientation, hyperalertness, short-term memory impairment, impaired reasoning, psychomotor agitation, and hallucinations signifying delirium. These symptom types may occur alone or in combination. The older term *delirium tremens* may be used in this context to describe the combined symptoms of confusion (type C), hyperadrenergic state (type B), and CNS excitation (type A). The AWS Type Indicator is a validated diagnostic tool that produces subscores for numbers of symptoms in withdrawal types A, B, and C (**Figure 1**).³

Signs and symptoms of AWS typically develop in alcohol-dependent patients within 6 to 24 hours of abstinence. Central nervous system excitation usually occurs within 12 to 48 hours after the last drink. Autonomic hyperactivity usually peaks between 24 and 48 hours after cessation of alcohol consumption. Delirium typically occurs later, with a variable time course.^{3,4} Techniques for managing AWS have evolved over the past several decades and include the use of barbiturates, paraldehyde, ethanol, and more recently, benzodiazepines. For the present protocol, we classify AWS symptoms into 3 distinct groups (using the AWS Type Indicator), and

each is addressed with distinct pharmacologic approaches. In addition, and in contrast to earlier recommendations of prophylactic benzodiazepine treatment for patients at risk,⁵ we use medication only when symptoms manifest, and we use a different class of drug for each AWS subtype. This symptom-triggered therapy requires frequent assessment for symptoms of AWS.

Type A symptoms are treated preferentially with lorazepam, a benzodiazepine with an intermediate half-life of 10 to 20 hours and no active metabolites. After chronic alcohol use, sobriety may reveal a compensated state of CNS excitability. Alcohol enhances the function of the inhibitory neurotransmitter γ -aminobutyric acid (GABA) and blocks the excitatory *N*-methyl-D-aspartate (NMDA) receptors. Because no NMDA receptor antagonists are available for use in humans, treatment of type A symptoms, or CNS excitation, currently depends on promoting GABA-related chloride channel-mediated neurotransmission with benzodiazepines. Lorazepam is available in both intravenous and enteral forms and does not require refrigeration or preparation. It has no active metabolites and thus delivers a relatively predictable duration of action.⁶ The availability of flumazenil as an injectable agent for reversal of benzodiazepine activity adds an element of safety in benzodiazepine use. Carbamazepine may be used in nonpregnant patients when benzodiazepines are contraindicated—when severe cognitive or liver dysfunction or high blood alcohol level is present.

Differentiating type A withdrawal symptoms from other conditions is important before proceeding with treatment. Class II hemorrhagic shock, for example, results in anxiety, and hypoglycemia may also mimic type A

symptoms. Psychiatric disorders such as generalized anxiety, posttraumatic stress disorder, affective disorders, and mania or hypomania may also manifest symptoms mimicking those of type A withdrawal.³

Elevated blood catecholamine levels account for type B symptoms, the type most likely to be associated with significant morbidity and mortality from alcohol withdrawal. Therefore, the present protocol calls for the treatment of type B symptoms until they are eliminated. In contrast to earlier recommendations against the use of β -blockers or α 2 agonists because of concern for masking the progression to more severe AWS status,⁷⁻⁹ we use clonidine, a central α 2 agonist, as the first-choice therapy for type B symptoms. Clonidine suppresses the release of catecholamines. Propranolol or labetalol are alternatives. Cardiac complications of type B symptoms include myocardial ischemia and the development of atrial fibrillation or flutter due to increased circulating epinephrine—termed the *holiday heart* syndrome. Since benzodiazepines treat type B symptoms ineffectively, titrating their use to minimize the adrenergic hyperactivity risks respiratory depression and thus should be avoided. Clinical assessment of type B signs and symptoms (adrenergic hyperactivity) may be challenging because of their non-specific nature in acutely ill patients immediately after surgery. The differential diagnoses for type B symptoms include pain, intravascular volume depletion, alcoholic gastritis with nausea and vomiting, hypoglycemia, myocardial ischemia, and diaphoresis from fever.³ The present protocol involves notifying the physician for evaluation of these diagnoses.

For type C symptoms, attempting to reorient the patient is the first-line therapy. If this attempt fails, butyrophenone neuroleptic haloperidol is the mainstay of treatment, while benzodiazepine use is avoided in most circumstances despite some prior recommendations.⁵ The most common error in the management of type C alcohol withdrawal symptoms is the indiscriminant use of benzodiazepines to control the agitated patient. Use of benzodiazepines decreases sensory input and inhibition and may exacerbate psychomotor agitation. While very high doses of benzodiazepines can control these symptoms, they also carry the risk of respiratory compromise through the loss of airway integrity and pneumonia.³

Use of prophylactic ethanol is poorly documented in the literature, and our experience is that discriminating between ongoing withdrawal symptoms and drunkenness becomes difficult, especially when a patient's speech is affected by surgery. Furthermore, use of flumazenil allows reversal of the effects of benzodiazepines, while there is no reversal agent for the potentially serious effects of an overdose of ethanol.

Alcoholics frequently develop deficiencies of folic acid and vitamin B₁ (thiamine hydrochloride) as a result of a poor diet and poor gastrointestinal absorption leading to anemia and possibly a predisposition to seizures. These deficiencies must be treated. A deficiency of thiamine may be asymptomatic until the administration of intravenous glucose converts it into Wernicke-Korsakoff syndrome, which can involve a variety of neurologic symptoms, the most common being encephalopathy, gait ataxia, and oculomotor dysfunction (nystagmus and palsies). In

alcohol withdrawal, the neurologic disturbances due to thiamine deficiency can lead to an agitated delirium, which may eventually lead to stupor, coma, or even death if untreated. The present protocol provides multivitamin, thiamine, and folic acid supplementation.

METHODS

We present our experience from March 2003 until March 2005 with 26 consecutive patients prospectively treated for AWS using a standardized care protocol from among 652 patients admitted for head and neck surgical procedures. Inclusion criteria consist of age older than 18 years, squamous cell carcinoma of the upper aerodigestive tract, and hospital admission of more than 2 days during which the AWS protocol was implemented for alcohol withdrawal signs or symptoms. Two of the 26 patients who were enrolled in the AWS protocol were excluded from analysis because they exhibited no alcohol withdrawal signs.

The care plan began in the preoperative setting and used the 4-question CAGE¹⁰ screening tool as part of the preoperative history and physical examination:

- Have you ever felt you ought to Cut down on your drinking?
- Have people Annoyed you by criticizing your drinking?
- Have you ever felt bad or Guilty about your drinking?
- Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (Eye opener)?

Reported alcohol intake of at least 1 to 2 drinks daily or a CAGE score greater than 0 was considered predictive of AWS, and the patient was enrolled. Three patients had a CAGE score of 0, but their respective daily alcohol intake was 2, 5, and at least 8 drinks. These 3 patients (13%) were enrolled late in the protocol—that is, only when AWS symptoms manifested postoperatively.

Per the protocol, postoperative nursing evaluations every 2 hours included use of the AWS Type Indicator, a validated diagnostic scale,³ to identify symptoms of AWS and to determine which symptom type or types predominated (Figure 1). Graded use of benzodiazepines, sympatholytics, and neuroleptic agents was directed at the 3 subtypes: central nervous system excitation (type A), adrenergic hyperactivity (type B), and delirium (type C), respectively.³ Preprinted standardized orders for physician review and signature are shown in **Figure 2**. The protocol pathway also incorporated standardized nutritional supplementation. Outcomes measured included number of days of restraint use; occurrence of falls, seizures, and violent episodes; wound complications; postoperative intubations; transfers to the ICU and number of days in the ICU; cardiac or respiratory arrest; and quantities of haloperidol, clonidine, and lorazepam use.

A retrospective comparison group of 14 patients met the inclusion criteria but were treated from March 2000 to December 2002, prior to the use of the AWS protocol. These patients were from a group of 981 patients admitted for major head and neck surgery. They were included in the study if a diagnosis of AWS was entered as a discharge diagnosis in the medical record. In all patients, determination of alcohol withdrawal as the cause for symptoms was a clinical diagnosis, aided by consultation, laboratory, and imaging techniques as needed.

Data were extracted from the paper and electronic medical charts to an encrypted FileMaker Pro 5.5 database (FileMaker Inc, Santa Clara, California). Drinks per day were numerically encoded according to the patient's report. Ranges (eg, "4 to 6 beers a day") were averaged, and qualifications were ignored (eg, "up to 12 beers per day," or "at least 6 drinks per day" were encoded as 12 and 6 drinks, respectively). Qualitative data such as "drinks socially" or "occasionally" were not included in ag-

1. Assess patient q2h using AWS type indicator
 2. Thiamine 100 mg po/DHT q day
 3. Folic acid 1 mg po/DHT q day
 4. MVI 1 po/DHT q day
 5. If Type A score ≥ 1 : lorazepam 1-2 mg IV q1h prn until Type A score = 0 or patient is calm and cooperative
 6. If Type B score ≥ 1 : Call MD to eval DDX (hypoglycemia, electrolyte disturbances, dehydration, cardiac, etc)
 7. If Type B score attributed to AWS: MD to order clonidine 0.2 mg po/Dobhoff tube q3h prn $\times 2$
 8. If BP still $> 140/90$ ($160/90$ if age > 65 yrs), notify MD for further clonidine order
 9. Discontinue clonidine if SBP decreases by > 30 mm Hg or DBP decreases by > 20 mm Hg with any one dose of clonidine and notify MD
 10. If Type C score ≥ 1 and unable to redirect or reorient patient, call MD and (see below—next order)
 11. Prior to giving haloperidol, patient must have had previous dose of lorazepam and 12 lead EKG. Stop lorazepam once haloperidol is started
 12. After above is completed, MD to order haloperidol 2-5 mg IV q2h prn $\times 2$ until Type C subscore ≤ 6 and patient not agitated. Call MD for further haloperidol orders
 13. Continue to assess with "AWS Type Indicator" q2h or before each dose
- Follow-up with maintenance/taper orders

Figure 2. Preprinted, standardized orders for physician review and signature at a patient's enrollment in the alcohol withdrawal syndrome (AWS) protocol. BP indicates blood pressure; DBP, diastolic BP; DHT, Dobhoff tube; DDX, differential diagnosis; EKG, electrocardiogram; eval, evaluate; IV, intravenous; MVI, multivitamin; po, by mouth; prn, as needed; q, every; SBP, systolic BP.

gregate calculations. We used the Wilcoxon rank sum test and JMP IN 5.1 software (SAS Institute, Cary, North Carolina). The comparative analysis was approved by the University of Michigan institutional review board.

RESULTS

The protocol and preprotocol groups were demographically similar. The protocol cohort was 81% male, with a mean (SD) age of 61.0 (10.0) years. The preprotocol group was aged 54.6 (10.6) years ($P = .06$). The number of encoded drinks per day was 6.7 (1.6) in the preprotocol group and 5.1 (1.3) in the protocol group ($P = .92$). The mean CAGE score among protocol enrollees was 1.8.

Twenty-four patients demonstrated some AWS signs or symptoms (92%). The 2 without symptoms reported CAGE scores of 1 and 3, with usual daily intake of 4 to 6 and 6 drinks elicited preoperatively. Outcome measures of the protocol and preprotocol cohorts are summarized in **Table 1**.

PROTOCOL ADMINISTRATION

Overall, preoperative identification of patients experiencing postoperative AWS was achieved in 92% of subjects ($n = 24$), improving from 85% in the first half of the study ($n = 11$) to 100% in the second half ($n = 13$). A CAGE score was determined for 42% of patients placed on this protocol ($n = 11$). The first half of the protocol had only 31% of patients' CAGE scores documented ($n = 4$) compared with an improved 54% in the second half ($n = 7$). Patient's usual intake of alcohol was elicited in 92% of preprotocol patients ($n = 12$) and 92% of protocol patients ($n = 12$) ($P = .95$). None of the preprotocol patients had a CAGE score documented ($P = .004$).

Late enrollment for patients who failed to meet screening criteria but manifested alcohol withdrawal symp-

toms postoperatively occurred in 3 protocol patients (11%). The statistically significant differences in clinical outcomes in this subgroup compared with the remainder of the protocol group are summarized in **Table 2**. Of 26 patients enrolled in the protocol, 2 failed to exhibit AWS symptoms (8%). Thus, the AWS protocol enrollment criteria were 92% sensitive and 99.7% specific for predicting the occurrence of postoperative AWS symptoms.

CLINICAL OUTCOMES

During the study periods, the overall rate of AWS among postoperative inpatients with head and neck cancer hospitalized for 2 or more days was 2.45% (40 of 1633): 1.43% among patients in the preprotocol period (14 of 981) and 3.99% among patients in the protocol period (26 of 652).

Patients enrolled in the protocol spent a mean (SD) of 7.4 (3.9) days (range, 3-20 days) receiving protocol care and had an overall length of stay of 13.0 (8.2) days. Preprotocol patients' length of stay was 9.6 (4.6) days ($P = .18$). Speech was affected postoperatively by surgical treatment involving tracheostomy, glossectomy, composite resection, or laryngectomy in all protocol patients ($n = 26$) and 71% of preprotocol patients ($n = 10$) ($P = .01$).

Transfers from the regular inpatient unit to the ICU for AWS-related cause occurred at a rate of 29% in the preprotocol patients ($n = 4$) vs 4% in the protocol patients ($n = 1$) ($P = .03$). Transfers to the ICU for any reason, including bed availability and general postoperative issues, occurred in 27% of protocol patients ($n = 7$) and 43% of preprotocol patients ($n = 6$) ($P = .31$). For patients with an ICU stay, the mean (SD) ICU length of stay was 3.7 (2.1) days among preprotocol patients and 4.9 (2.7) days among protocol patients ($P = .47$). The AWS-related length of ICU stays were 2.3 (2.7) days and 0.9 (2.6) days, respectively ($P = .12$).

Respiratory arrest occurred in 14% of preprotocol patients ($n = 2$) vs 4% of protocol patients ($n = 1$) ($P = .28$).

Mechanical restraints were used in 57% of preprotocol patients ($n = 8$) and in 42% of the protocol cohort ($n = 11$) ($P = .37$). Preprotocol patients needing mechanical restraints used them for 3.6 (1.4) days compared with 6.1 (1.2) days in the protocol group ($P = .15$).

Delirium was present in 79% of preprotocol patients ($n = 7$) and 29% of protocol patients ($n = 11$) ($P = .004$). When present, delirium lasted a mean (SD) of 3.2 (0.7) days in the preprotocol group and 3.3 (0.9) days in the protocol group ($P = .93$).

Violence (such as biting, scratching, kicking, verbal outbursts, and other violent manifestations) was present in 36% of the preprotocol group ($n = 5$) and 8% of the protocol group ($n = 2$) ($P = .04$). Among those exhibiting violence, the preprotocol group averaged 1.2 (0.4) episodes before discharge, and the protocol group averaged 3.0 (1.4) ($P = .08$).

One or more wound complications were present in 50% of the preprotocol cohort ($n = 7$) and 46% of the protocol group ($n = 12$) ($P = .82$). When complications were present, preprotocol and protocol patients had a mean (SD) of 1.3 (0.8) and 1.3 (0.5) separate wound complications, respectively ($P = .71$).

Table 1. Clinical Outcomes^a

Characteristic	Preprotocol Group	Protocol Group	P Value ^b
Patients, No.	14	24	NR
Rate of CAGE ¹⁰ documentation	0	9 (37)	.01
Speech affected postoperatively	10 (71)	24 (100)	.006
Length of stay, d	9.6 (4.6)	13.0 (8.2)	.23
Length of stay, median, d	8	9	NR
Transfers to ICU for AWS-related cause	4 (29)	1 (4)	.03
ICU length of stay for AWS-related cause, d	2.3 (2.7)	0.9 (2.6)	.12
ICU length of stay for any reason, d	3.7 (2.1)	4.9 (2.7)	.47
Respiratory arrest	2 (14)	1 (4)	.28
Mechanical restraint use	8 (57)	10 (42)	.37
Duration of mechanical restraint use, d	3.6 (3.1)	6.1 (4.5)	.15
Delirium present	11 (79)	7 (29)	.004
Duration of delirium, d	3.2 (0.7)	3.3 (0.9)	.93
Violence present	5 (36)	2 (8)	.04
Violent episodes, No.	1.2 (0.4)	3.0 (1.4)	.08
Wound complications	7 (50)	11 (46)	.82
Wound complications, No.	1.3 (0.8)	1.3 (0.5)	.71
Locoregional complications	6 (43)	11 (46)	.87
Locoregional complications, No.	1.0 (0.1)	1.2 (0.1)	.32
Distant complications	2 (14)	1 (4)	NS
Benzodiazepine used	14 (100)	23 (96)	.48
Cumulative benzodiazepine dose, mg	39 (30)	30 (46)	.11
Maximum cumulative benzodiazepine dose, mg	108	218	NR
Duration of lorazepam use, d	4.6 (3.8)	7.3 (4.9)	.08
Clonidine used	2 (14)	11 (46)	.053
Cumulative clonidine dose, mg	0.50 (0.57)	0.80 (0.90)	.62
Maximum cumulative clonidine dose, mg	1.0	8.8	NR
Haloperidol used	7 (50)	9 (38)	.47
Cumulative haloperidol dose, mg	21.5 (25.9)	22.9 (25.5)	.47
Maximum cumulative haloperidol dose, mg	150.5	206.0	NR
Consultation for AWS	3 (21)	4 (17)	.63

Abbreviations: AWS, alcohol withdrawal syndrome; ICU, intensive care unit; NR, not reported; NS, nonsignificant—low sample size precluded meaningful comparison.

^aUnless otherwise indicated, data are reported as number (percentage) of patients or mean (SD) values.

^bWilcoxon rank sum test. Boldface indicates statistical significance.

When complications were segregated by site, we found that locoregional complications occurred in 43% of patients in the preprotocol group (n=15) and 46% of the protocol cohort (n=12) ($P=.87$). Among patients with at least 1 locoregional complication, preprotocol patients developed a mean (SD) of 1.0 (0.1) head and neck complications vs 1.2 (0.1) in the protocol group ($P=.32$). One or more distant complications occurred in 2 preprotocol patients (14%) and 1 protocol patient (4%). One preprotocol patient had 2 distant complications (bilateral pneumothorax and pneumonia), and the other had 1 (pneumonia). The protocol patient with a distant complication developed wound breakdown in the abdominal rectus free tissue transfer donor site.

All preprotocol patients received benzodiazepines; the physician determined the most appropriate type to administer (ranging from short to long acting). The total dose of all benzodiazepines administered to the patient was summed for comparison of the 2 groups. Ninety-six percent of protocol patients received lorazepam for type A symptoms (n=25). The protocol patients received cumulative doses ranging from 0 to 218 mg of benzodiazepine (solely lorazepam in this group) vs 3.5 to 108 mg in the preprotocol group. The preprotocol group received a mean (SD) dose of 39 (30) mg of

Table 2. Worse Outcomes and More Needed Therapy for Late Enrollees to the Protocol vs Immediate Enrollees^a

Outcome or Therapy	Late Enrollees	Immediate Enrollees	P Value ^b
AWS-related ICU transfer	1 (33)	0	.01
Respiratory arrest	1 (33)	0	.01
Use of mechanical restraints	3 (100)	7 (30)	.02
Haloperidol use	3 (100)	6 (26)	.02
Duration of haloperidol treatment, d	3.7 (4.6)	1.4 (4.8)	.04
Clonidine use	3 (100)	8 (35)	.04
Duration of clonidine treatment, d	2.7 (1.5)	1.6 (4.3)	.047

Abbreviations: AWS, alcohol withdrawal syndrome; ICU, intensive care unit.

^aUnless otherwise indicated, data are reported as number (percentage) of patients or mean (SD) values.

^bWilcoxon rank sum test. Boldface indicates statistical significance.

benzodiazepines, and excluding the patient not receiving any benzodiazepines, the protocol group received 30 (46) mg of lorazepam ($P=.11$). The minimum and maximum 24-hour lorazepam doses for preprotocol patients were 2 and 19 mg, respectively. Protocol patients'

Table 3. Cost Outcomes

Cost Item	With AWS		Without AWS	
	Preprotocol	Protocol	Preprotocol	Protocol
Patients, No.	14	26	967	626
APR-DRG-CMI ^a	3.89	3.52	2.11	1.88
Average variable direct costs, \$	8965	11 945	6006	6359
Adjusted average variable direct costs, \$	2306	3393	3294	3851
Length of stay, mean, d	9.60	13.00	6.64	6.61

Abbreviations: APR, all-patient refined; CMI, case-mix index; DRG, diagnosis-related group.

^aThe APR-DRG-CMI is a measure of case complexity and severity of illness based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnoses that are recorded in administrative (billing) data.¹¹

minimum and maximum daily doses were 0 and 34 mg, respectively.

Fourteen percent of preprotocol patients exhibited type B symptoms and thus were given clonidine (n=2), while clonidine was administered to 46% of protocol patients (n=12) (P=.053). Among those receiving clonidine, preprotocol patients' cumulative dose was a mean (SD) of 0.5 (0.57) mg (range, 0.1-0.9 mg), while protocol patients accumulated an average of 0.8 (0.90) mg (range, 0.1-3.3 mg) (P=.62). The minimum and maximum 24-hour clonidine doses were 0 and 0.2 mg, respectively, for preprotocol patients and 0 and 0.4 mg, respectively, for protocol patients.

Fifty percent of preprotocol patients exhibited type C symptoms and thus received haloperidol (n=7), while haloperidol was administered to 35% of protocol patients (n=9) (P=.47). Preprotocol patients receiving any haloperidol accumulated a mean (SD) dose of 22 (26) mg (range, 2-62) mg, while protocol patients requiring this drug averaged 23 (26) mg (range, 5-85 mg) (P=.47). The minimum and maximum 24-hour haloperidol doses were 0 and 25 mg, respectively, for preprotocol patients and 0 and 30 mg, respectively, for protocol patients.

Consultation of another specialist for AWS diagnosis or management occurred in 21% of the preprotocol population (n=3) and 17% of the protocol group (n=4) (P=.63).

No seizures, falls, or deaths occurred in either cohort during the inpatient stay. No patient developed delirium tremens. Although the CAGE questionnaire was sensitive and specific in identifying patients at risk for AWS, clinical outcomes correlated poorly with preoperative CAGE scores and quantified usual daily intake of alcohol (data not shown).

COST OUTCOMES

Several hospital cost figures were available for this analysis, but variable direct costs were chosen because they most accurately reflect costs of patient care (ie, operating room, nursing, drugs, imaging, laboratory tests, and other costs) and do not include fixed or indirect costs (ie, equipment, administrative staff, or other indirect costs). For this analysis, patients were divided into 4 categories depending on the presence of AWS and their enrollment in the protocol to determine the impact of the

protocol on costs and utilization between the groups adjusting for differences in case mix and case complexity.

First and foremost, as is evident in **Table 3**, the length of stay for patients with AWS in general was significantly longer than for patients without AWS (9.60 preprotocol and 13.00 protocol days vs 6.64 preprotocol and 6.61 protocol days, respectively). Furthermore, the case-mix index (CMI) was significantly higher in patients with AWS than in those without AWS (3.89 preprotocol and 3.52 protocol vs 2.11 preprotocol and 1.88 protocol, respectively). Although the average variable direct cost was higher in patients with AWS (\$8965 preprotocol and \$11 945 protocol) than in those without AWS (\$6006 preprotocol and \$6359 protocol), the costs adjusted for comorbidities were not significantly different (\$2306 preprotocol and \$3393 protocol vs \$3294 preprotocol and \$3851 protocol, respectively). Finally, protocol patients with AWS compared with preprotocol patients with AWS did not illustrate a difference in average (\$11 945 vs \$8965) or adjusted average (\$3851 vs \$3294) direct variable costs.

COMMENT

In this study, we compared the outcomes of 2 similar groups of postoperative patients with head and neck cancer. One group was treated with the use of a prospectively applied standardized AWS evaluation and management protocol, and the other was treated prior to the implementation of this protocol. The most salient features of the protocol are the formalized evaluation and treatment responses. These measures promote earlier detection of even subtle AWS symptoms and expedite management. By enabling the nursing staff to complete the assessment and treat accordingly, the preprinted orders avert unnecessary communication delays and standardize treatment across nursing shifts. The AWS Type Indicator guides proper symptom-triggered and directed pharmacologic management with lorazepam, clonidine, or haloperidol for the appropriate AWS symptom types A, B, and C respectively.

The important findings in this study begin with the incidence of postoperative AWS, which occurred in 16 of 981 patients in the preprotocol period (1.4%), 24 of 652 patients in the protocol period (3.7%), and 40 of all

1633 patients admitted following major head and neck surgery at the University of Michigan Health System (2.45%). Not surprisingly, patients with AWS had higher comorbidity indices, longer lengths of stay, and higher average variable direct hospital costs than patients who did not have AWS. The implementation of a standardized AWS protocol resulted in significantly decreased rates of ICU transfer, delirium, and violence compared with patients undergoing alcohol withdrawal symptoms prior to the implementation of protocol. There were also decreases noted in the length of ICU stays and the number of respiratory arrests, although these differences did not reach statistical significance. The protocol did not significantly add cost or decrease wound complication rates, but it did allow for symptom-triggered therapy, which decreased the use of benzodiazepines and haloperidol and increased the use of clonidine.

Unlike many other surgical patients, the characteristics of the postoperative patient with head and neck cancer add a level of complexity to the diagnosis and management of AWS. Altered speech function, present in all patients in the protocol cohort (n=26) and 71% of the preprotocol cohort (n=10), may impede assessment of withdrawal symptoms that are usually expressed verbally, such as anxiety, lability of mood, and a sense of foreboding (type A symptoms), nausea and chills (type B symptoms), and attention deficit, disorientation, and impaired reasoning (type C symptoms). Furthermore, verbal responses facilitate the detection of adverse effects of pharmacotherapy, such as sedation and disinhibition (related to benzodiazepine use) and confusion (an occasional reaction to haloperidol). Frequent scheduled comprehensive nursing evaluations using the AWS Type Indicator are therefore especially useful in this population. The checklist prompts the nurse to obtain and record information that might otherwise remain undiscovered in an aphonic patient.

Preoperative identification of individuals at risk for postoperative AWS is challenging. While the CAGE score and information on the usual daily quantity of alcohol intake act as indicators and prompt enrollment in the AWS protocol, neither datum predicts clinical outcomes or severity of AWS. The poor correlation of CAGE scores and quantified usual daily intake of alcohol with clinical outcomes attests to the clinical dilemma of identifying at-risk individuals.

Late enrollees accounted for a significant portion of our patients with AWS (13%; n=3) and represent the additional challenge of delay in diagnosis and treatment compared with those already on the protocol. The 92% sensitivity of this screening protocol compares favorably with other screening questionnaires,² but improved sensitivity might lessen postoperative morbidity. Poorer outcomes among patients enrolled late in the care protocol appear to result from loss of some of the greatest advantages of the protocol—frequent active assessments and rapid intervention. That is, the delay in diagnosis appeared to allow AWS to progress unchecked to an extent that caused a delay in symptom control, despite high medication requirements, and worse outcomes than were achieved by patient enrolled in the protocol preoperatively.

No accurate and objective indicator of alcohol dependence that can be used preoperatively exists. The utility of measuring serum ethanol levels is limited because it measures only instantaneous alcohol concentration. Newer tests such as one that screens for the ethanol metabolite ethyl glutaraldehyde, show promise because of their sensitivity and ability to positively detect the presence of ethanol several days after alcohol ingestion.¹² While this may assist in identifying at-risk patients preoperatively, it may have low specificity for alcohol dependence, and the cost-effectiveness of this method is unproven.

An important yet unavoidable limitation of our study was the method by which we identified our retrospective, historical controls (preprotocol patients). We extracted the patients' records from our hospital database using a discharge diagnosis of alcohol dependence and/or withdrawal and compared them to findings of patients prospectively observed under our current AWS standardized protocol. The results revealed a decreased percentage of patients who exhibited alcohol withdrawal in the preprotocol period, which may indicate that we failed to capture all preprotocol patients who had AWS. Although this is unlikely to have occurred because we are very diligent in documenting such diagnoses in the medical record, it raises a valid concern of selection bias toward the worst outcomes in the preprotocol period compared with all patients in the protocol period. The only way to address this study design limitation would be to perform a prospective, randomized study and evaluate for differences in the 2 groups. But given the relatively small number of patients with AWS, it may be difficult to prove efficacy, even under ideal study design conditions. Regardless of this concern, all of the health care providers involved agree that the protocol simplified and standardized the care of these difficult patients and continue to enthusiastically support its use. A particular improvement noted through the use of the protocol was the early identification and symptom-triggered treatment of patients with AWS in the protocol period. This advantage was highlighted by the worse outcomes in those patients who were late enrollees to the protocol.

In summary, the use of this standardized algorithm facilitates the care of alcohol-dependent postoperative patients by (1) identifying at-risk patients preoperatively, (2) facilitating efficient treatment of the 3 symptom types with appropriate and graded pharmacologic therapy through frequent nursing assessment, and (3) optimizing management that yields a favorable outcome in a non-ICU inpatient setting. Implementation of the protocol requires the cooperation of numerous health care providers, including nurses, nursing aids, residents, physician assistants, and physicians—a phenomenon evidenced by the improved rate of identification of at-risk patients in the second half of the study. Overall, the protocol simplifies and standardizes therapy in this diverse patient population, leading to improved patient care.

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