

Alcohol-Related Predictors of Delirium After Major Head and Neck Cancer Surgery

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Objective: To identify specific alcohol-related predictors of postoperative delirium.

Design: Inception cohort, logistic regression with stepwise selection.

Setting: Ohio State University Comprehensive Cancer Center, Columbus.

Patients: A total of 774 patients undergoing major resection of head and neck squamous cell carcinoma.

Main Outcome Measures: The correlation of 19 variables with postoperative delirium. One variable was an alcohol-related blood test: mean red blood cell volume (MCV). Eight variables were patient responses to alcohol-related questions.

Results: Eighty-nine of 774 surgical procedures (11.5%) were complicated by delirium. Six variables were significantly associated with delirium: age older than 69 years (odds ratio [OR], 2.43; $P < .01$), preexisting cognitive impairment (OR, 3.83; $P < .01$), surgery duration greater

than 6 hours (OR, 2.40; $P < .01$), MCV greater than 95.0 femtoliters (OR, 2.23; $P < .01$), ever being advised to cut back on alcohol (OR, 2.25; $P = .01$), and not abstaining from alcohol for at least 1 continuous week in the preceding year (OR, 2.16; $P = .02$). The number of variables stratified delirium risk (0 variables: 198 patients, 2.5% incidence of delirium; 1 variable: 278 patients, 6% incidence of delirium; 2 variables: 206 patients, 18% incidence of delirium; and >2 variables: 92 patients, 34% incidence of delirium).

Conclusions: Three clinical variables not related to alcohol drinking (age, preexisting cognitive impairment, and surgery duration), an alcohol-related laboratory test (MCV), and 2 alcohol-related questions (“At any time in your life, has anyone ever suggested that you should cut back on your drinking?” and “What is the greatest number of days in a row you have gone without an alcoholic drink in the past year?”) may help in estimating a patient’s risk for postoperative delirium.

Arch Otolaryngol Head Neck Surg. 2012;138(3):266-271

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HALF OF ALL PEOPLE OLDER than 13 years in the United States report consuming alcohol at least monthly, and the per capita annual consumption of ethanol is over 2.3 gallons.¹ Heavy alcohol consumption is associated with a higher risk of surgical complications, including blood loss, infection, and heart failure, and with longer, more expensive hospital stays.²⁻⁷ Heavy alcohol consumption is also associated with postoperative delirium, including delirium tremens (DTs), and patients who develop DTs after surgery are up to 3 times more likely to die.^{2-6,8}

Despite the potential adverse impact of heavy alcohol consumption on postoperative outcomes, screening for alcohol consumption prior to surgery is often haphazard. In one survey, just over one-third of people who had received medical care

in the previous 2 years reported being asked about their alcohol consumption.⁹ There are several questionnaires validated to detect problem alcohol use, but these questionnaires were developed to identify people with various different types of alcohol use disorders, and none of them was developed to identify patients at risk for postoperative complications. Therefore, currently available questionnaires to detect problem alcohol use may not effectively or efficiently identify patients at risk for alcohol use–related postoperative complications.

The aim of this study was to determine which alcohol use–related questions and which laboratory tests best identified patients at risk for postoperative delirium. We chose to study patients undergoing major head and neck squamous cell cancer surgery because these patients have both a high prevalence of heavy

alcohol consumption and a high incidence of postoperative delirium.^{10,11} Our ultimate goal is to more effectively and efficiently identify patients who might benefit from interventions to reduce alcohol consumption before surgery and from treatments to prevent alcohol withdrawal delirium after surgery.

METHODS

DATA SOURCE

The study population was an inception cohort of 978 medical evaluations performed by one of us (H.G.W.) from July 1994 through January 2004 prior to major surgery performed by one of the other authors (A.A., E.O., or D.E.S.) to resect squamous cell carcinoma of the head and neck at the Comprehensive Cancer Center—Arthur G. James Cancer Hospital and Richard J. Solove Research Institute at the Ohio State University, Columbus. Preoperative data were collected prospectively using a structured questionnaire. Sixty-four of the patients (6.5%) had been treated with chemotherapy at some time in their lives prior to their head and neck cancer surgery, 46 within the 24 months before surgery, and 26 in the 12 months before surgery. Five had been treated with chemotherapy for colorectal cancer; 4 for leukemia or lymphoma; 1 each for bladder, ovarian, and skin cancer; and the remaining 52 for head and neck cancer. Only the first surgery was analyzed if a patient had undergone more than 1 procedure. Of the 978 preoperative evaluations, 173 surgical procedures were excluded because data were incomplete or because the surgery did not last at least 2 hours, 30 were excluded for being the second surgery, and 1 was excluded for being the third surgery. The 204 excluded patients and surgical procedures were similar to the 774 whose data were studied, with regard to age (mean, 64 years; median, 63 years [range, 33-92 years]; *t* test, *P* > .05), sex (male, 72%; χ^2 test, *P* > .05), self-reported race (white, 91%; χ^2 test, *P* > .05), duration of surgery (mean duration, 384 minutes; median, 348 minutes [range, 115-1081 minutes]; *t* test, *P* > .05), and prevalence of preexisting cognitive dysfunction (prevalence, 6%; χ^2 test, *P* > .05). Hospital records were reviewed to determine the occurrence of postoperative delirium, defined as agitation or confusion noted after the first postoperative day.

VARIABLES

Nineteen variables were analyzed for correlation with postoperative delirium. The variables were chosen because of their previously demonstrated associations either with postoperative delirium or with alcoholism.¹²⁻¹⁴ The 4 demographic variables were age, sex, self-reported race, and self-reported living-alone status. The 5 medical variables were cachexia; markedly abnormal serum sodium, potassium, or glucose levels; preexisting cognitive impairment; poor self-reported functional class; and elevated mean corpuscular volume.¹⁵ The 2 surgical variables were American Society of Anesthesiology (ASA) class and duration of surgery. Rhinophyma, a physical finding associated with chronic heavy alcohol consumption, was considered as a variable, but too few patients had this finding to make it statistically useful. Markedly abnormal serum sodium, potassium, or glucose levels were defined as serum sodium levels lower than 130 or higher than 150 mEq/L (<130 or >150 mmol/L); potassium level lower than 3.0 or higher than 6.0 mEq/L (<3.0 or >6.0 mmol/L); or glucose level lower than 60 mg/dL or higher than 300 mg/dL (<3.3 or >16.7 mmol/L). Preexisting cognitive impairment was defined as any history or physical findings of stroke, transient ischemic attack, or de-

mentia. Functional class was measured using the Specific Activity Scale (SAS), which has been validated against formal exercise testing.¹⁶ Age and duration of surgery were converted to dichotomous variables. For age, a cutoff of 69 years was used to make a model comparable with the model of Marcantonio et al.¹² For duration of surgery, a cutoff of 6 hours was used, because there was a 7.1% incidence of delirium for surgical procedures lasting less than 6 hours but a 14.6% incidence of delirium for procedures lasting longer than 6 hours. The other variables were analyzed as binary variables: sex (male or female); self-reported race (white, black, or other); self-reported living alone status (living alone or not); cachexia (body mass index [BMI], calculated as weight in kilograms divided by height in meters squared, <18.5 or \geq 18.5); markedly abnormal serum sodium, potassium, or glucose levels (any abnormal or all normal); preexisting cognitive impairment (impaired or not); poor self-reported functional class (4 or <4); elevated mean corpuscular volume (>95.0 or \leq 95.0); and higher ASA class (>2 or \leq 2).

The patients' responses to 8 questions about alcohol drinking were also analyzed for correlation with postoperative delirium:

Type	Question
Introductory disclaimer	Next, I'm going to ask you several questions about alcohol. I don't mean to imply anything by asking these questions. I ask everyone the same questions. I'm just trying to learn how people use alcohol.
1. Most recent use	When did you most recently have any alcoholic beverage to drink? By alcoholic beverage I mean beer or wine or any drink containing alcohol.
2. Time without alcohol	What is the greatest number of days in a row you have gone without an alcoholic drink in the past year?
3. Eye opener	In the past year, how often have you needed a drink first thing in the morning to get yourself going? Every day? Once a week? Once a month? Less than once a month? Never?
4. Blackouts	In the past year, how often have you been unable to remember what happened the night before because you had been drinking? Every day? Once a week? Once a month? Less than once a month? Never?
5. Feelings of guilt	In the past year, how often have you felt guilty or regretful about your drinking? Every day? Once a week? Once a month? Less than once a month? Never?
6. Advised to cut down	At any time in your life, has anyone, for example a friend or a family member, ever suggested that you needed to cut back on your drinking?
7. Feeling need to cut down	Have you ever felt that you needed to cut back on your drinking?
8. Shakes, delirium tremens, or seizures	Have you ever had the shakes from drinking? Did you ever see or hear things that weren't there? Did you ever have the DTs [delirium tremens]? Have you ever had a seizure?

The 8 questions consisted of modified versions of the 4 CAGE questions and 4 additional questions about recent alcohol drinking, abstinences from alcohol during the preceding 12 months, history of alcohol withdrawal symptoms, and history of memory loss episodes (blackouts) associated with heavy drinking. Strategies recommended by Isaacson and Schorling¹⁷ were used to make alcohol use-related questions less threatening, including asking the questions in the flow of history taking, after asking about adverse medication reactions, medications, medical history, surgical history, family history, and smoking history, and after a brief introductory disclaimer. The responses to all of the alcohol-drinking questions were analyzed as binary variables: most recent use of alcohol (\leq 2 days or >2 days), longest time without alcohol in the past year (<7 days or \geq 7 days), having an "eye opener" early morning alcoholic drink in the preceding 12 months (yes or no), blackout episodes in the preceding 12 months (yes or no), feeling guilty about drinking al-

Table 1. Patient Characteristics for 774 Major Head and Neck Cancer Surgical Procedures at the Arthur G. James Cancer Hospital, Columbus, Ohio, 1994-2004

Characteristic	No. (% of Total)	No. With Delirium (% of Characteristic)
Totals	774 (100)	89 (11)
Male	548 (71)	70 (13)
Race/ethnicity, self-reported		
White	720 (93)	85 (12)
Black	46 (6)	3 (7)
Other ^a	8 (1)	1 (1)
Living alone, self-reported	155 (20)	20 (13)
BMI		
<18.5	74 (10)	13 (18)
18.5-24.9	327 (42)	37 (11)
25.0-29.9	227 (29)	29 (13)
30.0-40.0	129 (17)	10 (8)
>40.0	17 (2)	0
Preexisting cognitive impairment	39 (5)	11 (28)
Poor functional status	17 (2)	4 (24)
Tumor stage		
I	30 (4)	2 (7)
II	108 (14)	9 (8)
III	127 (16)	13 (10)
IV	333 (43)	49 (15)
Recurrent	176 (23)	16 (9)
Alcohol-drinking questions		
Most recent, ≤2 d	181 (23)	31 (17)
Period of time without alcohol in past year <7 d	85 (11)	22 (26)
Eye opener	61 (8)	10 (16)
Blackouts	56 (7)	11 (20)
Felt guilty	104 (13)	19 (18)
Advised to cut down	134 (17)	29 (22)
Felt need to cut down	338 (44)	46 (14)
Shakes, DTs, or seizures	111 (14)	15 (14)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DTs, delirium tremens.

^aOther: 8 East Asian, South Asian, Native American, or Mexican.

cohol in the preceding 12 months (yes or no), ever having been advised to cut back (yes or no), ever feeling the need to cut back (yes or no), and ever having shakes, seizures, or DTs (yes to any, or no to all).

STATISTICAL ANALYSIS

Logistic regression with step-wise selection was used to analyze the data, because the outcome was dichotomous. Only characteristics correlated with $P < .05$ by univariate analysis were included in the final model. The ASA class was not included in the multivariate analysis because ASA class is subjective and is, by itself, a type of multivariate analysis, a gestalt based on the many variables in the medical history, physical examination, and laboratory findings. The Hosmer-Lemeshow goodness-of-fit test was applied to the final model. We performed statistical analysis with Stata statistical software package (version 10.0; StataCorp Inc, College Station, Texas).

After creating the main effects model, 7 interaction terms were created by multiplying the coded values of selected pairs of predictors. Only those predictors for which interaction was plausible were tested. The tested pairs were as follows: being advised to cut back by others and time without alcohol, being advised to cut back by others and mean red blood cell volume

(MCV) level, being advised to cut back by others and cognitive status, time without alcohol and MCV level, time without alcohol and cognitive status, MCV level and cognitive status, and cognitive status and age. The findings of step-wise multivariate logistic regression were unchanged when run with these 7 additional terms. No interaction terms were significant, and thus none of them were included in the final model. The Hosmer-Lemeshow goodness-of-fit test yielded a χ^2 value of 5.44 and P value of .49, implying an adequate fitting of the model to the data set.

All data were abstracted from the medical records, deidentified, encrypted, and password protected. The institutional review board of the Ohio State University's Office of Responsible Research Practices approved the study.

RESULTS

The 774 patients were predominantly white (93%), and male (71%) (**Table 1**). They ranged in age from 24 to 90 years, with a mean and a median age of 63 years. Almost half (44%) reported feeling, at some time in their lives, that they needed cut back on drinking alcohol. Twenty-three percent reported having had an alcoholic drink in the 2 days preceding preoperative evaluation; 17% reported having been advised by others to cut back on their drinking at some time in their lives; and 14% reported prior shakes, seizures, or DTs. Surgical procedures lasted from 2.0 hours to more than 16.0 hours, with a median duration of 5.5 hours. Ninety-two of the procedures (11.5%) were complicated by postoperative delirium.

UNIVARIATE ANALYSIS

Ten variables correlated significantly with postoperative delirium by univariate analysis (**Table 2**). The only demographic variable significantly correlated with postoperative delirium was age older than 69 years (odds ratio [OR], 2.06). The 2 medical variables significantly correlated with postoperative delirium were preexisting cognitive impairment (OR, 3.31) and an MCV greater than 95.0 femtoliters (fL) (OR, 2.72). Both surgical variables correlated significantly with postoperative delirium: ASA class of 3 or 4 (OR, 3.01), and duration of surgery greater than 6 hours (OR, 2.35). Five of the questions about alcohol drinking were significantly correlated with postoperative delirium: drinking alcohol in the 2 days before preoperative medical evaluation (OR, 1.91), not going without alcohol for at least 1 week in the preceding 12 months (OR, 3.24), having 1 or more blackouts in the preceding 12 months (OR, 2.01), feeling guilty about drinking in the preceding 12 months (OR, 1.92), and ever having been advised by others to cut back (OR, 2.67).

MULTIVARIATE ANALYSIS

Six variables remained significantly correlated with postoperative delirium after multivariate logistic regression: age older than 69 years, preexisting cognitive impairment, MCV greater than 95.0 fL, duration of surgery greater than 6 hours, not going without alcohol for at least 1 week in the preceding 12 months, and ever having been advised by others to cut back on alcohol use (**Table 3**). There were no significant interaction terms.

Table 2. Odds Ratios (ORs) for Univariate Predictors of Postoperative Delirium After Major Head and Neck Cancer Surgery, 1994-2004

Selected Predictors for Delirium	OR (95% CI)	P Value
Patient demographics		
Age >69 y	2.06 (1.31-3.24)	<.01 ^a
Male sex	1.60 (0.94-2.72)	.09
White race, self-reported	1.67 (0.59-4.75)	.33
Living alone	1.18 (0.69-2.01)	.54
Medical predictors		
BMI <18.5	1.75 (0.92-3.33)	.09
Abnormal laboratory values		
Sodium	1.19 (0.26-5.35)	.82
Potassium	0.96 (0.12-7.78)	.97
Glucose	0.51 (0.07-3.89)	.51
Any abnormal laboratory value	0.96 (0.33-2.78)	.94
Cognitive impairment	3.31 (1.59-6.91)	<.01 ^a
Poor functional status	2.43 (0.78-7.63)	.13
Surgical predictor		
ASA class ≥3	3.01 (1.19-7.59)	.02 ^a
Duration of surgery >6 h	2.35 (1.49-3.71)	<.01 ^a
Alcohol-related laboratory values		
Elevated MCV, >95.0	2.72 (1.72-4.31)	<.01 ^a
Alcohol-drinking questions		
Period of time without alcohol in past year, <7 d	3.24 (1.88-5.60)	<.01 ^a
Most recent, ≤2 d	1.91 (1.19-3.06)	<.01 ^a
Blackouts	2.01 (1.00-4.04)	.05 ^a
Shakes, DTs, or seizures	1.24 (0.69-2.26)	.47
CAGE questions		
Felt need to cut down	1.51 (0.97-2.33)	.07
Advised by others	2.67 (1.64-4.36)	<.01 ^a
Felt guilty	1.92 (1.10-3.34)	.02 ^a
Eye opener	1.57 (0.77-3.22)	.22

Abbreviations: ASA, American Society of Anesthesiology; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DTs, delirium tremens; MCV, mean red blood cell volume.

^aSignificant at the .05 α level.

A PROPOSED CLINICAL PREDICTION RULE

The ORs in the final model enabled creation of a clinical prediction rule to quantify an individual's risk of postoperative delirium. We assigned 1 point for each of the following variables: age older than 69 years, preexisting cognitive impairment, surgery lasting more than 6 hours, MCV greater than 95.0 fL, not abstaining from alcohol for at least 1 week in the preceding 12 months, and ever having been advised to cut back on alcohol intake. The prediction rule stratified the patients into 4 cohorts with risk of postoperative delirium increasing from under 3% in the lowest risk cohort to over 30% in the highest risk cohort (**Table 4**).

COMMENT

Alcoholism is associated with postoperative delirium, and postoperative delirium is associated with worse surgical outcomes.^{2-6,8} Despite the potential adverse impact of alcoholism on surgical outcomes, screening for alcoholism prior to surgery remains problematic. There is no reliable blood test for alcoholism. Patients are often embarrassed and fur-

Table 3. Multivariate Predictors of Delirium After Major Head and Neck Cancer Surgery, 1994-2004

Selected Predictors for Delirium	OR (95% CI)	P Value
Patient demographics		
Age >69 y	2.43 (1.46-4.06)	<.01
Medical		
Preexisting cognitive impairment	3.83 (1.70-8.63)	<.01
MCV >95.0	2.23 (1.33-3.72)	<.01
Surgical		
Duration of surgery >6 h	2.40 (1.48-3.89)	<.01
Alcohol-drinking questions		
Time without	2.16 (1.12-4.16)	.02
Advised by others	2.25 (1.25-4.05)	.01

Abbreviations: MCV, mean red blood cell volume; OR, odds ratio.

Table 4. Performance of 2 Prediction Rules for Postoperative Delirium in 774 Head and Neck Cancer Surgical Procedures, 1994-2004

Points	Patients	No. (%) With Delirium
Shah Rule^a		
0	198	5 (2.5)
1	278	16 (5.7)
2	206	37 (18.0)
≥3	92	31 (33.7)
Marcantonio Rule^b		
0	261	10 (4.2)
1	320	41 (10.0)
2	169	30 (22.5)
≥3	24	8 (33.3)

^aThis study.

^bSee Marcantonio et al.¹²

tive about how much they actually drink. Even cohabitant family members often do not know how much alcohol a patient is drinking. Furthermore, the same amount of alcohol has different effects on different people. Alcoholism screening questionnaires, such as the CAGE and Michigan Alcohol Screening Test, can be effective in identifying patients with alcoholism; however, they have limitations: (1) they do not solicit information on the amount, frequency, or pattern of alcoholic drinking; (2) they do not distinguish between current and past alcohol drinking; (3) they are designed to detect alcohol dependence but not other types of problem alcohol drinking; and (4) they require the time to ask multiple questions.¹⁸ The Alcohol Use Disorders Identification Test questionnaire includes questions on the amount, frequency, and pattern of alcohol drinking, and it specifically asks about drinking in the past year. However, it takes time to administer because it consists of 10 questions.¹⁸ The National Institute on Alcohol Abuse and Alcoholism recommends a single screening question, "How many times in the past year have you had x or more drinks in a day?", where x is 5 for men and 4 for women, and a response of once or more is considered indicative of some type of alcoholism.¹⁹ This question has been demonstrated to accurately identify un-

healthy alcohol drinking in a sample of primary care patients,¹⁹ but, to our knowledge, its ability to predict postoperative complications has not been studied.

We undertook this study to identify specific clinical variables related to alcohol drinking that correlate with postoperative delirium. We analyzed 19 variables previously associated either with postoperative delirium or with heavy alcohol drinking. Although ASA class has been associated with postoperative delirium and was associated with postoperative delirium in our univariate analysis, we did not include it in our multivariate analysis because ASA class is subjective and is, by itself, a type of multivariate analysis, a gestalt based on the many variables in the medical history, physical examination, and laboratory evaluation. We analyzed a number of alcohol drinking–related questions, because we sought to identify a few specific alcohol-related questions that clinicians can ask so that they can adequately evaluate alcohol-related risk without wasting their time and their patients' time during the preoperative evaluation by asking questions that are not helpful.

We intended to analyze 10 specific variables related to alcohol drinking, including 1 physical finding (rhinophyma) and 1 blood test (MCV); however, too few patients had the physical finding of rhinophyma for it to be analyzed. Four of the 8 questions related to alcohol drinking were derived from the CAGE questionnaire. The other 4 questions were about the most recent alcohol drinking, abstinences from alcohol during the preceding 12 months, history of alcohol withdrawal symptoms, and history of blackouts associated with heavy drinking. We sought to avoid confrontation and patient furtiveness by structuring the questions so as not to ask patients about current amount and frequency of alcohol drinking. We also carefully worded the questions to minimize emotional content. For example, we changed the CAGE question, "Have people annoyed you by criticizing your drinking?" to "Has anyone ever advised you to cut back on your drinking?" It seems to us less embarrassing to report having been advised than to admit to having been criticized and annoyed. We found that responses to 2 of these alcohol-drinking–related questions and the MCV were correlated with postoperative delirium.

This study confirmed some of the previously identified predictors of postoperative delirium and suggests 3 additional predictors that are associated with heavy alcohol consumption. In 1994, Marcantonio et al¹² published a clinical prediction rule for delirium after elective noncardiac surgery (hereinafter, the Marcantonio rule), which assigns 1 point for each of 6 predictors: (1) age older than 69 years; (2) poor preoperative cognitive status; (3) high-risk surgery; (4) poor preoperative functional status; (5) markedly abnormal serum sodium, potassium, or glucose levels; and (6) heavy alcohol drinking, as defined by self-reported consumption of more than 2 drinks daily. We previously applied the Marcantonio rule to 138 major head and neck cancer surgical procedures, and it stratified them into 3 cohorts of increasing prevalence of postoperative delirium (9%, 19%, and 25%).¹³ However, the Marcantonio rule did not identify a cohort of patients at low risk for postoperative delirium, perhaps because it did not distinguish different degrees of alcohol drinking in the population of patients with head and neck cancer, a popula-

tion with a high prevalence of alcohol drinking. In the current study we analyzed the predictors previously identified by Marcantonio et al,¹² and we found that, while advanced age, impaired cognitive status, "high-risk" surgery (defined as surgery lasting >6 hours in our population), and self-reported uninterrupted daily alcohol drinking were correlated with postoperative delirium, a poor SAS functional status of 4 and markedly abnormal preoperative levels of serum sodium, potassium, or glucose were not (Table 2). This may have been because Marcantonio et al¹² included laboratory findings up to the day of surgery, whereas the laboratory findings we analyzed were obtained 1 to 2 weeks prior to surgery, and the abnormal findings were addressed and usually corrected prior to surgery. For example, electrolytes were replaced, medications were adjusted, and diabetes mellitus was controlled several days, if not a week or more, prior to surgery.

The abnormal laboratory test that was correlated with postoperative delirium in the current study was an MCV greater than 95.0 fL, a marker of heavy daily alcohol consumption. An MCV greater than 100 fL has been shown to predict alcohol withdrawal delirium in hospitalized medical patients.²⁰ The MCV is also often elevated for several months after cytotoxic antineoplastic chemotherapy.²¹ At the time MCV was determined, 11 of the patients in this study had undergone antineoplastic chemotherapy in the previous 6 months, and 21 had done so in the previous 12 months. In addition, an elevated MCV is associated with increasing age and myelodysplastic syndrome; however, an MCV greater than 95.0 fL remained correlated with postoperative delirium after controlling for age. Finally, an elevated MCV is also associated with inadequate intake or absorption of vitamin B₁₂, which can also impair neurologic function. Although vitamin B₁₂ deficiency may explain some of the correlation of an elevated MCV with postoperative delirium, most of the patients with postoperative delirium were not clinically malnourished, and many were also taking multivitamin supplements either as a tablet or in a liquid nutritional supplement. Therefore, the association of elevated MCV with alcoholism seems the most likely explanation for its correlation with postoperative delirium in this study. If this is true, then the fact that elevated MCV remained associated with postoperative delirium after controlling for self-reported alcohol drinking also suggests that there was underreporting of alcohol drinking by some patients. That is, considering the MCV improved the detection of risk compared with only asking the alcohol-drinking related questions, and, likewise, asking the alcohol-drinking–related questions improved the detection of risk compared with only considering the MCV. Other studies have also found that considering the MCV improves the sensitivity of alcohol-drinking screening questions.²⁰

In the current study, the Marcantonio rule¹² stratified patients into cohorts of increasing prevalence of postoperative delirium (4%, 10%, 23%, and 33%), but it did not identify a low-risk cohort. The proposed "Shah rule" developed in this study did stratify a significant number of patients into a low-risk cohort (198 patients, <3% risk). It also stratified a greater number of patients into a high-risk cohort than did the Marcantonio rule (92 patients at >30% risk vs 24 patients at 33% risk). At least some of the

comparative advantage of the Shah rule is likely due to data fitting, the fact that the rule was derived from the data to which we are applying it. Nonetheless, these findings suggest that, in addition to considering age, preexisting cognitive impairment, and expected duration of surgery, asking patients (1) whether anyone has ever advised them to cut back on their drinking and (2) the greatest number of days in a row they have gone without an alcoholic drink in the past year and (3) also noting whether their preoperative MCV is higher than 95.0 fL may help to identify patients at both low and high risk for postoperative delirium. Although not addressed in this study, patients who are identified as being at risk for postoperative delirium based on risk factors related to alcohol drinking might reasonably be expected to benefit from special assistance with alcohol abstinence before surgery^{22,23} and from symptom-triggered treatment with benzodiazepines after surgery to prevent postoperative alcohol withdrawal delirium.²⁴

Application of the findings of this study should be guided by its limitations, including that the questions were asked, and the patients' responses were interpreted, by a single observer; that it was performed at a single institution; that some medical records were excluded from analysis owing to missing data; and that the findings have not been externally validated.

In conclusion, in 774 patients undergoing major resection of head and neck cancer, multivariate analysis identified 6 predictors of postoperative delirium: advanced age (>69 years), preexisting cognitive impairment, longer duration of surgery (>6 hours), ever having been advised to cut back on alcohol drinking, not abstaining from alcohol for at least 1 week in the preceding year, and an MCV greater than 95.0 fL. The findings of this study suggest that, in addition to advanced age, preexisting cognitive impairment, and long surgery, 2 specific questions regarding alcohol drinking and MCV may help to identify patients at risk for postoperative delirium.

Submitted for Publication: March 3, 2011; final revision received November 1, 2011; accepted December 5, 2011.

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Author Contributions: Dr Weed had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. **Study concept and design:** Shah, Weed, Ozer, and Schuller. **Acquisition of data:** Weed, Ozer, and Schuller. **Analysis and interpretation of data:** Shah, Weed, He, and Agrawal. **Drafting of the manuscript:** Shah, Weed, and Ozer. **Critical revision of the manuscript for important intellectual content:** Shah, Weed, He, Agrawal, and Schuller. **Statistical analysis:** Shah and He. **Administrative, technical, and material support:** Schuller. **Study supervision:** Weed. **Decision making and planning care:** Ozer.

Financial Disclosure: None reported.

Funding/Support: Dr Weed was supported in part by Department of Health and Human Services Primary Care Research Initiative Grant No. 5D12 HP00027-02. Dr Schuller was supported in part by grant P30 CA16058, National Cancer Institute, Bethesda, Maryland; The Ohio

State University Comprehensive Cancer Center Head and Neck Oncology Group, Columbus; and the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus.

Previous Presentation: This study was presented as a poster at the Society of General Internal Medicine Annual Meeting; May 15, 2009; Miami, Florida.

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