Risk factors and prevalence of perioperative cognitive dysfunction in abdominal aneurysm patients

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Background: **Perioperative delirium is common in high-risk surgery and is associated with age, education, preoperative cognitive functioning, pre-existing medical conditions, and postoperative complications. We investigated these factors as well as lifestyle and demographic variables by using cognitive measures that were more sensitive than those used in previous studies.**

Methods: **Extensive medical and demographic data were collected on 102 patients between 41 and 88 years of age to identify comorbidities and lifestyle considerations preoperatively. Elective abdominal aortic aneurysm surgery was performed under combined general/epidural anesthesia with postoperative epidural analgesia. A battery of sensitive, cognitive measures was administered preoperatively, at the time of discharge from hospital, and 3 months postoperatively. Symptoms of delirium were assessed during the first 6 postoperative days using *Diagnostic and Statistical Manual of Mental Disorders-4th Edition* criteria. Intraoperative and postoperative data, including medications, vital signs, conduct of the surgery and anesthesia, complications, and details of pain control, were collected.**

Results: **Delirium occurred in 33% of the patients during the first 6 days after surgery. Longer duration of delirium was related to lower education, preoperative depression, and greater preoperative psychoactive medication use. Characteristics of the surgery and hospital stay were unrelated to the development of delirium. Patients who were diagnosed with delirium had lower cognitive scores during each of the three assessment periods, even when controlling for age and education. Logistic regression analysis indicated that the most powerful preoperative predictors of delirium were number of pack years smoked ($P = .001$), mental status scores ($P = .003$), and number of psychoactive medications ($P = .005$).**

Conclusion: **A significant proportion of patients undergoing elective abdominal aortic aneurysm repair are susceptible to the development of delirium and are at risk for cognitive dysfunction after surgery. Our findings have implications for promoting long-term lifestyle changes, including smoking cessation and improved management of mental health as risk-reduction strategies. (J Vasc Surg 2005;42:884-90.)**

Delirium is an acute mental disorder and is a common postoperative complication, especially in the elderly. It is associated with increased morbidity, mortality, and length of hospital stay in elective surgical patients.[1] Delirium can be the presenting symptom of an underlying physical illness, and failure of diagnosis leads to a delay in intervention. It can occur in both patients with pre-existing cognitive deficits and in those with apparently normal cognition. Many patients do not recover cognitively after an episode of severe delirium.[2]

In previous studies, the accurate diagnosis of delirium has been clouded by confusion surrounding terminology. The development of precise diagnostic criteria by the American Psychiatric Association published in the *Diagnostic and Statistical Manual of Mental Disorders-4th Edition* (DSM-IV)[3] has clarified the diagnosis (Table I). *Delirium* is now the appropriate term for an organic brain syndrome that develops acutely, has a fluctuating clinical course, and is characterized by disturbances of attention, memory, orientation, perception, psychomotor behavior, and sleep.

The incidence of postoperative delirium varies widely, with reported rates of 10% to 55%.[1,2] A number of major factors affecting incidence have been identified, including patient characteristics such as age, education, ethanol consumption, previous head trauma, pre-existing medical conditions, and preoperative cognitive status.[4,5] Surgical procedures and postoperative complications have also been shown to influence the incidence of delirium.[6,7]

Some studies[5] suggest that the preoperative cognitive status of elderly patients may be a major factor determining the degree of cognitive impairment after surgery. A feared

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Table I. DSM-IV criteria for delirium

1. Disturbance of consciousness (ie, reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.
2. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia.
3. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.

DSM-IV, Diagnostic and Statistical Manual of Mental Disorders-4th Edition.

complication of surgery and anesthesia by the elderly is permanent cognitive impairment. Although most elderly people have no deterioration in cognitive function after an uneventful anesthetic, there is evidence that a subset of patients may be susceptible to long-term cognitive impairment.[4,8]

Many previous studies have failed to recognize potentially important risk factors such as lifestyles and demographics that may affect the development of delirium. The cognitive functioning measures selected have often lacked the sensitivity to detect subtle cognitive changes. Some studies have neglected to correct for the effect of age and education on cognitive test performance and have not properly controlled for these variables in their statistical analysis.

This prospective multidisciplinary study is designed to examine the factors associated with postoperative cognitive impairment in a group of patients undergoing elective repair of abdominal aortic aneurysm. This procedure was chosen because of the reported high incidence of postoperative delirium.[6] The objectives in our study were to:

1. measure the incidence and duration of postoperative delirium in a known high-risk group of elective surgical patients;
2. identify perioperative risk factors for the development of delirium; and
3. determine whether there is significant cognitive decline after surgery.

METHODS

Ethical approval for the study protocol was obtained from the University of Manitoba Research Ethics Board, and all procedures were followed in accordance with the Declaration of Helsinki and the Tri-Council Policy. All patients who entered into the study provided written informed consent. Patient recruitment began on December 29, 2000, and was completed on December 4, 2003. One hundred two patients between the ages of 41 and 88 years were recruited prospectively from consecutive cases seen in the outpatient clinic for elective management of abdominal aortic aneurysm (AAA). Exclusion criteria included patients with a language barrier, visual or auditory impairment, illiteracy, or any other reason that made them unable to perform the cognitive testing.

Preoperative period. A standardized history and physical form was completed to document pertinent patient information, with special emphasis on patterns of smoking and ethanol consumption. All study patients attended the multidisciplinary Preoperative Assessment Clinic, where preoperative evaluation and teaching is performed by anesthesiology, nursing, physiotherapy, occupational therapy, and other medical consultants as required.

Appropriate laboratory investigations were determined by the procedure and patient history. Pulse oximetry was recorded when significant respiratory disease was suspected. Nonsurgical management of the aneurysm was pursued in patients with oxygen saturations <90%. Each patient underwent cognitive testing performed by the study nurse who was trained and supervised by a neuropsychologist. The Geriatric Depression Scale[9] (GDS) was administered to explore potential effects of emotional factors. All measures were completed 2 weeks before surgery.

Perioperative period. The anesthetic management of patients was consistent. All patients had a combined general and epidural anesthetic technique with postoperative epidural analgesia. The surgery performed was at the discretion of the attending surgeon. All surgery was performed by one of three surgeons who practice as a team and use similar operative techniques.

Intraoperative data collection included duration of surgery, aortic cross-clamp time, length of surgical intensive care unit stay, and hospital stay. Patients were admitted to the surgical intensive care unit postoperatively and then to the surgical ward. All patients were assessed twice daily by the Acute Pain Service for the management of their epidural analgesia, which is staffed by a pain nurse supervised by an anesthetist who is on 24-hour call.

Postoperative data collection included medications administered, medical and surgical complications, pain scores, and cognitive status. The patient's chart was reviewed, nursing staff were consulted, and standardized neuropsychological tests were administered. Clinical researchers with either medical or neuropsychological training conducted all assessments.

An abbreviated Mini Mental State Examination was used to test for orientation, attention and memory problems. Symptoms of delirium were monitored using DSM-IV criteria. If there were symptoms suggesting delirium, patients were further assessed using the clinician-rated Delirium Index.[10] This is a seven-item instrument that rates symptoms of impaired attention, disorganized thinking, altered levels of consciousness, disorientation, memory impairment, perceptual disturbances, and abnormal motor activity. Postoperative cognitive testing and the GDS were repeated on postoperative day 6 or before discharge.

Late postoperative period. Once discharged from the hospital, patients were followed in the Outpatient Clinic or through home visits. At 3 months postoperatively, patients repeated the cognitive assessment battery and the GDS.

Cognitive assessment battery. The cognitive assessment battery consisted of neuropsychological tests selected to be sensitive to mild and diffuse organic brain dysfunction and that could all be completed in <45 minutes. The battery consisted of nine tests:

1. Standardized Mini Mental State Examination[11] was included given the common usage of this test in medical settings (different word lists were used for each administration);
2. Wechsler Logical Memory test,[12] a measure of verbal memory where the patient tries to recall a short story that has just been read (alternate stories were used to reduce practice effects);
3. Rey-Osterrieth Complex Figure,[13] a measure of perceptual organization and motor functioning where the patient is asked to copy a geometric line drawing containing 18 elemental details;
4. Time Months of the Year Backward (TMYB), an item from the Short Blessed Test for dementia[14] measuring central processing speed and sensitive of brain dysfunction;
5. The Time to Print the Alphabet in capital letters, an item drawn from the HIV Dementia Scale[15] that measures graphomotor speed;
6. Trail Making Test (parts A and B),[16] which measures visual conceptual and visuomotor tracking;
7. Animal (Category) Naming,[17] a test of word fluency where the patient generates as many animal names as they can in one minute;
8. Delayed recall scores for Wechsler Logical Memory test; and
9. Delayed recall for the Rey-Osterrieth Complex Figure.

Statistical analysis. We compared continuous variables using the Student's *t* test for normally distributed data and the Mann-Whitney *U* test for nonparametric data. Categoric variables were compared with the χ^2 test or Fisher's exact test. To control for type I errors with multiple comparisons, Bonferroni corrections were applied. Differences in cognitive test scores between patients diagnosed with delirium and those without delirium were analyzed presurgery, postsurgery, and 3 months postsurgery by a repeated measure of a multiple analysis of covariance (MANCOVA) design with age and education as covariates. Time of measurement (pre-, post-, 3 months post-) was the within patient factor, and presence of delirium, age, and education were between patient factors. A logistic regression analysis was performed on statistically significant discriminating preoperative variables to predict the likelihood of delirium post-surgery. We took $P < .05$ as the level of significance in all analyses and used SPSS (version 10.0) (SPSS Inc, Chicago, Ill) for the analysis of the data. Data are expressed as means ± standard deviation (SD).

RESULTS

Incidence of delirium. Thirty-four (33%) of the 102 patients were diagnosed with at least one episode of delirium (an episode was defined as a diagnosis of delirium using DSM-IV criteria on any post-operative day) during the first 6 postoperative days. For patients who developed delirium, the mean number of days on which delirium occurred was 2.18 (range, 1 to 6 days). Most of the delirium episodes occurred on the second (24.3%), third (21.6%), and fourth (20.3%) days after surgery. Of the 34 patients diagnosed with delirium, 17 had it only 1 day, and 17 had it ≥2 days. Patients with ≥2 days of delirium had significantly less education (9.35 ± 1.46 years) than those with only 1 day (11.47 ± 3.78 years) ($P = .039$). Patients with ≥2 days of delirium also had significantly higher GDS scores (5.29 ± 3.16) than the 1-day patients (1.56 ± 5.29) ($P = .0004$) and took significantly more preoperative psychoactive medications (0.76 ± 0.83) than the 1-delirium-day group (0.24 ± 0.56) ($P = .038$). Some patients had episodes of delirium beyond the 6-day follow-up, but it resolved in all patients before discharge.

Preoperative medical predictors of delirium. Patients who developed delirium did not differ significantly in height, weight, systolic or diastolic blood pressure, or history of head injury or other neurologic conditions compared with patients without delirium (Table II). There were no differences between the two groups in terms of the presence of pre-existing medical conditions. However, patients diagnosed with delirium were taking significantly more psychoactive medications before surgery than nondelirium patients and significantly fewer vasoactive medications than nondelirium patients. Psychoactive agents included benzodiazepines or hypnotics, antidepressants, and antipsychotics; the vasoactive agents included antihypertensive and antianginal agents.

Demographic predictors of delirium. Patients ranged in age from 41 to 88 years (70.80 ± 8.17 years), and although the mean age of the delirium group was 3 years older, the difference was not statistically significant (Table III). However, the 12 patients who were aged ≥80 years had a much higher incidence of delirium (75%) than patients aged <80 years (27.8%) ($P = .002$). There was no difference in gender, education, or living situation between patients who developed delirium and those who did not. Patients diagnosed with delirium were significantly more likely to be single, widowed, separated, or divorced. Most of the patients (n = 95, 93.1%) had a history of smoking, but 66 (64.7%) reported they had quit smoking at some point before surgery (14.91 ± 13.73 years). Patients diagnosed with delirium had a significantly higher number of pack years smoked. The incidence of delirium was not related to current smoking status or to the number of years since quitting smoking.

Virtually all of the patients (n = 101, 99.0%) had a history of ethanol consumption: 67 (65.7%) described themselves as mild drinkers, 22 (21.6%) as moderate drinkers, and 11 (10.8%) as heavy drinkers. Eighty-one (79.4%) were current drinkers, and 20 (19.6%) former drinkers who had abstained for an average of 18.08 ± 14.22 years. Unexpectedly, the patients who developed delirium consumed fewer drinks per year than those who did not develop delirium, although the difference only approached statistical significance.

Perioperative variables and delirium. We examined characteristics of the AAA operation and of the hospital stay

Table II. Preoperative medical predictors of delirium

Variable	*Delirium (yes)* (n = 34)*	*Delirium (no)* (n = 68)*	P
Height (cm)	171.17 ± 9.24	172.51 ± 8.01	.462
Weight (kg)	78.72 ± 16.96	84.19 ± 14.43	.100
Blood pressure			
Systolic (mm Hg)	140.44 ± 19.54	138.19 ± 24.91	.647
Diastolic (mm Hg)	76.71 ± 11.47	76.46 ± 12.26	.924
Other neurologic disease			
Yes	10 (29.4)	11 (16.4)	.128
No	24 (70.6)	56 (83.6)	
History of head injury			
Yes	9 (26.5)	18 (26.5)	1.000
No	25 (73.5)	50 (73.5)	
Depression (GDS)	3.48 ± 3.13	2.51 ± 2.39	.087
Number of psychoactive meds†	0.50 ± 0.75	0.18 ± 0.42	.020
Number of vasoactive meds	0.41 ± 0.50	0.78 ± 0.79	.017

GDS, Geriatric Depression Scale.
*Data expressed as number (%) or mean ± SD.
†Mann-Whitney *U* test.

Table III. Patient characteristics predictive of delirium

Variable	*Delirium (yes)* (n = 34)*	*Delirium (no)* (n = 68)*	P
Gender			
Males	26 (76.5)	53 (77.9)	.867
Females	8 (23.5)	15 (22.1)	
Age (years)	72.88 ± 8.62	69.76 ± 7.79	.069
Total years of education	10.41 ± 3.02	10.76 ± 2.58	.550
Marital status			
Married	18 (52.9)	51 (75.0)	.025
Other†	16 (47.1)	17 (25.0)	
Living Situation			
Lives with others	21 (61.8)	51 (75.0)	.167
Lives alone	13 (38.2)	17 (25.0)	
No. of alcoholic drinks/year‡	206.03 ± 487.08	386.35 ± 854.46	.060
No. of pack years smoked	46.78 ± 27.53	31.15 ± 19.47	.002
Quit smoking			
Yes	24 (72.7)	42 (67.7)	.649
No	9 (27.3)	20 (32.3)	
No. years since quitting	14.52 ± 13.67	15.13 ± 13.25	.772

*Data are expressed as number (%) or mean ± SD.
†Single, widowed, divorced, separated.
‡Mann-Whitney *U* test.

Table IV. Perioperative variables predictive of delirium

Variable	*Delirium (yes)* (n = 34)*	*Delirium (no)* (n = 68)*	P
Length of AAA operation (hrs)	2.82 ± 1.06	2.89 ± 0.81	.693
Maximum AAA diameter (cm)	6.12 ± 0.89	5.97 ± 0.97	.475
Aortic cross-clamp time (mins)	70.50 ± 34.62	63.81 ± 25.06	.110
Days in ICU†	1.39 ± 2.40	0.63 ± 0.65	.156
Days in hospital†	12.34 ± 23.68	7.08 ± 2.77	.067
Surgical procedure			
Aortoaortic	23 (39.7)	35 (60.3)	.297
Aortobifemoral	8 (26.7)	22 (73.3)	
Aortobiiliac	3 (30.0)	7 (70.0)	
Endovascular repair	0 (0)	4 (100.0)	

AAA, Abdominal aortic aneurysm; *ICU,* intensive care unit.
*Data are expressed as number (%) or mean ± SD.
†Mann-Whitney *U* test.

to see if they were related to the presence of delirium after surgery (Table IV). There was no statistically significant difference in the incidence of delirium between the different aortic surgical procedures. The length of operation, maximum diameter of AAA (cm), and aortic clamp time did not differ between the two groups. The incidence of perioperative medical and surgical complications was similar in both groups.

A two-way repeated-measures analysis of variance (ANOVA) indicated that patients diagnosed with delirium did not differ from nondelirium patients in the number of psychoactive, vasoactive, cardiac, antibiotic or other medications administered on the day of surgery or during the 6 postoperative days. We found no difference in the use of narcotics and sedatives between delirium and nondelirium patients in the postoperative period.

Although patients who developed delirium spent a longer time in the intensive care unit (1.39 days) than nondelirium patients (0.63 days) and had a longer length of stay in the hospital (12.34 days vs 7.08 days), neither difference was statistically significant.

Cognitive functioning and delirium. Cognitive test measures whose scores were normally distributed were entered into a MANCOVA analysis with age and education as covariates. Research has demonstrated that these two variables are related to cognitive test performance, especially in the elderly.[5] The 76 patients who completed all of the tests on all three measurement periods were included in

Table V. MANCOVA analysis of cognitive measures predictive of delirium

		*Within effects**			*Between effects*			
Measure	*Delirium*	*Pre*	*Post*	*3 Months*	*Time*	*Delirium*	*Age*	*Education*
Trails A (time in secs)†	Yes	44.57 ± 16.68	49.24 ± 22.51	51.74 ± 21.96	F = 3.26	F = 0.82	F = 2.42	F = 3.45
	No	43.68 ± 20.35	44.55 ± 20.21	43.17 ± 21.51	*P* = .043	*P* = .367	*P* = .125	*P* = .067
Trails B (time in secs)	Yes	148.48 ± 67.56	164.13 ± 79.32	137.91 ± 62.57	F = 1.03	F = 2.37	F = 4.22	F = 11.13
	No	123.08 ± 61.61	135.08 ± 73.53	119.17 ± 63.20	*P* = .358	*P* = .128	*P* = .044	*P* = .001
Rey Figure‡ (score/36)	Yes	23.54 ± 5.66	23.32 ± 6.61	24.00 ± 5.38	F = 0.28	F = 4.46	F = 0.01	F = 4.25
	No	26.08 ± 5.01	24.93 ± 5.13	26.78 ± 4.47	*P* = .755	*P* = .038	*P* = .927	*P* = .043
Rey Figure Recall‡ (score/36)§	Yes	12.09 ± 4.93	13.82 ± 6.21	13.63 ± 4.72	F = 0.57	F = 0.00	F = 0.31	F = 2.03
	No	10.87 ± 4.99	13.39 ± 4.92	15.33 ± 5.98	*P* = .562	*P* = .969	*P* = .578	*P* = .158
The Months of the Year Backwards (time in secs)	Yes	21.78 ± 20.52	23.70 ± 18.73	15.70 ± 8.29	F = 0.61	F = 1.49	F = 0.00	F = 3.97
	No	16.81 ± 12.13	17.51 ± 13.22	15.47 ± 10.78	*P* = .521	*P* = .226	*P* = .974	*P* = .050
Time to print Alphabet (time in secs)	Yes	27.61 ± 7.36	29.14 ± 7.88	27.65 ± 7.83	F = 0.82	F = 2.33	F = 1.00	F = 14.00
	No	25.23 ± 7.74	26.47 ± 7.28	24.96 ± 6.55	*P* = .431	*P* = .132	*P* = .320	*P* = .000
Animal Names (number of animals)	Yes	18.17 ± 4.16	17.04 ± 4.13	17.78 ± 4.07	F = 0.43	F = 2.67	F = 7.30	F = 2.45
	No	18.91 ± 4.92	18.81 ± 5.15	20.64 ± 5.20	*P* = .630	*P* = .107	*P* = .009	*P* = .122
Wechsler Logical) Memory‡ (Immediate (score/25)	Yes	9.74 ± 3.80	10.74 ± 4.06	11.70 ± 3.73	F = 0.19	F = 5.49	F = 5.05	F = 5.77
	No	11.75 ± 4.42	13.09 ± 4.37	13.60 ± 4.02	*P* = .815	*P* = .022	*P* = .028	*P* = .019
Wechsler Logical Memory‡ (Delayed) (score/25)	Yes	9.22 ± 4.53	9.30 ± 4.52	10.09 ± 4.70	F = 1.62	F = 7.53	F = 6.66	F = 6.14
	No	11.02 ± 4.59	11.92 ± 4.43	13.21 ± 3.82	*P* = .204	*P* = .008	*P* = .012	*P* = .016

MANCOVA, Multiple analysis of covariance.
Data are expressed as mean ± SD.
*Used Greenhouse-Geisser correction.
†Visit by age interaction (F = 5.02, *P* = .008).
‡High scores represent better test performance.
§Visit by delirium interaction (F = 3.89, *P* = .024).

Table VI. Logistic regression analysis predictors of delirium

Variable	*B*	*S.E.*	*Wald*	*df*	*Sig*	*Exp(B)*
Pack years smoked	−.050	.014	11.756	1	.001	.952
MMSE	.742	.252	8.695	1	.003	2.100
No. psychoactive meds	−1.918	.688	7.779	1	.005	.147
No. vasoactive meds	1.343	.556	5.825	1	.016	3.830
No. ethanol drinks/year	.001	.001	2.539	1	.111	1.001

MMSE, Mini Mental State Examination.

the analysis. The rate of delirium for this subset of patients (30.3%) was similar to the total sample (33.3%).

Patient scores on all cognitive measures were within 1 SD of the normal range for this age group. Patients diagnosed with delirium performed consistently more poorly on all nine cognitive tests than nondelirium patients (Table V). The MANCOVA analysis shows that the covariate of age and education was a significant factor in accounting for the variability of scores for four of the nine cognitive tests, and the covariate of education for six of the tests. However, the presence of delirium was still a statistically significant between-subjects factor for the Rey Figure test and both the Immediate and Delayed Recall scores of the Wechsler Logical Memory Test.

Emotional functioning. GDS scores were analyzed by repeated-measures ANOVA with the presence of delirium as the between-patients factor. Patients who developed delirium had higher preoperative GDS scores (3.30 ± 3.05) than nondelirium patients (2.34 ± 2.31), but this between-group difference disappeared in the period after surgery and 3 months postsurgery. However, there was a statistically significant change for both groups across the three measurement periods ($F_{2,82}$ = 10.60, P =.0006). Post hoc analysis indicated a quadratic contrast in which depression scores increased significantly immediately after surgery and then returned to preoperative levels at 3 months after surgery. This increase in GDS scores immediately postoperatively is likely related to the shortcomings of the GDS instrument measuring discomfort and fatigue rather than true depression.

Logistic regression analysis. Preoperative variables discriminating between patients who did and did not develop delirium were entered into a forward stepwise (Wald) logistic regression analysis in which presence of delirium was the dependent variable. The most statistically significant predictors of postoperative delirium were (1) a greater number of pack years smoked, (2) a lower Mini Mental State Examination score, (3) a greater number of psychoactive medications, and (4) a lower number of vasoactive medications (Table VI). The model correctly predicted 84% of the cases. The Cox and Snell $R^2 = 0.375$.

DISCUSSION

The incidence of delirium after elective AAA repair was 33%, which is lower than the 46% as previously reported by Marcantonio et al.[6] Although diagnostic criteria for delirium were similar, the number of patients was quite different—102 in our study vs 35 in Marcantonio's study—and the time period of data collection was approximately a decade apart. Our patients had a high incidence of delirium despite a relative absence of serious medical problems. Most cases of delirium occurred on postoperative days 2, 3, and 4, as previously reported in the literature.[6] This might have been due to the stress of surgery with resultant physiologic instability, combined with withdrawal of regular habits and medications, in the patient with a vulnerable brain.

Our study confirmed previous work[1] that increasing age was a risk factor, especially in patients aged ≥80 years. Despite this trend, delirium occurred in all age groups. Patients who were not married and living alone had a higher incidence of delirium, but this was associated with increasing age. The level of education was not related to the incidence of delirium, but it was related to its severity. Previous research has shown a significant relationship between lower levels of education and both postoperative cognitive dysfunction[5] and dementia.[18] Less education was also associated with poorer scores on our cognitive test battery.

The strongest predictor of delirium was the amount smoked in pack years. Although heavy lifetime exposure to cigarettes has not been previously associated with postoperative delirium, there is evidence that smoking correlates with dementia,[19] errors on cognitive tests,[20] and diminished cognition.[21] This may reflect either a direct neurotoxic effect of tobacco or microvascular changes in the brain that produce a diminished executive function and cognitive reserve. The stress of surgery and all of its accompanying effects may uncover subtle deficits that are not functionally significant. Clearly, this finding is another reason to stop smoking. Our finding of pack years smoked, rather than current smoking status, suggests that smoking cessation may be insufficient to reduce the risk of cognitive sequelae.

Ethanol consumption was not significantly related to the incidence of delirium, although there was an association of increasing consumption with less delirium. Previous research has also shown contradictory associations of ethanol use and delirium. While some studies have demonstrated a positive relationship between ethanol abuse and delirium,[22] other studies have reported no relationship.[23] The accuracy of self-reported data on ethanol consumption is suspect: drinkers are notorious for denying or minimizing drinking levels. We believe this may explain the inconsistent finding both in our study and in others.

Preoperative psychoactive medication use was associated with an increased incidence of delirium, which is consistent with previous research.[24,25] Our study did not evaluate interventions such as preoperative tapering of psychoactive medications or changing from short-acting to long-acting drugs. Also, we did not categorize the clinical indication for these drugs. These would be further avenues of investigation to determine if this is a modifiable factor in diminishing risk of delirium. Our results suggest that aggressive management of cardiovascular disease with vasoactive agents is of benefit in preventing delirium.

It was interesting to see that delirium was associated with weaker pre- and postsurgery cognitive performance overall, even after controlling for the effects of age and education. These differences reached statistical significance only in the case of the Rey Complex Figure test and the Wechsler Logical Memory tests, which are more mentally challenging tasks compared with most of the other tests that involve more basic concentration and psychomotor abilities. It may be that once the effects of a postoperative delirium have cleared, the patient's cognitive function returns to a level roughly equivalent to that of the nondelirious postsurgery patient, apart from some subtle higher-order changes. It is noteworthy as well that these differences, found shortly after surgery, tended to persist at 3 months. Nevertheless, those patients with both delirium and low scores were still within the normal range of cognitive function for their age group. This may be a reflection of the lack of sensitivity of current methods to assess cognition, and it is unclear whether any of these differences have clinical significance beyond their ability to predict an increased risk of postoperative delirium.

Interestingly, the difference in cognitive test scores between patients with and without delirium was of approximately the same magnitude at each test interval. Again, the scores for these two groups of patients at the preoperative stage were within the normal range expected for people in their age group, and the differences were subtle. These subtle cognitive differences that are associated with delirium could account for later mild cognitive differences that are seen 3 months after surgery, without invoking a direct effect of delirium itself. Whether subtle cognitive dysfunction is a cause of delirium, or whether both cognitive dysfunction and delirium are the result of some third factor, cannot be distinguished by this study.

Preoperative depression as measured by the GDS was associated with more days of delirium. This may explain why there was also an association between delirium and living alone or being widowed, separated, or divorced. Because we also found a link between delirium and the use of preoperative psychoactive medication, one wonders whether preoperative emotional difficulties play a direct role in the increased risk of delirium, or whether the effect is indirect, leading to over-use of psychoactive drugs. The question of whether there are vulnerabilities directly associated with psychological stress would require further research to answer. Notably, GDS scores were not significantly different overall between patients who did or did not develop delirium. It is also possible that our measure of depression was not sensitive enough to detect group differences.

We identified several weaknesses in our study. Our original protocol had included both early and late preoperative cognitive assessments, a minimum of 3 months apart, to allow measurement of any possible downward trajectory in cognitive function. This became impractical because most patients had earlier surgical dates than anticipated. It may be possible that future research can study a group of patients who are appropriate for earlier preoperative cognitive measurements. The 6-day postoperative follow-up period in our protocol caused us to underestimate the length of delirium symptoms in some patients. Cognitive testing before discharge was occasionally problematic due to patient fatigue, and some patients were unable to complete the tests.

The strengths of our study included a prospective design, precise definition of delirium, and standardized cognitive tests sensitive to subtle cognitive changes with established norms that allow comparison with other populations. Our multidisciplinary research team included surgeons, anesthesiologists, a geriatric psychiatrist, a neuropsychologist, and a statistician. This allowed us to explore a variety of characteristics in our patients and identify specific risk factors for delirium. Informed consent should be extended to a discussion of risk, management**, i**mplications of and prognosis of an episode of delirium.

It is hoped that identification of these risk factors will lead to risk-reduction strategies and improved patient outcomes. Future research can be designed to achieve these goals.

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