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Brief Preoperative Screening for Frailty and Cognitive Impairment Predicts Delirium after Spine Surgery

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ABSTRACT

Background: Frailty and cognitive impairment are associated with postoperative delirium, but are rarely assessed preoperatively. The study was designed to test the hypothesis that preoperative screening for frailty or cognitive impairment identifies patients at risk for postoperative delirium (primary outcome).

Methods: In this prospective cohort study, the authors administered frailty and cognitive screening instruments to 229 patients greater than or equal to 70 yr old presenting for elective spine surgery. Screening for frailty (five-item FRAIL scale [measuring fatigue, resistance, ambulation, illness, and weight loss]) and cognition (Mini-Cog, Animal Verbal Fluency) were performed at the time of the preoperative evaluation. Demographic data, perioperative variables, and postoperative outcomes were gathered. Delirium was the primary outcome detected by either the Confusion Assessment Method, assessed daily from postoperative day 1 to 3 or until discharge, if patient was discharged sooner, or comprehensive chart review. Secondary outcomes were all other-cause complications, discharge not to home, and hospital length of stay.

Results: The cohort was 75 [73 to 79 yr] years of age, 124 of 219 (57%) were male. Many scored positive for prefrailty (117 of 218; 54%), frailty (53 of 218; 24%), and cognitive impairment (50 to 82 of 219; 23 to 37%). Fifty-five patients (25%) developed delirium postoperatively. On multivariable analysis, frailty (scores 3 to 5 [odds ratio, 6.6; 95% CI, 1.96 to 21.9; $P = 0.002$]) *versus* robust (score 0) on the FRAIL scale, lower animal fluency scores (odds ratio, 1.08; 95% CI, 1.01 to 1.51; $P = 0.036$) for each point decrease in the number of animals named, and more invasive surgical procedures (odds ratio, 2.69; 95% CI, 1.31 to 5.50; $P = 0.007$) *versus* less invasive procedures were associated with postoperative delirium.

Conclusions: Screening for frailty and cognitive impairment preoperatively using the FRAIL scale and the Animal Verbal Fluency test in older elective spine surgery patients identifies those at high risk for the development of postoperative delirium.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Postoperative delirium is a common complication in older surgical patients.
- Frailty and cognitive impairment are associated with postoperative delirium but are rarely assessed preoperatively. This may be due to the time and burden required for screening.

What This Article Tells Us That Is New

- Screening for frailty and cognitive impairment preoperatively using the brief FRAIL (measuring fatigue, resistance, ambulation, illness, and weight loss) scale and the Animal Verbal Fluency test in older elective spine surgery patients identifies those at high risk for the development of postoperative delirium.

POSTOPERATIVE delirium is a common complication that afflicts 20 to 80% of older surgical patients.[1] As such, guidelines recommend that older surgical patients undergo preoperative screening for geriatric conditions associated with postoperative delirium and poor surgical outcomes.[2,3] Chief among these are frailty, a geriatric syndrome often described as cumulative impairments in functional reserve, and cognitive impairment. About 10 to 40% of older community-dwelling persons are prefrail or frail and a similar proportion has cognitive impairment or overt dementia.[4] Likewise, both conditions are common in older surgical patients and are associated with a higher risk of developing postoperative delirium, other in-hospital complications, prolonged hospital length of stay, discharge not to home, hospital readmission, and mortality.[5–10] Nonetheless, preoperative

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screening for frailty or cognitive impairment are not typically performed before a surgical procedure.

There are myriad reasons for this, but one is the perception that such screening is unduly burdensome and time-consuming for a surgical setting.[8,11–13] This has been addressed to some degree in the case of preoperative cognitive screening, with work by several groups, including us, demonstrating that brief instruments such as the Mini-Cog and Animal Verbal Fluency can identify patients at risk for poor surgical outcomes.[10,11,14,15] Similarly, there are numerous validated tools to assess frailty, but little consensus about which are best suited to the preoperative setting. Thus far, investigations of the relationship between frailty and adverse surgical outcomes have largely relied on instruments such as the Frailty Index or the Frailty Phenotype which, are relatively time consuming and labor intensive and therefore unlikely to be widely accepted or adopted in a high throughput preoperative setting. Given the prevalence of frailty and its association with poor surgical outcomes, preoperative assessment of frailty remains an important clinical initiative.

With this in mind, we hypothesized that frailty or cognitive screening using brief tools will identify patients at high risk for postoperative delirium and other complications. Hence, we designed a prospective study wherein older patients scheduled for elective spine surgery were screened preoperatively for frailty with the FRAIL (measuring fatigue, resistance, ambulation, illness, and weight loss) scale, a validated five-item questionnaire for predicting decline in health or mortality, and cognition with the Mini-Cog and Animal Verbal Fluency tests, which we and others have previously demonstrated can stratify older surgical patients at risk of postoperative delirium and other adverse outcomes.[8,10,11,15–17] Our secondary aims were exploratory in nature and investigate associations between perioperative variables, including frailty and cognitive performance, with all in-hospital complications, discharge to place other than home and hospital length of stay.

Materials and Methods

The Partners Human Research Committee/Institutional Review Board approved this prospective observational cohort study (No. 2016P000012) that was also registered in ClinicalTrials.gov (NCT02922634). This is a primary analysis of data. Between April 17, 2017 and October 9, 2018, study staff members recruited patients greater than or equal to 70 yr of age who were scheduled for elective spine surgery at the Brigham and Women's Hospital (Boston, Massachusetts) and were expected to have an inpatient admission after their procedure. We selected this patient population because spine surgery is the third most common surgical procedure in older persons[18] and our previous work showed that nearly 20% of this surgical demographic develops delirium postoperatively.[19] This type of surgery is relatively homogeneous and grouped within tiers of invasiveness. Eligible patients were identified by review of the preoperative evaluation schedule in the electronic medical record. Exclusion criteria included planned outpatient surgery; history of overt stroke or brain tumor; uncorrected vision or hearing impairment (unable to see pictures or read or hear instructions); limited use of the dominant hand (limited ability to draw); and/or inability to speak, read, or understand English.

We planned to prospectively enroll a total of 229 patients in the study based on a power calculation of the number of patients required for 85% power to detect a 50% difference in postoperative delirium (primary outcome) at the $P = 0.05$ level between patients with and without a positive cognitive or frailty screen, assuming a baseline incidence of postoperative delirium of 15% and approximately a 10% loss to follow up. After obtaining written informed consent, patients were screened using the FRAIL scale to identify frailty and the Mini-Cog and Animal Verbal Fluency tests to evaluate cognitive performance in the Brigham and Women's Hospital Weiner Center for Preoperative Evaluation (Boston, Massachusetts) on the day of the patient's scheduled preoperative evaluation which takes place no more than 4 weeks before surgery.[9,10] The FRAIL scale[8,16] is a simple five-point screen that measures fatigue, resistance (ability to climb one flight of stairs), ambulation (ability to walk one block), illness (more than five past or current diagnoses), and weight loss (more than 5%). Each positive response within a domain scores 1 point, yielding a maximum score of 5. Higher scores indicate increased frailty; as described by others, we defined "frail" as a score of 3 or more and "prefrail" as a score of 1 to 2. We selected the Mini-Cog and Animal Verbal Fluency tests for cognition because they are brief, have been used previously in older surgical populations, and have been shown to be associated with the development of postoperative delirium.[9–11,15] The Mini-Cog is a simple and validated cognitive screening tool that includes a three-item recall of memory and a clock drawing component that is graded on a five-point scale, where a score of 2 or less is considered probable cognitive impairment. Animal Verbal Fluency is a similarly simple and brief cognitive screening tool where the subject is asked to name as many animals as possible in 60 s; a score of 16 or less has previously been demonstrated to be associated with postoperative delirium.[11,20] For the primary analysis, both Mini-Cog and Animal Verbal Fluency scores were analyzed linearly. We categorized the complexity and invasiveness of the surgical procedure according to an established four-tier rating system: microdiscectomy is a tier 1 procedure; lumbar laminectomy, anterior cervical procedures, or minimally invasive fusions are tier 2; lumbar fusion, trauma, or posterior cervical fusion procedures are tier 3; and tumor, infection, deformity, or combined anterior and posterior cervical procedures are tier 4.[21] For the analysis, we grouped tiers 1 and 2 (less complex) and 3 and 4 (more complex) together as there were few patients in categories 1 or 4. Other demographic and medical information such as age, sex, body mass index, highest level of education, American Society of Anesthesiologists (ASA) functional status, metabolic equivalent of task, total number of medications, preoperative use of opioids, alcohol consumption, and past medical history of depression and psychiatric comorbidities were obtained from the medical record.

Incidence of postoperative delirium was the primary outcome. Postoperative delirium was identified both by chart review using published criteria and by direct, independent assessment with the Confusion Assessment Method.[10,22,23] The Confusion Assessment Method was administered once per day on postoperative days 1 to 3, or until discharge if the patient was discharged early, by an investigator blinded to chart review information. We used both methods because they are complementary. Delirium typically waxes and wanes so it can be missed if the Confusion Assessment Method is administered during the waning period. Conversely, chart review reflects events during an entire day but may miss hypoactive postoperative delirium, the most common form.[1] The secondary outcomes included all in-hospital cardiopulmonary (myocardial infarction, congestive heart failure, cardiac arrest, new onset arrhythmia, pulmonary embolism, reintubation, and deep venous thrombosis), infectious (wound infections, pneumonia, sepsis, and urinary tract infection), renal (acute renal injury), or cerebrovascular (stroke and transient ischemic accident) complications, discharge to place other than home and hospital length of stay.

Study data were managed using Research Electronic Data Capture hosted at Partners Healthcare (Somerville, Massachusetts).[24]

Statistical Analysis

Data were analyzed by several methods using two-tailed testing. We first evaluated data for normality and outliers, and no action was required. We performed a missing data analysis (numbers reported in the results and tables) and a complete case analysis was performed. For univariate analysis, we used Mann–Whitney U test for nonnormal distributions (data reported as median [25th, 75th percentiles]) or the independent samples *t* test for normally distributed continuous variables (data reported as mean ± SD), and chi-square test for categorical variables (data reported as count [%]) to compare differences between postoperative delirium and no postoperative delirium groups. For multivariable analysis, all the covariates with $P \leq 0.1$ on univariate analysis (body mass index, ASA physical status, metabolic equivalent of task, total number of medications, preoperative use of opioids, animal fluency test score, FRAIL scale score, and invasiveness of the surgical procedure) were entered into a backwards stepwise logistic regression model for prediction of the primary outcome: incidence of postoperative delirium. Age as a continuous variable and Mini-Cog score were forced into the multivariable model. These variables were selected to account for possible confounding, no variables were analyzed as effect modifiers. The Hosmer–Lemeshow goodness of fit test was performed to evaluate model-fitting of the logistic multivariable model. Variables included in the model were tested for multicollinearity using the variance inflation factor and correlation matrix. We performed the same univariate statistical analysis previously described for having complications other than postoperative delirium, discharge to place other than home, and hospital length of stay (secondary outcomes), and further used the Spearman rank-order correlation test and Kruskal–Wallis rank sum test as appropriate. We performed a *post hoc* analysis to investigate the association between the FRAIL scale scores and the ASA physical status (both as ordinal variables) using the Spearman rank-order correlation test. A sensitivity model was conducted *post hoc* where we forced possible confounders based on theory (to further include alcohol consumption, depression and psychiatric history) into the model with the relevant pre-screening predictors. The significance threshold was set at $P < 0.05$. All analyses were performed with statistical software IBM SPSS Statistics for Macintosh, Version 25.0 (IBM Corp, USA).

Results

During the study period, the Weiner Center evaluated 439 patients aged 70 yr or older who were scheduled for elective spine surgery (fig. 1). Of these, 33 were ineligible, 41 could not be approached because study personnel were occupied with another enrollment, and 3 declined participation at the front desk. Of the remaining 362 patients, 125 declined and 8 were determined to be ineligible. Of the 229 who gave informed consent, 5 asked to be unenrolled during the study and were excluded, and 5 did not have their procedure. Data from the remaining 219 patients were included in this analysis.

As shown in table 1, of the 219 patients, 2 (0.9%) patients had missing data for body mass index, 7 (3.2%) for highest level of education, 10 (4.6%) for metabolic equivalent of task, 26 (11.9%) for alcohol consumption, 1 (0.5%) for FRAIL scale, 1 (0.5%) for hospital length of stay, and 1 (0.5%) for discharge place.

The median age of the cohort was 75 yr with 57% (N = 124 of 219) being male (table 1) and 24% (N = 53 of 219) scored as frail. Based on the Mini-Cog and verbal fluency scores, 23% (N = 50 of 219) and 37% (N = 82 of 219) had probable cognitive impairment, respectively. Postoperative delirium developed in 25% (N = 55 of 219), with 32 of 219 (58%) detected by chart review only, 2 of 219 (4%) detected by Confusion Assessment Method only, and 21 of 219 (38%) detected by chart review and Confusion Assessment Method. On univariate analysis, higher body mass index, ASA physical score greater than or equal to 3, metabolic equivalent of task less than or equal to 4, higher number of medications, chronic use of opioids, fewer animals named on the verbal fluency test, frailty, and more invasive procedures were associated with postoperative delirium (table 2).

On the multivariable model, frailty (FRAIL scale score greater than or equal to 3) (odds ratio, 6.6; 95% CI, 1.96

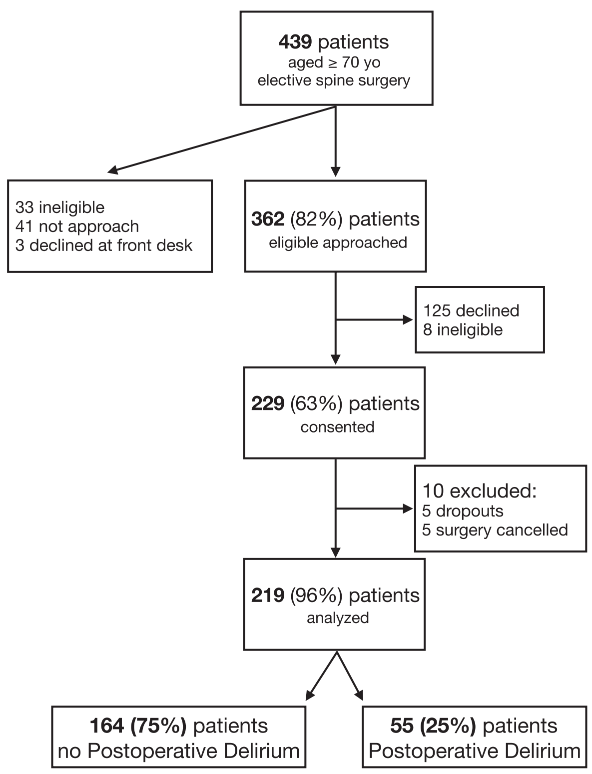

Fig. 1. Flow diagram on recruitment, retention and postoperative delirium.

to 21.9; $P = 0.002$) was a strong independent predictor of postoperative delirium but this was not the case for prefrailty (FRAIL scale score 1 or 2) (odds ratio, 1.95; 95% CI, 0.60 to 6.3; $P = 0.266$). Naming fewer animals on the verbal fluency test was associated with increased odds of postoperative delirium (odds ratio, 1.08; 95% CI, 1.01 to 1.51; $P = 0.036$ for each point decrease in the number of animals named). In contrast, lower scores on the Mini-Cog were not associated with increased risk for postoperative delirium. Finally, more invasive surgery was associated with greater risk for postoperative delirium (odds ratio, 2.69; 95% CI, 1.31 to 5.50; $P = 0.007$) (table 3).

All in-hospital complications other than postoperative delirium (N = 219) occurred in 68 patients (31%) and, on univariate analysis, higher body mass index, ASA physical status greater than or equal to 3, metabolic equivalent of task less than 4, total number of medications, chronic use of opioids, alcohol consumption, Animal Verbal Fluency test score, frailty, and more invasive procedures were associated with other in hospital complications. (Supplemental Digital Content, table 1, http://links.lww.com/ALN/C469)

Seventy-seven patients (36%) admitted from home (N = 215) were discharged to a place other than home. On univariate analysis, older age, female sex, ASA physical status greater than or equal to 3, metabolic equivalent of tasks less than 4, total number of medications, psychiatric history, Animal Verbal Fluency test score, FRAIL scale score greater than or equal to 3, and more invasive procedures were associated with discharge to other place than home. (Supplemental Digital Content, table 2, http://links.lww.com/ALN/C470)

On univariate analysis, variables associated with longer hospital length of stay after surgery included higher body mass index, ASA physical status, metabolic equivalent of task less than 4, total number of medications, chronic use of opioids, depression, FRAIL scale score, and more invasive surgical procedures. (Supplemental Digital Content, table 3, http://links.lww.com/ALN/C471)

No in-hospital or 30-day mortality was recorded.

On the *post hoc* analysis, ASA physical status was weakly correlated with the FRAIL scale scores ($r_s = 0.179$; $P = 0.008$). The sensitivity model consisting of theoretically important confounders yielded consistent results to significant association between verbal fluency test (odds ratio, 1.08; 95% CI, 1.002 to 1.15; $P = 0.043$), frailty (FRAIL scale score greater than or equal to 3 [odds ratio, 7.1; 95% CI, 1.84 to 27.2; $P = 0.004$]), and more invasive surgical procedures (odds ratio, 3.05; 95% CI, 1.42 to 6.54; $P = 0.004$).

Discussion

This study demonstrates that frailty is prevalent in older patients undergoing elective spine surgery and, along with cognitive impairment and the invasiveness of the surgical procedure, frailty is associated with postoperative delirium. Unlike most previous work, we assessed and identified frailty using a simple, brief screening tool, the FRAIL scale, rather than a lengthy battery and demonstrate that it is sufficient to identify patients at risk for unfavorable surgical outcomes. This is crucial in a preoperative setting, where time is limited and geriatric expertise many not be available. Furthermore, we concurrently screened patients for cognitive impairment, a common feature of frailty and a well-established independent risk factor for development of postoperative delirium.[3] Confirming previous work, we demonstrate that the older surgical population has a high prevalence of cognitive impairment and that poor cognition is associated with a high incidence of postoperative delirium. Therefore, while both frailty and cognitive impairment are common in older elective surgical patients and predict greater risk for postoperative cognitive and medical complications, frailty appears to be the stronger risk factor of the two.

Frailty is an age-related syndrome featuring multi-organ loss of reserve and resiliency and increased vulnerability to stressors. It is common in the community, with a prevalence between 10 and 65%, depending upon age and the tool used to assess it, and more than 40% are prefrail.[4,8,24] Frailty is also common in older elective surgical populations; 38 to 54% of those greater than or equal to age 70 score as prefrail

Table 1. Baseline Characteristics

	Total = 219
Age, yr, median [25th, 75th percentile]	75 [73, 79]
Sex, n (%)	
Male	124 (57)
Female	95 (43)
Body mass index, kg/m^2, median [25th, 75th percentile]*	28 [25, 32]
College degree or higher, n (%)†	144 (66)
ASA physical status ≥ 3, n (%)	149 (68)
Metabolic equivalent of task < 4, n (%)‡	70 (32)
Total number of medications, median [25th, 75th percentile]	8 [5, 11]
Chronic use of opioids, n (%)	55 (25)
Alcohol consumption, n (%)§	125 (57)
Depression, n (%)	39 (18)
Psychiatric history, n (%)	22 (10)
Mini-Cog score, median [25th, 75th percentile]	4 [3, 5]
Animal Verbal Fluency test, mean ± SD	18 ± 6
FRAIL scale, n (%)‖	
Score 0 (robust)	48 (22)
Scores 1 and 2 (prefrail)	117 (54)
Scores 3 and 5 (frail)	53 (24)
Surgical invasiveness#, n (%)	
Tier 1 + 2	111 (51)
Tier 3 + 4	108 (49)

*N = 217. †N = 212. ‡N = 209. §N = 193. ‖N = 218. #Tiers 1 and 2: microdiscectomy, lumbar laminectomy, or anterior cervical procedures, minimally invasive fusions; tiers 3 and 4: lumbar fusion, trauma, or posterior cervical fusion procedures, tumor, infection, deformity, or combined anterior and posterior cervical procedures.
ASA, American Society of Anesthesiologists.

and 35 to 41% as frail on comprehensive frailty measures.[7] However, longer, detailed frailty instruments have been used in nearly all frailty studies in surgical patients which, due to time constraints, are unlikely to be widely adopted in clinical practice, and the few that used brief measures were conducted retrospectively and/or involved urgent or emergency surgery.[8] There is no agreement about the optimal tool for assessing frailty and prevalence estimates vary somewhat with the criteria and instrument used. We chose the FRAIL scale because it is brief and requires neither measurements (*e.g.,* walking speed, grip strength) nor medically-trained personnel. The scale has high specificity but low sensitivity, so may underestimate the prevalence of frailty. Nonetheless, it performed well in our setting as judged by the fact that the percentage of our cohort who scored as frail is similar to that reported in surgical populations by others using longer instruments and that the brief screen for frailty verified associations of this geriatric syndrome with postoperative delirium and all-cause complications. Therefore, the FRAIL scale appears to be well-suited for a high-throughput environment such as the preoperative evaluation clinic. While there is some correlation between ASA physical status and the FRAIL scale score (our *post hoc* analysis suggests a weak yet statistically significant positive correlation), the ASA physical status does not predict perioperative risks, but when used with other factors such as the type of surgery, frailty scores, and other markers of deconditioning it can be helpful in predicting perioperative risks.[25,26] The FRAIL score measures fatigue, resistance, ambulation, illnesses, and loss of weight and is very objective. In contrast, the ASA physical status is a subjective assessment of the fitness of patients before surgery and measures their medical comorbidities.

Frail persons are often cognitively impaired as well, and poor cognition is a risk factor for development of postoperative delirium and other unfavorable surgical outcomes. As such, we screened patients separately for baseline cognitive status. We used the Mini-Cog and Animal Verbal Fluency tests because both tools are brief and easy to administer and have previously been shown to predict risk for postoperative delirium in older surgical patients.[10,11] Our results compare well with previous work in geriatric patients scheduled for various elective surgical procedures, with most reporting that 15 to 63% of patients are cognitively impaired before surgery. In fact, the 23% incidence of probable cognitive impairment by Mini-Cog and 37% by Animal Verbal Fluency identified in this study are consistent with the findings of others. Likewise, our data show that poor preoperative cognitive status is associated with a greater prevalence of postoperative delirium, a relationship identified previously using different tests and surgical populations.[11,15] Here, however, contrary to our previous work and the work of others, poor preoperative cognition was associated with postoperative delirium by Animal Verbal fluency but not Mini-Cog.[10] The reasons for this discrepancy are not clear but may be related to several factors. Animal Verbal Fluency is scored on an unlimited-point scale whereas the Mini-Cog is scored on a five-point scale and this may reduce the statistical power of the latter to detect differences; or perhaps because Animal Verbal Fluency has high sensitivity and low specificity as suggested by a higher incidence of cognitive impairment (37%) than the Mini-Cog (23%).

This work has a number of weaknesses. This was a single-center study of older surgical spine patients, so caution is warranted in generalizing these results to other geriatric surgical patients. In addition, nearly 35% of the patients who were eligible for the study declined participation and it is not known whether the results would be different if they had enrolled (*i.e.*, selection bias). Our data may also underestimate the risk of developing postoperative delirium after this type of surgery, as more than 65% of the subjects in this study had at least a college education; this is relevant because educational attainment is associated with a lower risk of cognitive impairment and, hence, delirium. Similarly, because we administered the Confusion Assessment Method just once per day during the first 3 postoperative days, we may have missed cases of postoperative delirium. However, we complemented this evaluation with chart review, which complements the Confusion Assessment Method and reflects the waxing and waning course of delirium throughout the day. There were other sources of potential bias during this study, such as

Table 2. Univariate Associations with Postoperative Delirium

N = 219	Postoperative Delirium No = 164 (75%)	Postoperative Delirium Yes = 55 (25%)	*P* Value
Age, years, median [25th, 75th percentile]	75 [73, 79]	77 [72, 80]	0.508*
Sex, n (%)	108 (67)	36 (72)	0.720†
Male	94 (57)	30 (55)	
Female	70 (43)	25 (46)	
Body mass index, kg/m^2, median [25th, 75th percentile]‖	28 [25, 32]	30 [26, 34]	0.025*
College degree or higher, n (%)#	108 (67)	36 (72)	0.480†
ASA physical status ≥ 3, n (%)	105 (64)	44 (80)	0.028†
Metabolic equivalent of tasks < 4, n (%)**	45 (29)	25 (49)	0.007†
Total number of medications, median [25th, 75th percentile]	8 [5, 10]	9 [7,12]	0.002*
Chronic use of opioids, n (%)	34 (21)	21 (38)	0.010†
Alcohol consumption, n (%)††	98 (68)	27 (55)	0.101†
Depression, n (%)	26 (16)	13 (24)	0.192†
Psychiatric history, n (%)	14 (9)	8 (15)	0.200†
Mini-Cog score, median [25th, 75th percentile]	4 [3, 5]	4 [2, 5]	0.333*
Animal Verbal Fluency test, mean ± SD	19 ± 5	17 ± 5	0.005‡
FRAIL scale, n (%)‡‡			< 0.001†
Score 0 (robust)	43 (26)	5 (9)	
Scores 1 and 2 (prefrail)	92 (56)	25 (46)	
Scores 3 and 5 (frail)	29 (18)	24 (44)	
Surgical invasiveness§, n (%)			0.002†
Tier 1 + 2	93 (57)	18 (33)	
Tier 3 + 4	71 (44)	37 (67)	

*Mann–Whitney U test. †Chi-square test. ‡Independent samples *t* test. §Tiers 1 and 2: microdiscectomy, lumbar laminectomy or anterior cervical procedures, minimally invasive fusions; tiers 3 and 4: lumbar fusion, trauma, or posterior cervical fusion procedures, tumor, infection, deformity, or combined anterior and posterior cervical procedures. ‖N = 217. #N = 212. **N = 209. ††N = 193. ‡‡N = 218.

ASA, American Society of Anesthesiologists.

interviewer bias or bias from misclassification of exposure and/or outcome that were acknowledged and addressed: we used a standardized protocol for data collection; investigators were trained to score the Mini-Cog and Confusion Assessment Method before study enrollment; the Mini-Cog clock drawing test was scored by a second blind investigator and, in case of conflicting scores, by a third blind investigator; and Confusion Assessment Method and chart review for postoperative delirium were checked by an independent investigator. We performed a multivariable regression analysis to account for possible confounders, but the role of other unidentified variables cannot be ruled out.

Table 3. Variables Associated with Postoperative Delirium on Multivariable Analysis

	Postoperative Delirium Odds Ratio (95% CI)	*P* Value
Body mass index	1.06 (0.996, 1.14)	0.067
Animal Verbal Fluency test	1.08* (1.01, 1.51)	0.036
Scores 3 to 5 (frail) *vs.* score 0 (robust)	6.6 (1.96, 21.9)	0.002
Scores 1 and 2 (prefrail) *vs.* score 0 (robust)	1.95 (0.60, 6.32)	0.266
Surgical invasiveness	2.69 (1.31, 5.50)	0.007

Hosmer–Lemeshow goodness of fit test, *P* = 0.234. Variables entered in the logistic model: age, body mass index, American Society of Anesthesiologists physical status, metabolic equivalent of task, total number of medications, preoperative use of opioids, Mini-Cog score, animal fluency test score, FRAIL questionnaire score and invasiveness of the surgical procedure.

*Odds ratio as per one animal decrease.

In conclusion, as suggested by The American College of Surgeons and the American Geriatrics Society guidelines, we found that older patients who screen positively for preoperative frailty or cognitive impairment using brief screening tools are at increased risk of developing postoperative delirium and all-cause morbidity.

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Competing Interests

Dr. Culley is the Director of the American Board of Anesthesiology, a member of the American Board of Medical Specialties Committee on Continuous Certification, an Accreditation Council for Graduate Medical Education

– Resident Review Committee ex-officio member, Executive Editor of Anesthesiology, an American Society of Anesthesiologists committee member, and reports receiving grant funding from National Institute on Aging and National Institute of General Medical Sciences (Bethesda, Maryland). Dr. Friese reports financial support for this work from Foundation for Anesthesia Education and Research; Dr. Crosby reports an ongoing financial relationship with International Anesthesia Research Society outside the submitted work; Dr. Groff reports current financial relationships with Depuy Spine (Raynham, Massachusetts), Biomet Spine (Parsippany-Troy Hills, New Jersey), and Nuvasive Spine (San Diego, California) outside the submitted work; and Dr. Chi reports a current financial relationship with Stryker Spine (Kalamazoo, Michigan) outside the submitted work. The other authors declare no competing interests.

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References

1. Inouye SK: Delirium in older persons. N Engl J Med 2006; 354:1157–65
2. Chow WB, Rosenthal RA, Merkow RP, Ko CY, NF; American College of Surgeons National Surgical Quality Improvement Program; American Geriatrics Society: Optimal preoperative assessment of the geriatric surgical patient: A best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. J Am Coll Surg 2012; 215:453–66
3. Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Audisio R, Borozdina A, Cherubini A, Jones C, Kehlet H, MacLullich A, Radtke F, Riese F, Slooter AJ, Veyckemans F, Kramer S, Neuner B, Weiss B, Spies CD: European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. Eur J Anaesthesiol 2017; 34:192–214
4. Woo J, Yu R, Wong M, Yeung F, Wong M, Lum C: Frailty screening in the community using the FRAIL scale. J Am Med Dir Assoc 2015; 16:412–9
5. Gleason LJ, Schmitt EM, Kosar CM, Tabloski P, Saczynski JS, Robinson T, Cooper Z, Rogers SO Jr, Jones RN, Marcantonio ER, Inouye SK: Effect of delirium and other major complications on outcomes after elective surgery in older adults. JAMA Surg 2015; 150:1134–40
6. Makhani SS, Kim FY, Liu Y, Ye Z, Li JL, Revenig LM, Vaughan CP, Johnson TM II, García PS, Ogan K, Master VA: Cognitive impairment and overall survival in frail surgical patients. J Am Coll Surg 2017; 225:590–600.e1
7. Cooper Z, Rogers SO Jr, Ngo L, Guess J, Schmitt E, Jones RN, Ayres DK, Walston JD, Gill TM, Gleason LJ, Inouye SK, Marcantonio ER: Comparison of frailty measures as predictors of outcomes after orthopedic surgery. J Am Geriatr Soc 2016; 64:2464–71
8. Gleason LJ, Benton EA, Alvarez-Nebreda ML, Weaver MJ, Harris MB, Javedan H: FRAIL questionnaire screening tool and short-term outcomes in geriatric fracture patients. J Am Med Dir Assoc 2017; 18:1082–6
9. Culley DJ, Flaherty D, Reddy S, Fahey MC, Rudolph J, Huang CC, Liu X, Xie Z, Bader AM, Hyman BT, Blacker D, Crosby G: Preoperative cognitive stratification of older elective surgical patients: A cross-sectional study. Anesth Analg 2016; 123:186–92
10. Culley DJ, Flaherty D, Fahey MC, Rudolph JL, Javedan H, Huang CC, Wright J, Bader AM, Hyman BT, Blacker D, Crosby G: Poor performance on a preoperative cognitive screening test predicts postoperative complications in older orthopedic surgical patients. Anesthesiology 2017; 127:765–74
11. Long LS, Wolpaw JT, Leung JM: Sensitivity and specificity of the animal fluency test for predicting postoperative delirium. Can J Anaesth 2015; 62:603–8
12. Flexman AM, Charest-Morin R, Stobart L, Street J, Ryerson CJ: Frailty and postoperative outcomes in patients undergoing surgery for degenerative spine disease. Spine J 2016; 16:1315–23
13. Shoultz TH, Moore M, Reed MJ, Kaplan SJ, Bentov I, Hough C, Taitsman LA, Mitchell SH, So GE, Arbabi S, Phelan H, Pham T: Trauma providers' perceptions of frailty assessment: A mixed-methods analysis of knowledge, attitudes, and beliefs. South Med J 2019; 112:159–63
14. Robinson TN, Wu DS, Pointer LF, Dunn CL, Moss M: Preoperative cognitive dysfunction is related to adverse postoperative outcomes in the elderly. J Am Coll Surg 2012; 215:12–7; discussion 17–8
15. Dworkin A, Lee DS, An AR, Goodlin SJ: A simple tool to predict development of delirium after elective surgery. J Am Geriatr Soc 2016; 64:e149–53
16. Morley JE, Malmstrom TK, Miller DK: A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012; 16:601–8
17. Valdatta L, Perletti G, Maggiulli F, Tamborini F, Pellegatta I, Cherubino M: FRAIL scale as a predictor of complications and mortality in older patients undergoing reconstructive surgery for non-melanoma skin cancer. Oncol Lett 2019; 17:263–9
18. Deiner S, Westlake B, Dutton RP: Patterns of surgical care and complications in elderly adults. J Am Geriatr Soc 2014; 62:829–35
19. Susano MJ, Scheetz SD, Grasfield RH, Cheung D, Xu X, Kang JD, Smith TR, Lu Y, Groff MW, Chi JH,

Crosby G, Culley DJ: Retrospective analysis of perioperative variables associated with postoperative delirium and other adverse outcomes in older patients after spine surgery. J Neurosurg Anesthesiol 2019; 31:385–91
20. Fong TG, Hshieh TT, Wong B, Tommet D, Jones RN, Schmitt EM, Puelle MR, Saczynski JS, Marcantonio ER, Inouye SK: Neuropsychological profiles of an elderly cohort undergoing elective surgery and the relationship between cognitive performance and delirium. J Am Geriatr Soc 2015; 63:977–82
21. Armaghani SJ, Lee DS, Bible JE, Archer KR, Shau DN, Kay H, Zhang C, McGirt MJ, Devin CJ: Preoperative opioid use and its association with perioperative opioid demand and postoperative opioid independence in patients undergoing spine surgery. Spine (Phila Pa 1976) 2014; 39:E1524–30
22. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI: Clarifying confusion: The confusion assessment method. A new method for detection of delirium. Ann Intern Med 1990; 113:941–8
23. Kuhn E, Du X, McGrath K, Coveney S, O'Regan N, Richardson S, Teodorczuk A, Allan L, Wilson D, Inouye SK, MacLullich AM, Meagher D, Brayne C, Timmons S, Davis D: Validation of a consensus method for identifying delirium from hospital records. PLoS One 2014; 9:e111823
24. Aprahamian I, Cezar NOC, Izbicki R, Lin SM, Paulo DLV, Fattori A, Biella MM, Jacob Filho W, Yassuda MS: Screening for frailty with the FRAIL scale: A comparison with the phenotype criteria. J Am Med Dir Assoc 2017; 18:592–6
25. Fitz-Henry J: The ASA classification and peri-operative risk. Ann R Coll Surg Engl 2011; 93:185–7
26. Mayhew D, Mendonca V, Murthy BVS: A review of ASA physical status – historical perspectives and modern developments. Anaesthesia 2019; 74:373–9

ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

Jolly Holly Greetings from Pittsburgh: Advertising Analgesia Formulated by King William III's Physician

Adorned in holly, an infant dressed as a jester sends late nineteenth century holiday greetings from R. Monroe Kennedy, whose Pittsburgh-based firm manufactured the popular cure-all "Dr. Radcliffe's Seven Seals" (*bottom*). An alcoholic elixir of ether, chloroform, capsicum, and peppermint oil, Seven Seals promised to ease woes and bring holiday cheer. The face of the baby jester's wand grins in the background with knowing delight. This Kennedy remedy was an American version of one popularized by Dr. John Radcliffe (1650 to 1714), British Parliamentarian and royal physician to William and Mary. Radcliffe's bustling London practice had treated patients as notable as Isaac Newton, Alexander Pope, and Jonathan Swift. An Oxford graduate, Radcliffe gave his alma mater a gift that was far from seasonal; his lavish trust has funded Oxonian ventures for centuries. As homage to his generosity, several university buildings, including the Radcliffe Science Library and the John Radcliffe Hospital, still bear his name. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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