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Preoperative Frailty in Older Surgical Patients is Associated with Early Postoperative Delirium

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Abstract

Among older noncardiac surgical patients, we investigated whether preoperative frailty provides information about the development of postoperative delirium that is in addition to traditional geriatric risk factors. One-third of patients had a frailty score ≥ 3 , which is considered 'frail' in others' research. Twenty-five percent of patients developed postoperative delirium, which was measured using the Confusion Assessment Method. Multivariable logistic regression showed that age, activities of daily living dependence, independent activities of daily living dependence and cognitive functioning did not contribute significantly to the prediction of postoperative delirium. Only preoperative symptoms of depression (OR=1.42; 95% CI=1.06–1.91; $p=0.018$) and the frailty score (OR=1.84; 95% CI=1.07–3.1; $p=0.028$) were independently associated with the development of postoperative delirium.

Introduction

Postoperative delirium is common among older surgical patients with rates ranging from 10% to 60% of patients (1). Successful targeting of interventions to reduce rates of postoperative delirium depends on evidence about which patients are at risk for developing delirium. Frailty is a common geriatric syndrome whose risks and consequences overlap with delirium. For example, advanced age and disease status are common risks for the development of both frailty and delirium. Functional dependence is an example of a common outcome for frailty and delirium. Due to common risks and consequences of these two geriatric syndromes, it is unclear whether preoperative assessments of frailty provide

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DISCLOSURES

Name: Jacqueline M Leung, M.D., M.P.H.

Contribution: Study design, data analysis, conduct of study, and manuscript preparation

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prognostic information about the development of postoperative delirium that is in addition to currently recognized risks for delirium such as advanced age, presurgical disease status, functional dependence and cognitive impairment. Accordingly, our study aimed to determine whether preoperative frailty is an independent predictor for postoperative delirium after considering common risks and consequences of these two geriatric syndromes. We hypothesized that preoperative frailty provides prognostic information that is in addition to commonly recognized risks and consequences for both.

Methods

This pilot study was approved by the institutional committee on human research, and informed oral and written consent were obtained preoperatively from each study patient. Patients included were a subset of a larger study that began in 2001, investigating the pathophysiology of postoperative delirium. Inclusion criteria included English-speaking patients ≥ 65 years of age undergoing noncardiac surgery requiring anesthesia and who were anticipated to stay in the hospital for longer than 48 hours. We began measuring preoperative frailty in 2007 in consecutive patients.

Preoperatively, patients were evaluated for depressive symptoms, pain, functional and cognitive status. The Telephone Interview for Cognitive Status (TICS) (2), modified from the Mini Mental State Examination, was used to measure baseline cognitive status. The Geriatric Depression Scale (GDS) was used preoperatively to measure symptoms of depression (3).

Frailty status also was measured preoperatively using 5 criteria: unintentional weight loss ≥ 10 pounds in the past year, self-reported exhaustion, weak grip strength, slow walking time, and low physical activity (4). Grip strength was measured using the Jamar hydraulic hand dynamometer (Model 5030J1, Sammons Preston Rolyan, Inc., Bolingbrook IL). The average of three measurements was used to determine grip strength. Weak grip strength was identified when the strength was below that adjusted for gender and body mass index. Walking time was measured by asking the subjects to walk at a comfortable pace down a 15-foot hallway. Slow walking pace was identified when the walking time was longer than a predefined time adjusted for height and gender. Each criterion present was given 1 point to create a composite frailty score between 0 and 5 (4).

Independence in functional status was measured by the Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL).

A trained research assistant conducted structured interviews preoperatively and on the first two postoperative days to determine the presence of delirium, defined using the Confusion Assessment Method (5). All cases were validated by a second investigator. In a separate analysis to determine the duration of postoperative delirium, in addition to the Confusion Assessment Method diagnosis of delirium, medical records were also reviewed. We chose two days of measurement in this study because nearly one in three patients in this noncardiac surgical cohort were discharged two days after surgery, hence we chose delirium assessment in the first two days as our primary outcome measurement to minimize missing data. The secondary outcome was delirium assessment by any method.

Preoperative disease status was measured by the ASA classification. Surgical type, duration of surgery, and intraoperative blood loss were measured. Preoperative pain level was measured by a verbal version of the Visual Analog Scale.

Analyses were first directed at determining risks for delirium that are associated with frailty status. This was accomplished by computing bivariate associations between risks for

delirium and frailty score using chi-square tests or Fisher test for nominal categorical variables and Mantel-Haenszel chi-square tests for trend were used for ordinal variables, and Pearson correlation coefficients were computed for associations with continuously valued variables. A second set of bivariate analyses was conducted to determine whether risks for delirium were associated with delirium status in this sample. A multivariable logistic regression analysis using forward stepwise regression based on the likelihood ratio was computed in two steps. The variables entered in step 1 were those variables associated with frailty or delirium status with a p-value of 0.20 or less. These variables were age, ADL dependence, IADL dependence, and the TICS and GDS scores. The only variable that was retained by the forward stepwise likelihood ratio criteria after step 1 was the GDS score. In the second step of the equation, the frailty score was entered. The fit of the final model was assessed using the Hosmer-Lemeshow test. Analyses were performed using SPSS V18.0. A P values < 0.05 (two-tailed) was considered statistically significant.

Results

The preoperative characteristics of patients are shown in Table 1. Higher frailty score was associated with higher risk for delirium ($p=0.004$). Figure 1 shows that the incidence of delirium increased steadily from 0% for those with frailty scores of 0 to 57% for those with frailty scores of 4 or more. Patients' risk factors that were associated with higher frailty scores are shown in Table 2. Sixteen of 63 patients (25%) developed delirium postoperatively. Table 1 shows that of the nine risks assessed, only ADL dependence ($p=0.02$), IADL dependence ($p=0.05$), the TICS score ($p=0.004$) and the GDS score ($p=0.002$) were significantly associated with the development of delirium. The final solution revealed that preoperative GDS score ($b=0.35$; $OR=1.24$; 95% CI 1.06–1.91) and the frailty score ($b=0.61$; $OR=1.84$; 95% $CI=1.07$ –3.15) were significantly associated with postoperative delirium (Table 3).

Discussion

Our study is one of the first to show that preoperative frailty is prevalent in older patients awaiting major noncardiac surgery, and that it is independently associated with postoperative delirium occurrence.

Our finding that one-third of the patients had a frailty score of 3 or more is similar to that reported by a previous study showing that 27% of older patients admitted to a Veterans Hospital were considered frail (6). Patients awaiting major surgery may have co-existing surgical conditions such as osteoarthritis that may produce symptoms similar to those observed in the frail elders. However, our finding that preoperative frailty independently predicts postoperative delirium suggests that the frailty score reveals risk that is not captured by traditional risk factors for delirium such as advanced age, functional dependence, cognitive frailty and depression.

A previous study in older surgical patients found that frailty, as defined by the Edmonton Frail Scale, was associated with postoperative complications, but the measurement of postoperative delirium in this study was only through chart review and likely underestimated its occurrence (7). In the Rush Memory and Aging Project, a longitudinal study of aging (8) increasing frailty was found to be associated with incident Alzheimer's disease and rate of cognitive decline. Other studies reported that signs of frailty such as grip strength, gait disturbance, and body composition, have been related to mild cognitive impairment (9–12).

Taken together, factors associated with the development of frailty and cognitive changes may share a common etiology. For example, a history of cerebrovascular disease has been

related to both postoperative delirium (13) and frailty (14). Inflammatory markers such as C-reactive protein or proinflammatory interleukins have been implicated in frailty (15) and cognitive impairment (16), but their relationship to postoperative delirium remains to be defined, and should be considered in future investigations (17,18). Alternatively, frailty may actually operate as a marker of delirium, or *vice versa*. Although the criteria proposed by Fried *et al.* remains the most widely used construct (4), there is controversy as to whether other common age-related conditions such as cognitive impairment should be included in the definition of the syndrome (19). Another important consideration is whether frailty is dynamic and potentially reversible. Considering that half of the patients in our study were pre-frail, whether interventions would reduce the development of frailty is clinically relevant.

We focused on measuring delirium in the early postoperative period; as a result, incidents of later onset delirium may have been missed. Second, our study sample size is relatively small and the results should be confirmed by a larger study.

In summary, including frailty assessment in the preoperative setting may improve preoperative risk assessment of older patients, particularly in identifying the patients at risk for postoperative delirium. Furthermore, expanding frailty research to the surgical setting may also advance our understanding of the pathophysiology of postoperative delirium.

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Figure 1. Incidence of Postoperative Delirium Across Frailty Scores

Shown on the Y axis is the incidence of postoperative delirium, and on the X axis is the frailty score. The n and % below each bar represents the number and percentage of patients within each frailty score category with delirium.

Table 1

Preoperative Characteristics of Patients with and without Postoperative Delirium

Demographic data	Delirium (n=16)	No delirium (n=47)	P value
Age (in years)	74.2 ± 6.0	71.9 ± 6.3	0.21
Gender Female, n (%)	8 (50)	26 (55)	0.71
ADL Dependence, n (%)	7 (44)	7 (9)	0.02
IADL Dependence, n (%)	12 (75)	22 (47)	0.05
TICS score	32.6 ± 4.9	35.4 ± 2.4	0.0035
GDS	4.3 ± 2.3	2.3 ± 2.0	0.0016
ASA Classification Class ≥3, n (%)	8 (50)	24 (51)	0.94
Surgical type General, n (%) Arthroplasty, n (%) Spine, n (%) Thoracic, n (%)	0 4 (25) 11 (69) 1 (6)	2 (4) 23 (49) 17 (36) 5 (11)	0.18
Change in pain score from pre- to postoperative periods	1.93 ± 2.84	1.89 ± 2.91	0.96

ADL= activities of daily living

ASA = American Society of Anesthesiologists

GDS = geriatric depression scale

IADL = independent activities of daily living

TICS = telephone interview of cognitive status

The integers shown in each cell refer to the number of patients, and the rest of the data are shown as mean ± SEM

Table 2

Relationship Between Patient Factors and Preoperative Frailty Scores

Variable	
Age	$r=0.39$, $p=0.002$
ADL dependence	$\chi^2=18.53$, $p=0.001$
IADL dependence	$\chi^2=13.14$, $p=0.011$
TICS score	$r=-0.32$, $p=0.01$
GDS score	$r=0.29$, $p=0.02$
ASA classification	$\chi^2=5.49$, $p=0.24$
Surgical type	$\chi^2=19.63$, $p=0.22$
Change in pain score from pre- to postoperative periods	$r=0.004$, $p=0.97$

ADL= activities of daily living

ASA = American Society of Anesthesiologists

GDS = geriatric depression scale

IADL = independent activities of daily living

TICS = telephone interview of cognitive status

Table 3

Multivariate Logistic Regression of the Predictors of Postoperative Delirium

Variable	B	Odds Ratio	95% CI	P-value
Preoperative depression score	0.35*	1.42	1.06–1.91	0.018
Preoperative frailty score	0.61	1.84	1.07–3.15	0.028

B = regression coefficient

The Hosmer–Lemeshow test ($P = 0.74$) indicates that the overall model fit is good.