Predictors and Sequelae of Postoperative Delirium in a Geriatric Patient Population With Hip Fracture

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ABSTRACT

Introduction: Postoperative delirium is common for patients with hip fracture. Predictors of postoperative delirium and its association with preexisting dementia and adverse postoperative outcomes in a geriatric hip fracture population were assessed.

Methods: Patients with hip fracture aged 60 years and older were identified in the 2016 and 2017 National Surgical Quality Improvement Program Procedure Targeted Databases. Independent risk factors of postoperative delirium were identified. Associations with mortality, readmission, and revision surgery were evaluated using moderation and mediation analysis.

Results: Of 18,754 patients with hip fracture, 30.2% had preoperative dementia, 18.8% had postoperative delirium, and 8.3% had both preoperative dementia and postoperative delirium. Independent predictors of postoperative delirium were as follows: older age, male sex, higher American Society of Anesthesiologists score, dependent functional status, nongeneral anesthesia, preoperative diabetes, bleeding disorder, and preoperative dementia. Preoperative dementia and postoperative delirium each had an independent correlation with 30-day mortality (odds ratios = 2.06 and 1.92, respectively, with \( P < 0.001 \) for both). However, when both were present, those with preoperative dementia and postoperative delirium had an even higher odds of mortality based on moderation analysis (odds ratio = 2.25, \( P < 0.001 \)). Readmissions and reoperations were significantly correlated with postoperative delirium, but not with preoperative dementia. Preoperative dementia and postoperative delirium each had an independent correlation with 30-day mortality (odds ratios = 2.06 and 1.92, respectively, with \( P < 0.001 \) for both). However, when both were present, those with preoperative dementia and postoperative delirium had an even higher odds of mortality based on moderation analysis (odds ratio = 2.25, \( P < 0.001 \)).

Discussion: Postoperative delirium is a potentially preventable postoperative adverse outcome that was seen in 18.8% of 18,754
In the United States alone, approximately 300,000 geriatric patients experience hip fractures annually.\textsuperscript{1,2} Unfortunately, high morbidity and high mortality exist in this group.\textsuperscript{3,4} This warrants close attention, especially because it is estimated that the yearly incidence of hip fractures occurring yearly could climb to 840,000 by 2040, as the population ages.\textsuperscript{1} Postoperative delirium in the elderly has been associated with increased morbidity, mortality, and high rates of other adverse outcomes after hip fracture surgery.\textsuperscript{5-7}

A prospective study by Bellelli et al\textsuperscript{5} found that, for geriatric patients with hip fracture, each day of postoperative delirium increased the risk of mortality at 6 months by 17\%. Similarly, another prospective study by Holmes and House\textsuperscript{6} found that geriatric patients with hip fracture with a diagnosis of delirium within 5 days of surgery had prolonged hospital length of stay and increased the risk of 6-month mortality. In addition, a retrospective analysis of a Canadian database by Zywiel et al\textsuperscript{8} found that the development of delirium after hip fracture surgery led to markedly increased length of hospital stay and markedly increased episode-of-care costs.

The incidence of postoperative delirium in the hip fracture population has been reported with broadly variable incidence, ranging from 4.0 to 53.3\% of patients.\textsuperscript{9,10} Predictors of delirium for orthopaedic surgery include the following: preoperative functional status,\textsuperscript{11} low body mass index (BMI),\textsuperscript{12} fracture occurring indoors,\textsuperscript{12,13} advanced age,\textsuperscript{8,12,14} diabetes,\textsuperscript{14} substance use,\textsuperscript{14} polypharmacy,\textsuperscript{14} low postoperative hematocrit,\textsuperscript{11,14} and history of dementia.\textsuperscript{11}

Preoperative dementia is a factor that bears specific consideration for its relationship with postoperative delirium. As a related cognitive dysfunction, it has been shown to be related to the postoperative delirium in many clinical settings.\textsuperscript{12,14,15} Fick et al\textsuperscript{15} conducted a meta-analysis to study the prevalence of and outcomes associated with delirium superimposed on dementia in populations aged 65 years and older. Two of the 14 studies included in their analysis focused on geriatric hip fracture populations. The first study, a prospective cohort study by Edlund et al\textsuperscript{10} including 101 patients, found that most patients with postoperative delirium experienced drops in blood pressure or other postoperative complications such as infections. The second study, a randomized control trial by Marcantonio et al\textsuperscript{16} including 126 patients, found that proactive geriatric consultation beginning in the preoperative period reduced the incidence of postoperative delirium.

Studies evaluating risk factors for postoperative delirium have generally been limited in size to patient populations ranging from 10 to 562 patients.\textsuperscript{8,9,11,12,14,15,17} This study was conducted to study predictors of postoperative delirium and its sequelae in a patient population larger than previously assessed for such analysis. By studying a larger population, the potential moderating and mediating effects of delirium on the relationship between preoperative dementia and perioperative outcomes of interest could be assessed.

**Methods**

**Database/Study Population**

This study used the 2016 and 2017 National Surgical Quality Improvement Program (NSQIP) Procedure Targeted Hip Fracture Databases merged with the corresponding NSQIP Participant Use Data Files. Our Institutional Review Board has granted exemption for all studies that use NSQIP.

NSQIP variables include patient demographics, comorbidities, and 30-day postoperative events including morbidity and mortality for patients who have undergone surgical procedures.\textsuperscript{18} The targeted hip fracture database contains 17 additional variables and data on 9,390 patients from 117 different sites.\textsuperscript{19}

All patients in the hip fracture database who were 60 years of age and older were included in this study. This age limitation was implemented to narrow the scope to geriatric patients who had sustained a hip fracture. Patients with preoperative dementia and patients with postoperative delirium were identified according to database coding. Those patients diagnosed with both preoperative and postoperative delirium were not included in regression analyses to allow for analysis of only newly developed delirium after surgery and its relation to preexisting dementia.

**Demographic and Outcome Variables**

The NSQIP database includes patient demographic information: age, sex, height, weight, American Society of Anesthesiologists (ASA) score, and functional status. BMI was calculated from height and weight for each
patient. Additional data abstracted included diabetes, hypertension, smoking status, chronic obstructive pulmonary disease, congestive heart failure, use of corticosteroids, bleeding disorder, acute renal failure, and preoperative dementia.

The database also provides surgical information. This includes operations done based on common procedural terminology code, anesthetic type used, length of operation, and postoperative length of stay in the hospital. The NSQIP Procedure Targeted Hip Fracture Databases provides information on diagnoses of preoperative and postoperative dementia and delirium. The targeted databases were merged with the general NSQIP databases to form a data set with comprehensive information for patients with hip fracture.

The primary outcome of interest was mortality within 30 days of the principal surgery. Secondary outcomes of interest included return to the hospital (readmission) and return to the operating room (revision surgery) within 30 days of principal procedure.

Statistical Analysis
Statistical analysis was done using Stata. All figures presented were created with Microsoft Excel and Lucidchart.

Univariate and Multivariate Analyses
A series of chi square tests was done to characterize the study population by postoperative delirium status and to determine demographic, comorbidity, and procedural characteristics for which those with and without postoperative delirium differed. Significance was adjusted using Bonferroni correction to account for multiple comparisons.

Multivariate logistic regression was then done to determine independent risk factors for postoperative delirium. The model controlled for demographic factors including age, sex, ASA, BMI, and functional status. It also controlled for patient morbidities and surgical characteristics including preoperative dementia, smoking status, corticosteroid use, bleeding disorder, chronic obstructive pulmonary disease, renal failure, diabetes, hypertension, congestive heart failure, dyspnea, operation time, anesthetic type, and type of procedure performed. Significance was again adjusted using Bonferroni correction to account for multiple comparisons.

Moderation Analysis
Moderation analysis is also known as an analysis of the interaction between variables. It is usually done to determine when or in what context the effect of an independent variable (IV) on a dependent variable (DV) occurs or changes. Considering Figure 1, preoperative dementia is the IV, the adverse event, mortality, for example, is the DV, and postoperative delirium is the moderating variable (M). M is the factor that changes the magnitude of the effect of preoperative dementia on the adverse event. In this case, preoperative dementia directly affects the occurrence of the adverse event, but the interaction of preoperative dementia and postoperative delirium has the ability to modify the size of the effect.

Three logistic regression models were created to determine the moderating effects of postoperative delirium on the relationship between preoperative dementia and (1) mortality, (2) readmission, and (3) revision surgery.

Venn diagram showing the incidences of dementia and postoperative delirium
surgery. Each model controlled for all the aforementioned variables in the independent risk factor model and also contained an interaction term relating preoperative dementia and postoperative delirium. Significance was determined using a \( P \) value of 0.05.

### Mediation Analysis

Mediation analysis is commonly done to study how an outcome occurs by measuring the total effect of the IV on the DV, the direct effect of the IV on the DV, and the indirect effect of the IV on the DV through a mediating variable (M) that lies on the causal pathway between the IV and the DV.\(^{20,21}\) Considering Figure 2, preoperative dementia is the IV, the adverse event is the DV, and postoperative delirium is M. The variable \( c' \) represents the direct effect of preoperative dementia on the adverse event. The indirect effect of preoperative dementia on the adverse event occurs through postoperative delirium and is represented by \( ab \). The variable \( c \) represents the total effect of preoperative dementia on the adverse event and is equal to \( ab + c' \). The goal of the analysis is to determine the proportion of the total effect that occurs because of the indirect pathway through postoperative delirium.

### Table 1. Demographics by Delirium Status

| Characteristic                  | No Post-op Delirium (N = 15,235) | Post-op Delirium (N = 3,519) | \( P \) Value |
|--------------------------------|----------------------------------|-----------------------------|---------------|
| Age                            |                                  |                             | \(< 0.001\)   |
| 60-69                          | 2,010 (13.19)                    | 208 (5.91)                  |               |
| 70-79                          | 3,548 (23.29)                    | 602 (17.11)                 |               |
| 80+                            | 9,677 (63.52)                    | 2,709 (76.98)               |               |
| Sex                            |                                  |                             | 0.004         |
| Male                           | 4,451 (29.22)                    | 1,115 (31.69)               |               |
| Female                         | 10,784 (70.78)                   | 2,404 (68.31)               |               |
| BMI \( \leq 24 \text{ kg/m}^2 \)| 6,775 (44.47)                    | 1,621 (46.06)               | 0.008         |
| 25-29 \text{ kg/m}^2           | 4,019 (26.38)                    | 863 (24.52)                 |               |
| 30-34 \text{ kg/m}^2           | 1,582 (10.38)                    | 326 (9.26)                  |               |
| \( \geq 35 \text{ kg/m}^2 \)    | 2,859 (18.77)                    | 709 (20.15)                 |               |
| ASA \( \leq 2 \)               | 2,510 (16.48)                    | 328 (9.32)                  | \(< 0.001\)   |
| \( \geq 3 \)                   | 12,725 (83.52)                   | 3,191 (90.68)               |               |
| Functional status              |                                  |                             | \(< 0.001\)   |
| Independent                    | 12,116 (79.53)                   | 2,448 (69.57)               |               |
| Partially/completely dependent  | 3,119 (20.47)                    | 1,071 (30.43)               |               |
| Surgical characteristics       |                                  |                             | 0.131         |
| CPT                            |                                  |                             | \(< 0.001\)   |
| Hemiarthroplasty               | 5,518 (36.22)                    | 1,327 (37.71)               |               |
| Plate/screw fixation           | 1,996 (13.10)                    | 426 (12.11)                 |               |
| Cephalomedullary nail fixation  | 7,721 (50.68)                    | 1,766 (50.18)               |               |
| Anesthesia                     |                                  |                             | \(< 0.001\)   |
| General                        | 10,517 (69.69)                   | 2,327 (66.13)               |               |
| Other                          | 4,618 (30.31)                    | 1,192 (33.87)               |               |
| Operation time                 | 63.94 ± 40.82                    | 62.04 ± 35.07               | \(< 0.001\)   |
| Postoperative length of stay   | 5.46 ± 5.60                      | 7.50 ± 7.70                 |               |

ASA = American Society of Anesthesiologists, BMI = body mass index, CPT = common procedural terminology

Bolded values represent significance at \( P < 0.006 \) according to Bonferroni correction.
Following this mediation model, analysis was done using a generalized version of the Erickson method. The Hicks mediation package was used for confirmation. The mediating effect of postoperative delirium on the relationship between preoperative dementia and (1) mortality, (2) readmission, and (3) revision surgery was determined.

## Results

### Study Population

In total, 18,754 patients with hip fracture 60 years of age and older were identified. Of the total sample, 30.2% had preoperative dementia, 18.8% had a new diagnosis of delirium postoperatively, and 8.3% had both preoperative dementia and postoperative delirium (Figure 3). Of the 5659 patients who had preoperative dementia and 27.3% developed postoperative delirium.

### Postoperative Delirium Associations

Based on univariate analysis, the cohorts with and without postoperative delirium differed significantly based on several comorbidities: hypertension ($P < 0.001$), CHF ($P = 0.001$), bleeding disorder ($P < 0.001$), and preoperative dementia ($P < 0.001$) (Table 2).

Based on multivariate regression analysis, age, sex, ASA, functional status, anesthesia type, diabetic status, bleeding disorder, and preoperative dementia were independent risk factors for postoperative delirium. Odds ratios and confidence intervals are presented in Table 3.

The mortality rate was 8.7% among patients who developed delirium postoperatively and only 4.9% among patients who did not develop postoperative delirium ($P < 0.001$). Similarly, increases in the rates of the secondary adverse outcomes, readmission and revision surgery, were found to be significantly increased among patients who developed delirium in the postoperative period. The readmission rate was 12.3% among the cohort of patients who developed delirium after surgery and 7.5% among those who did not ($P < 0.001$). The revision surgery rate was 3.6% among those who developed delirium compared with 2.0% among those who did not develop delirium postoperatively ($P < 0.001$) (Table 4).

### Moderation Analysis

Moderation analysis was done to assess the interaction between preoperative dementia and postoperative delirium on mortality, readmission, and revision surgery.
Table 3. Independent Risk Factors for Post-op Delirium

| Characteristic/Comorbidity   | OR    | 99.4% CI        | Multivariate P Value |
|-----------------------------|-------|-----------------|----------------------|
| Age                         |       |                 | <0.001               |
| 70-79                       | 1.50  | 1.18-1.91       |                      |
| ≥80                         | 2.22  | 1.77-2.79       |                      |
| Sex                         |       |                 | <0.001               |
| Female                      | 0.85  | 0.76-0.96       |                      |
| ASA                         |       |                 | <0.001               |
| ≥3                          | 1.40  | 1.17-1.67       |                      |
| Functional status           |       |                 | <0.001               |
| Partially/completely dependent | 1.18 | 1.04-1.35       |                      |
| Anesthesia                  |       |                 | <0.001               |
| Other                       | 1.18  | 1.05-1.32       |                      |
| Diabetes                    |       |                 | <0.001               |
| Insulin dependent           | 1.30  | 1.06-1.59       |                      |
| Bleeding disorder           | 1.27  | 1.11-1.45       | <0.001               |
| Preoperative dementia       | 1.75  | 1.55-1.98       | <0.001               |

ASA = American Society of Anesthesiologists, OR = odds ratio
Bolded values represent significance at P < 0.006 according to Bonferroni correction.

Patients with only preexisting dementia were 2.06 times more likely than patients without dementia to die after hip fracture surgery (OR = 2.06, 95% CI, 1.57 to 2.35, P < 0.001) (Table 5). Those without preexisting dementia who developed postoperative delirium were 1.92 times more likely to die after surgery compared with those without postoperative delirium (OR = 1.92, 95% CI, 1.74 to 2.43, P < 0.001) (Table 5). Patients with postoperative delirium superimposed on preexisting dementia were 2.23 times more likely to die after hip fracture repair compared with those without dementia or delirium (OR = 2.25, 95% CI, 1.82 to 2.79, P < 0.001) (Table 5).

Readmission and revision surgery followed a similar pattern. Patients with only preexisting dementia were not significantly more likely to be readmitted or to have revision surgery than those without preexisting dementia (Table 5). However, those without preexisting dementia who developed delirium postoperatively were significantly more likely to be readmitted or to have revision surgery compared with those who did not develop postoperative delirium (Table 5). Patients with postoperative delirium superimposed on preoperative dementia were also significantly more likely to be readmitted or to have revision surgery than those without dementia or delirium (Table 5).

Mediation Analysis

Mediation analysis was done to assess the indirect effect of postoperative delirium on the relationship between preoperative dementia and mortality, readmission, and revision surgery (Table 6). The analysis determined that postoperative delirium was a significant mediator of the relationship between preoperative dementia and (1) mortality and (2) readmission.

The indirect effect of preoperative dementia on mortality through postoperative delirium accounted for 7% of the total effect of preoperative dementia on mortality (medeff = 7%, P < 0.001) (Table 6). In addition, the indirect effect of preoperative dementia on readmission through postoperative delirium accounted for 35% of the total effect of preoperative dementia on readmission (medeff: 35%, P < 0.001) (Table 6). Postoperative delirium was not a significant mediator of the relationship between preoperative dementia and revision surgery (P > 0.05) (Table 6).

Discussion

As the population ages, the incidence of hip fractures is expected to increase.24,25 Delirium is common after hip fracture surgery9,10 and has been associated with adverse outcomes such as death,16,26 functional decline,27 cognitive decline,27 longer hospitalization,28 and higher healthcare costs.29,30

This study recapitulates both the incidence of and the deleterious effects of delirium in the postoperative patient with hip fracture. Of the 18,235 patients included in the
study, 18.8% developed delirium in the postoperative period, which is congruent with Edlund et al<sup>10</sup> who determined the incidence of delirium in the postoperative patient with hip fracture to be 18.8%.

This study also determined that mortality was increased among patients who developed delirium postoperatively (8.7% vs 4.9%, <i>P</i> < 0.001), which is concordant with established literature<sup>**16,26</sup>. In addition, the study’s secondary adverse outcomes, readmission and revision surgery, were found to be increased among patients who developed delirium postoperatively (12.5% vs 7.5% and 3.6% vs 2.0%, respectively and both <i>P</i> < 0.001). Although these results are consistent with the literature,<sup>31</sup> to our knowledge, this is the first study to evaluate moderation and mediation effects of postoperative delirium on the relationship between preexisting dementia and the occurrence of adverse postoperative events.

Preoperative dementia was present in 30.2% of the study population of which 27.3% developed postoperative delirium. Moderation analysis was done to determine whether the development of postoperative delirium affected the likelihood of mortality, readmission, and revision surgery among patients with preoperative dementia. Mediation analysis was used to study how the development of postoperative delirium affected postoperative outcomes. It determined the proportion of the total effect of preoperative dementia on each outcome of interest that could be accounted for by the development of postoperative delirium. The moderation analysis first showed that postoperative delirium influenced the likelihood of mortality, readmission, and revision surgery as follows:

### Table 5. Moderating Effects of Post-op Delirium

| Adverse Event                        | Odds Ratio | 95% CI       | <i>P</i> Value |
|--------------------------------------|------------|--------------|---------------|
| Mortality                            |            |              |               |
| No pre-op dementia                   | Reference  | —            | —             |
| Pre-op dementia                      | 2.06       | 1.57-2.35    | <0.001        |
| No post-op delirium                 | Reference  | —            | —             |
| Post-op delirium                    | 1.92       | 1.74-2.43    | <0.001        |
| No pre-op dementia or post-op delirium | Reference  | —            | —             |
| Pre-op dementia + post-op delirium   | 2.25       | 1.82-2.79    | <0.001        |
| Readmission                          |            |              |               |
| No pre-op dementia                   | Reference  | —            | —             |
| Pre-op dementia                      | 1.10       | 0.95-1.28    | 0.193         |
| No post-op delirium                 | Reference  | —            | —             |
| Post-op delirium                    | 1.57       | 1.34-1.84    | <0.001        |
| No pre-op dementia or post-op delirium | Reference  | —            | —             |
| Pre-op dementia + post-op delirium   | 1.75       | 1.47-2.10    | <0.001        |
| Reoperation                          |            |              |               |
| No pre-op dementia                   | Reference  | —            | —             |
| Pre-op dementia                      | 0.88       | 0.66-1.18    | 0.396         |
| No post-op delirium                 | Reference  | —            | —             |
| Post-op delirium                    | 1.78       | 1.36-2.34    | <0.001        |
| No pre-op dementia or post-op delirium | Reference  | —            | —             |
| Pre-op dementia + post-op delirium   | 1.74       | 1.25-2.41    | 0.001         |

Bolded values represent significance at <i>P</i> < 0.05.

### Table 6. Mediating Effects of Post-op Delirium

| Adverse Event                        | Mediation Effect | <i>P</i> Value |
|--------------------------------------|------------------|---------------|
| Mortality                            |                  |               |
| Pre-op dementia + post-op delirium   | 7%               | <0.001        |
| Readmission                          |                  |               |
| Pre-op dementia + post-op delirium   | 35%              | 0.031         |

Significance determined at <i>P</i> < 0.05.
Dementia and Delirium in Patients With Hip Fracture

delirium significantly amplified the effects of preoperative dementia on mortality, readmission, and revision surgery (Figure 1). The mediation analysis demonstrated that a significant proportion of the total effect of preexisting dementia on mortality and readmission occurred through postoperative delirium (Figure 2).

Given the negative ramifications of untreated delirium, particularly among patients with hip fracture with preexisting dementia, identifying patients at risk for the development of delirium is paramount. This study’s multivariate regression analysis suggests that older age, male sex, higher ASA score, partially/completely dependent functional status, nongeneral anesthesia, insulin-dependent diabetic status, preexisting bleeding disorders, and preoperative dementia are independent risk factors for the development of postoperative delirium in patients with hip fracture (Table 3). Our determination of age, ASA score, functional status, bleeding disorder, and preoperative dementia are congruent with existing literature. Interestingly, our study found that although most of the study sample was female (70.3%) and most of those who had preexisting dementia were female (73.0%), male patients were markedly more likely to develop delirium after hip fracture repair. Therefore, based on this study’s findings and preestablished literature, these independent risk factors may be useful in the identification of patients who are at risk for developing delirium postoperatively and who are therefore at increased risk of experiencing adverse postoperative events.

This study does have limitations. The recognition of delirium and dementia can be challenging, but the NSQIP database does adhere to strict definitions of these conditions. Furthermore, other adverse outcomes and function measures aside from mortality, readmission, and revision surgery could not be studied in the current analyses because of parameters of the database.

In conclusion, hip fracture repair can be associated with preexisting dementia and postoperative delirium. The results of this study demonstrate that postoperative delirium is a moderating variable and markedly increases the risk of postoperative mortality, readmission, and revision surgery, particularly among patients with baseline dementia. In addition, mediation analysis demonstrates that delirium indirectly accounts for a notable proportion of the relationship between preoperative dementia, mortality, and readmission. Therefore, special attention should be given to patients who present with cognitive impairment and other risk factors for postoperative delirium at the time of surgery.

References
1. Shah SN, Wainess RM, Karunakar MA: Hemiarthroplasty for femoral neck fracture in the elderly surgeon and hospital volume-related outcomes. J Arthroplasty 2005;20:503-508.
2. Hip Fractures Among Older Adults. Atlanta, GA: Centers for Disease Control and Prevention, 2016.
3. Kiestil T, Röder C, Strotter C, et al: Impact of timing of surgery in elderly hip fracture patients: A systematic review and meta-analysis. Sci Rep 2018;8:13933.
4. Menzies IB, Mendelson DA, Kates SL, Friedman SM: The impact of comorbidity on perioperative outcomes of hip fractures in a geriatric fracture model. Geriatr Orthop Surg Rehabil 2012;3:129-134.
5. Belleri G, Mazzola P, Morandi A, et al: Duration of postoperative delirium is an independent predictor of 6-month mortality in older adults after hip fracture. J Am Geriatr Soc 2014;62:1335-1340.
6. Holmes J, House A: Psychiatric illness predicts poor outcome after surgery for hip fracture: A prospective cohort study. Psychol Med 2000;30:921-929.
7. Olofsson B, Lundstrom M, Bossen B, Nyberg L, Gustafsson Y: Delirium is associated with poor rehabilitation outcome in elderly patients treated for femoral neck fractures. Scand J Caring Sci 2005;19:119-127.
8. Zywiel MG, Hurley RT, Perruccio AV, Hancock-Howard RL, Coyle PC, Rampersaud YR: Health economic implications of perioperative delirium in older patients after surgery for a fragility hip fracture. J Bone Joint Surg Am 2015;97:829-836.
9. Bruce AJ, Ritchie CW, Blizard R, Lai R, Raven P: The incidence of delirium associated with orthopedic surgery: A meta-analytic review. Int Psychogeriatr 2007;19:197-214.
10. Edlund A, Lundström M, Brännström B, Bucht G, Gustafsson Y: Delirium before and after operation for femoral neck fracture. J Am Geriatr Soc 2001;49:1335-1340.
11. Demeure MJ, Fain MJ: The elderly surgical patient and postoperative delirium. J Am Coll Surg 2006;203:752-757.
12. Juliebø V, Bjøro K, Krogseth M, Skovlund E, Ranhoff AH, Wyller TB: Risk factors for preoperative and postoperative delirium in elderly patients with hip fracture. J Am Geriatr Soc 2009;57:1354-1361.
13. Fick DM, Steis MR, Waller JL, Inouye SK: Delirium superimposed on dementia is associated with prolonged length of stay and poor outcomes in hospitalized older adults. J Hosp Med 2013;8:500-505.
14. Gao R, Yang ZZ, Li M, Shi ZG, Fu Q: Probable risk factors for postoperative delirium in patients undergoing spinal surgery. Eur Spine J 2008;17:1531-1537.
15. Fick DM, Agostini JV, Inouye SK: Delirium superimposed on dementia: A systematic review. J Am Geriatr Soc 2002;50:1723-1732.
16. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM: Reducing delirium after hip fracture: A randomized trial. J Am Geriatr Soc 2001;49:516-522.
17. Robertson BD, Robertson TJ: Postoperative delirium after hip fracture. J Bone Joint Surg Am 2006;88:2060-2068.
18. Alluri RK, Leland H, Heckmann N: Surgical research using national databases. Ann Transl Med 2016;4:393.
19. Program ACoSNSQI: User Guide for the 2016 ACS NSQIP Procedure targeted Participant Use Data File (PUF), Chicago, IL: 2017.
20. Hayes AF, Rockwood NJ: Regression-based statistical mediation and moderation analysis in clinical research: Observations, recommendations, and implementation. Behav Res Ther 2017;98:39-57.
21. Hayes AF, Preacher KJ: Statistical mediation analysis with a multicategorical independent variable. *Br J Math Stat Psychol* 2014;67:451-470.

22. Buis ML: Direct and indirect effects in a logit model. *Stata J* 2010;10:11-29.

23. Hicks R, Tingley D: Causal mediation analysis. *Stata J* 2011;11: 605-619.

24. Brown CA, Starr AZ, Nunley JA: Analysis of past secular trends of hip fractures and predicted number in the future 2010-2050. *J Orthop Trauma* 2012;26:117-122.

25. Schneider EL, Guralnik JM: The aging of America. Impact on health care costs. *JAMA* 1990;263:2335-2340.

26. Sampson EL, Raven PR, Ndhllovu PN, et al: A randomized, double-blind, placebo-controlled trial of donepezil hydrochloride (Aricept) for reducing the incidence of postoperative delirium after elective total hip replacement. *Int J Geriatr Psychiatry* 2007;22:343-349.

27. Saczynski JS, Marcantonio ER, Quach L, et al.: Cognitive trajectories after postoperative delirium. *New Engl J Med* 2012;367:30-39.

28. Saravay SM, Kaplowitz M, Kurek J, et al.: How do delirium and dementia increase length of stay of elderly general medical inpatients? *Psychosomatics* 2004;45:235-242.

29. Postier A, Neidel J, Günther KP: Incidence of early postoperative cognitive dysfunction and other adverse events in elderly patients undergoing elective total hip replacement (THR). *Arch Gerontol Geriatr* 2011;53:328-333.

30. Rudolph JL, Marcantonio ER: Postoperative delirium: Acute change with long-term implications. *Anesth analgesia* 2011;112:1202.

31. Kates SL, Behrend C, Mendelson DA, Cram P, Friedman SM: Hospital readmission after hip fracture. *Arch Orthop Trauma Surg* 2015;135:329-337.

32. Pendlebury ST, Lovett NG, Smith SC, et al: Observational, longitudinal study of delirium in consecutive unselected acute medical admissions: Age-specific rates and associated factors, mortality and re-admission. *BMJ open* 2015;5:e007808.

33. Inouye SK: Delirium in older persons. *New Engl J Med* 2006;354: 1157-1165.

34. Robinson TN, Raeburn CD, Tran ZV, Angles EM, Brenner LA, Moss M: Postoperative delirium in the elderly: Risk factors and outcomes. *Ann Surg* 2009;249:173-178.

35. Elie M, Cole MG, Primeau FJ, Bellavance F: Delirium risk factors in elderly hospitalized patients. *J Gen Intern Med* 1998;13:204-212.

36. Bilge EU, Kaya M, Şenel GÖ, Ünver S: The incidence of delirium at the postoperative intensive care unit in adult patients. *Turk J Anaesthesiol Reanim* 2015;43:232-239.

37. Brouquet A, Cudennec T, Benoist S, et al: Impaired mobility, ASA status and administration of tramadol are risk factors for postoperative delirium in patients aged 75 years or more after major abdominal surgery. *Ann Surg* 2010;251:759-765.

38. Noimark D: Predicting the onset of delirium in the post-operative patient. *Age Ageing* 2009;38:368-373.

39. Böhner H, Hummel TC, Habel U, et al: Predicting delirium after vascular surgery: A model based on pre- and intraoperative data. *Ann Surg* 2003; 238:149-156.