Preoperative risk factors for delirium in hip-fracture surgery under regional anesthesia: A nationwide population-based study

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Abstract

Background

Delirium is common, but is frequently undetected by clinicians, despite the fact that it can be life-threatening. The objective of this study was to identify the incidence of delirium and the preoperative factors associated with postoperative delirium in elderly patients who underwent hip fracture surgery under regional anesthesia.

Methods

We retrospectively reviewed records of all patients ≥65 years who underwent hip fracture surgery under regional anesthesia, covered by the Korean National Health Insurance, between January 1, 2009 and December 31, 2015. A univariate and stepwise logistic regression model with the occurrence of delirium as the dependent variable was used to identify perioperative factors for this sample of patients.

Results

Among the 70696 patients who underwent hip fracture surgery, 58972 patients were who received regional anesthesia during surgery were included in our study. Delirium was detected in 8680 (14.7%) patients. Performing stepwise logistic regression, preoperative variables including female gender, included age ≥85 years, hospital type (medical center), ICU and ventilator care, neurodegenerative disorders, uncomplicated diabetes mellitus, peptic ulcer disease, psychoses, and depression (OR=1.491.42-1.58, 4.74.15-5.37, 13.37.57-23.8, 1.521.43-1.60, 1.191.01-1.40, 1.201.14-1.27, 1.091.04-1.14, 0.870.96-0.00, 2.231.48-3.37, and 1.381.32-1.46, respectively) were identified to be associated with delirium.

Conclusion

Delirium could occur in approximately 15% of elderly hip fracture surgery cases in which regional anesthesia is used. Multiple preoperative risk factors were found to be associated
with delirium.

Introduction

With a rapidly aging population, the incidence of hip fracture cases continues to increase in South Korea [1]. Elderly hip fracture patients suffer adverse complications, including mortality, which poses a medical and financial burden on society [2]. Although there has been improvement in the quality of surgical and anesthetic care over time, morbidity and mortality after hip fracture remain high [3]. One of the most common complications after hip fracture surgery is delirium, with a reported incidence varying between 4 and 53% [4]. Delirium is common, but it is frequently undetected by clinicians, despite the fact that it can be life-threatening and gives rise to serious preventable complications [5].

Postoperative delirium was known to associated with increased length of ICU and hospital stay, hospital costs, institutionalization, and mortality after surgery [6]. To decrease morbidity and mortality, including postoperative delirium, it is recommended that the anesthesia type used in hip fracture surgery be considered. Although the effects of the type of anesthesia on outcomes in elderly patients are debated, some studies have reported that regional anesthesia (RA) yields more favorable outcomes when used in hip fracture surgery. Despite the favorable results of RA in hip fracture surgery, delirium still occurs. Thus, the risk factors for delirium remain to be investigated so that postoperative complications can be reduced in geriatric patients. The objective of this study was to identify the incidence of delirium and the preoperative factors associated with postoperative delirium in elderly patients who underwent hip fracture surgery under regional anesthesia.

Methods

This study was reviewed and approved by the institutional review board of Seoul Paik
Hospital (IRB No 2019-05-005), and the need to obtain informed consent was waived since we used de-identified administrative data.

The NHIS is a single health insurer managed by the Korean government covering approximately 97% of Koreans. The remaining 3% of Koreans are covered by the Medical Aid Program (MAP) [7]. The National Health Information Database (NHID), created by the NHIS, is a public database on health care utilization, health screenings, sociodemographic variables, and mortality for the entire South Korean population, composed of data obtained between 2002 and 2015. The NHID is open to all researchers whose study protocols are approved by the official review committee. The NHID provides support through the NHIS for research activities in various sectors, such as in societal, economic, environmental, and industry, as well as in the policy and medical sectors, by providing data on the Sample cohort DB, Customized DB, Health Disease index, and others. Among these services, our data were “customized health information data” provided on request specifically for our study.

Participants
We included all patients 65 years old or older who underwent hip surgery under regional anesthesia in hospitals in Korea between January 1, 2009 and December 31, 2015 based on admission date. The inclusion and exclusion criteria used are described as follows.

Inclusion criteria
Principal diagnosis upon admission of femur neck fracture (S720) or trochanteric fracture (S721) based on the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code Admission with at least one of the following surgical operations based on procedure codes: Open Reduction of Fractured Extremity [Femur], Total Arthroplasty [Hip], Hemiarthroplasty [Hip] Who received spinal or epidural anesthesia

Exclusion criteria
Patients with a diagnosis of multiple traumas or fracture (“S00-S70”, “S73–99”, “T07”, or “T14”) Patients who underwent more than two such operations during the same admission period
Patients who had a diagnosis of psychiatric disease (F10-F29) and a medication history of haloperidol, risperidone, and quetiapine before admission date

Delirium was defined as a record of intravenous administration of haloperidol, risperidone, and quetiapine at least once during the hospital stay.

**Independent variables**

The patient characteristics recorded included sex, age, comorbid conditions, and hospital type (medical center=1, general hospital=2, or clinic=3). The Elixhauser Comorbidity method, which outperforms the Charlson Index in predicting inpatient death after orthopedic surgery, was used to identify patient comorbidities [8]. Elixhauser Comorbidity measures were calculated by the sum of weighted points based on the presence or absence of 31 different medical conditions. These included congestive heart failure, cardiac arrhythmias, valvular disease, pulmonary circulation disorders, peripheral vascular disorders, uncomplicated hypertension, complicated hypertension, paralysis, other neurologic disorders, chronic pulmonary disease, uncomplicated diabetes mellitus, complicated diabetes mellitus, hypothyroidism, renal failure, liver disease, peptic ulcer disease, AIDS/HIV infection, lymphoma, metastatic cancer, solid tumor without metastasis, rheumatoid arthritis, coagulopathy, obesity, weight loss, fluid and electrolyte disorders, blood loss anemia, deficiency anemia, alcohol abuse, drug abuse, psychoses, and depression. The comorbidities were followed by the list of ICD-10 codes defined by Quan et al. [9]. Stays in the intensive care unit (ICU) as well as ventilator care were also recorded.

**Statistical analysis**

All statistical analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC). For continuous variables, data are presented as the median (range), and groups were
compared using the Mann–Whitney U test. Descriptive variables were analyzed by chi-
squared analysis. Two-tail P values were used throughout analysis, and 95% confidence
intervals were reported with relative risks and odds ratios for variables significantly
associated with delirium. Using a univariate and stepwise logistic regression model with
the occurrence of delirium as the dependent variable, perioperative factors were identified
for this sample of patients. All statistical testing was two-sided at a significance level of
0.05.

Results

We identified 70696 patients who underwent hip fracture surgery under regional
anesthesia, who were 65 years old or older and who were admitted to the hospital during
2009–2015; of these, 363 patients were excluded due to missing data. To reduce
confounding bias, 11361 patients with diagnoses of psychiatric diseases (F10-F29) and
medication histories of haloperidol, risperidone, and quetiapine before the admission date
were excluded. In total, 58972 patients were included in our study (Figure 1).
The incidence of delirium in patients who underwent hip-fracture surgery under regional
anesthesia was 14.7% (8680/58972). Sex, age, Elixhauser Comorbidity score, and hospital
type were different between the two groups (Delirium versus No delirium, Table 1).
Covariates including congestive heart failure, cardiac arrhythmia, peripheral vascular
disorder, complicated hypertension, uncomplicated hypertension, neurologic disorder,
uncomplicated diabetes mellitus, renal failure, fluid and electrolyte disorder, deficiency
anemia, psychoses, and depression showed significant differences between the groups
(Table 1). Additionally, ICU stays, ventilator care, and mortality were significantly
different between the groups (Table 1).

Univariate factors associated with delirium included male gender (OR=1.26[1.19-1.33]),
age ≥85 (OR=4.5[4.0-5.1]), Elixhauser Comorbidity score ≥15 (OR=1.3[1.14-1.48]),
hospital type 1 (OR=26.8[9.25-28.6]), congestive heart failure (OR=1.15[1.09-1.21]),
cardiac arrhythmia (OR=1.15[1.09-1.21]), perivascular disease (OR=1.05[1.0-1.1]),
uncomplicated hypertension (OR=1.12[1.05-1.19]), complicated hypertension (OR=1[0.0-9.25]), neurodegenerative disorder (OR=1.26[1.26-1.33]), uncomplicated diabetes mellitus
(OR=1.02[1.00-1.10]), renal failure (OR=1.15[1.06-1.24]), fluid disorder (OR=1.07[1.01-1.12]), deficiency anemia (OR=1.06[1.0-1.11]), psychoses (OR=2.44[1.64-3.62]), and
depression (OR=1.33[1.27-1.39]). Additionally, ICU stay (OR=2.13[2.02-2.25]) and
ventilator care (OR=1.99[1.7-2.3]) were significant risk factors for delirium (Table2).

Adjusting for other factors by stepwise logistic regression, female gender (OR=1.49[1.42-1.58]),
age ≥85 (OR=4.7[4.15-5.37]), hospital type 1 (OR=13.3[7.57-23.8]), ICU stay
(OR=1.52[1.43-1.60]), ventilator care (OR=1.19[1.01-1.40]), neurologic disorder
(OR=1.20[1.14-1.27]), uncomplicated diabetes mellitus (OR=1.09[1.04-1.14]), peptic ulcer
disease (OR=0.87[0.96-0.00]), psychoses (OR=2.23[1.48-3.37]), and depression
(OR=1.38[1.32-1.46]) remained predictive of delirium (Table 3).

Discussion

The present study reports that delirium could occur in approximately 15% of elderly hip
fracture surgery cases in which regional anesthesia is used. Multiple preoperative risk
factors, including male gender, included age ≥85, hospital type (medical center), ICU and
ventilator care, neurodegenerative disorder, uncomplicated diabetes mellitus, peptic ulcer
disease, psychoses, and depression, are associated with delirium.

Elderly hip fracture patients require efficient and multidisciplinary perioperative
evaluation and management to improve postoperative outcomes. The most common
complication after hip fracture surgery is delirium, reported in up to 53% of cases [4].

However, in our study, the incidence of delirium requiring pharmacological intervention in
our population was 14.7%. The difference between these reported incidence rates may be
related to the definition of delirium and the anesthetic method used.

Some previous reports compared the use of general anesthesia and regional anesthesia to reduce morbidity and mortality, including delirium. These reported that regional anesthesia yielded more favorable outcomes than general anesthesia [3, 10, 11]. Therefore, we selected only patients who underwent regional anesthesia to reduce selection bias. It is known that regional anesthesia is associated with shorter times to mobilization and positive outcomes [12]. Even regional anesthesia can cause delirium requiring pharmacological intervention to some extent. Therefore, the ability to detect patients who have a high risk of postoperative delirium following hip surgery will reduce the incidence of delirium and help to prevent it.

Our results are consistent with those of previous studies. In line with previous reports, age ≥85 years was a significant predictor of delirium. It may be further suggested that age ≥85 could be the cutoff for delirium prevalence. Additionally, male patients had more developed delirium, similar to the study by Edelstein et al., which reported an incidence of delirium in male patients which was twice that in females [13].

Our study found that not only preoperative variables such as age, male gender, and comorbidities such as preoperative neurodegenerative disorder, diabetes mellitus, peptic ulcer disease, psychoses, and depression, but also ICU stay and ventilator care, may have strong associations with delirium. It has been recognized that duration of ICU stay and mechanical ventilation are precipitating factors of delirium [14, 15]. According to a meta-analysis of elderly hip fracture cases, patients with postoperative delirium had more than twice the risk of mortality than those without delirium [16]. Identification of patients who have a high risk of postoperative delirium will associate to increase both prevention and treatment strategies and to improve hip fracture surgery outcomes.
The strength of this study was its use of anonymized data from nearly an entire country’s population, which made its results less susceptible to selection bias. Additionally, we only selected patients who received RA to reduce the influence of other types of anesthesia. Nevertheless, this study had some limitations. First, this was a retrospective national claims data investigation, and thus, patient clinical data such as body weight, perioperative blood loss, and duration of surgery were not included due to the nature of the database. To minimize heterogeneity, we only included cases of femur neck fracture (S720) and trochanteric fracture (S721). Second, claims data can contain coding errors. Third, information on diagnosis and disease included in the healthcare utilization database may not have sufficient validity for identifying disease occurrence and prevalence, since the data have not been established for research purposes, but rather for medical services claims and reimbursement. Finally, as previously stated, the definition of delirium used in our study had limitations. Delirium not requiring pharmacological intervention, such as the hypoactive subtype of delirium, may have been ignored in this study. Because of these limitations, we could only determine associations between the type of anesthesia and mortality and not causal relationships. Therefore, careful interpretation should be applied.

Conclusions

We conducted a retrospective analysis of the data of nearly 6 million elderly patients who underwent surgery for hip fracture under regional anesthesia. Regional anesthesia requiring pharmacologic intervention was associated with multiple risk factors, including male gender, old age, preoperative neurodegenerative disorder, diabetes mellitus, peptic ulcer disease, psychosis, depression, ICU stay, and ventilator care, in elderly patients undergoing hip fracture surgery.

List Of Abbreviations
Regional anesthesia (RA)

Medical Aid Program (MAP)

National Health Information Database (NHID)

International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM)

**Declarations**

**Ethical approval and consent to participate**

The study was reviewed and approved by the institutional review board of Seoul Paik Hospital (IRB No 2019-05-005). The need to obtain informed consent was waived because we used de-identified administrative data.

**Availability of data and material** Data cannot be shared publicly because of confidentiality and privacy issues. Data may be available with a formal application to the institutional ethics committee (contact via https://nhiss.nhis.or.kr/bd/sey/bdaya001iv.do) for researchers who meet the criteria for access to confidential data.

**Competing interests**

There are no competing interests to declare.

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**Author contributions**

Eun-Jin Ahn contributed to data collection, data analysis, data interpretation, and writing of the manuscript. Si Ra Bang contributed to the literature review, figure preparation, study design, data collection, analysis, interpretation, and writing of the manuscript.

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Tables

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Figures

Figure 1
Flow diagram

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