

BMJ Open Comparison of general anaesthesia and regional anaesthesia in terms of mortality and complications in elderly patients with hip fracture: a nationwide population-based study

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ABSTRACT

Objective To evaluate the effects of anaesthesia on postoperative outcome in elderly patients who underwent hip fracture surgery.

Setting Nationwide National Health Insurance Sharing Service database of Korea.

Participants All patients aged ≥65 years old who underwent hip fracture surgery, covered by the Korean National Health Insurance, between 1 January 2009 and 31 December 2015.

Interventions Hip fracture surgery under general anaesthesia (group GA) or regional anaesthesia (group RA), with a principal diagnosis of femoral fracture.

Primary and secondary outcome measures The primary outcome was the anaesthetic-type effect on 30-day mortality and the secondary outcome was postoperative delirium requiring pharmacological intervention.

Results Among the 96 289 patients who underwent hip fracture surgery, 25 593 and 70 696 patients received GA and RA, respectively. After propensity score matching, 25 593 remained in each group. Postmatching mortality was lower in the RA than in the GA group (574 (2.24%) vs 654 (2.55%), $p=0.0047$, 95% CI -0.0099 to 0.0159). Delirium incidence was lower in the RA than in the GA group (5187 (20.27%) vs 5828 (22.77%), $p<0.0001$, 95% CI 0.019 to 0.045). The incidence of intensive care unit stay and ventilator care was lower in the RA than in the GA group (5838 (22.1%) vs 8055 (31.47%), $p<0.0001$, 95% CI 0.046 to 0.070 and 459 (1.73%) vs 1207 (4.72%), $p<0.0001$, 95% CI -0.0024 to 0.023 , respectively).

Conclusion RA was associated with better outcomes than GA, in terms of mortality, delirium, intensive care unit admission and ventilator care, in elderly patients who underwent hip fracture surgery.

INTRODUCTION

The ageing population is rapidly growing, particularly in developed countries. South Korea is rapidly turning into an aged society, defined as a society with the elderly population exceeding 14% of the total population.¹

Strengths and limitations of this study

- It was based on a large and representative national database that is widely used as a reliable research tool for identifying trends and demographics.
- We used more recent data (2009–2015) to reflect improvements in anaesthetic drugs, perioperative haemodynamic monitoring and perioperative pain management.
- The database did not include clinical data, and it may have contained coding errors.

Ha *et al*² reported that the incidence of hip fracture is continually increasing and that the predicted increases will cause a serious socioeconomic burden and a challenge for public healthcare management in Korea. Hip fractures are usually associated with adverse complications, including mortality, which lead to a medical and financial burden on society.³

One of the most common adverse complications of hip fracture in elderly patients is delirium. It is associated with an increased rate of cognitive decline, institutionalisation and mortality.⁴ To decrease the mortality rate and postoperative delirium, a careful consideration of the type of anaesthesia used in hip fracture surgery is recommended, although the effects of anaesthesia type on mortality and outcome in geriatric patients are debated. Some reports have stated that most anaesthesia-related complications are multifactorial. However, in hip fracture surgery, it has been reported that regional anaesthesia (RA) yields a more favourable outcome.

In this study, we used a nationwide database to evaluate the effects of anaesthesia on postoperative outcome in elderly patients who underwent hip fracture surgery. The primary

outcome of this study was the effect of the anaesthetic type on the 30-day mortality, and the secondary outcome was postoperative delirium requiring pharmacological intervention.

METHODS

The need to obtain informed consent was waived because we used deidentified administrative data. The study population consisted of all patients 65 years old or older, who underwent hip fracture surgery, covered by the Korean National Health Insurance Service (NHIS), between 1 January 2009 and 31 December 2015.

The NHIS is a single health insurer, managed by the Korean government, which covers approximately 97% of Koreans, while the remaining 3% of Koreans who cannot afford national insurance are covered by the Medical Aid Program (MAP).⁵ Claims submitted for reimbursement to NHIS and MAP are reviewed by the Health Insurance Review and Assessment Service, a central office in the Korean Ministry of Health. Our data were obtained from the National Health Information Database (NHID), created by the NHIS. The NHID is a public database of healthcare utilisation, health screening, sociodemographic variables and mortality for the entire population of South Korea and comprises data obtained between 2002 and 2015. The NHID can be accessed by the researchers whose study protocols are approved by the official review committee. Moreover, this study conformed to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting observational cohort studies (www.strobe-statement.org).

Patient and public involvement

No patients or members of the public were involved in the design of this study.

Participants

We included all patients 65 years old or older, who underwent hip surgery in hospitals in Korea between 1 January 2009 and 31 December 2015. The study period was based on admission date. The major inclusion criterion was admission with a principal diagnosis of femoral neck fracture (S720) and trochanteric fracture (S721), as identified from the patient's overall diagnosis based on the

code. We included the patients who were admitted with at least one of the following surgical operations based on procedure codes: open reduction of fractured extremity (femur), total arthroplasty (hip), hemiarthroplasty (hip) and revision of hemiarthroplasty (hip). We included patients who received general, spinal and epidural anaesthesia. We excluded patients who received both GA and RA. Patients with a diagnosis of multiple trauma or fracture ('S00–S70', 'S73–99', 'T07', 'T14') were excluded. Additionally, we excluded patients who underwent more than two such operations during the same period of admission. Thirty-day mortality was defined as death either

inside or outside the hospital due to any cause within 30 days of admission (in the hospital or after discharge).

Independent variables

Patients were classified into two groups according to the specific anaesthesia type (general anaesthesia (GA) or RA). The RA group was administered epidural anaesthesia, spinal anaesthesia or both. The patient characteristics that were recorded were sex, age, comorbid conditions and hospital type (medical centre, general hospital or clinic). The Elixhauser comorbidity method, which outperforms the Charlson Index in predicting hospital inpatient death after orthopaedic surgery, was used to identify the patients' comorbidities.⁶ The Elixhauser comorbidity method uses the sum of weighted points based on the presence or absence of 31 different medical conditions (including congestive heart failure, cardiac arrhythmias, valvular disease, pulmonary circulation disorders, peripheral vascular disorders, uncomplicated hypertension, complicated hypertension, paralysis, other neurological 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 tumour without metastasis, rheumatoid arthritis, coagulopathy, obesity, weight loss, fluid and electrolyte disorders, blood loss anaemia, deficiency anaemia, alcohol abuse, drug abuse, psychoses and depression). The hospital type was classified, according to the number of beds, into a medical centre, general hospital or clinic. Stay in the intensive care unit (ICU), ventilator care and cost during the hospital stay were also recorded.

The primary outcome was the 30-day mortality (defined as death due to any cause within 30 days of the indexed date, inside or outside the hospital). As a secondary outcome, we used the occurrence of delirium, defined by a record of intravenous administration of haloperidol, risperidone and quetiapine at least once during the hospital stay period.

Other complications, such as myocardial infarction, pulmonary embolism, cerebral haemorrhage, acute respiratory distress syndrome, pulmonary oedema, acute kidney injury, hepatic failure and sepsis, were also recorded.

Statistical analysis

To reduce selection bias and the potential baseline differences between the RA and GA groups, prior propensity score matching (PSM) was performed via the calliper matching method to match patients from the two groups in a 1:1 ratio. The propensity score was calculated by logistic regression analysis using the following covariates: age, sex, hospital type and comorbid conditions using the Elixhauser method to examine the association of anaesthesia type with 30-day mortality, other complications and delirium after hip fracture surgery.

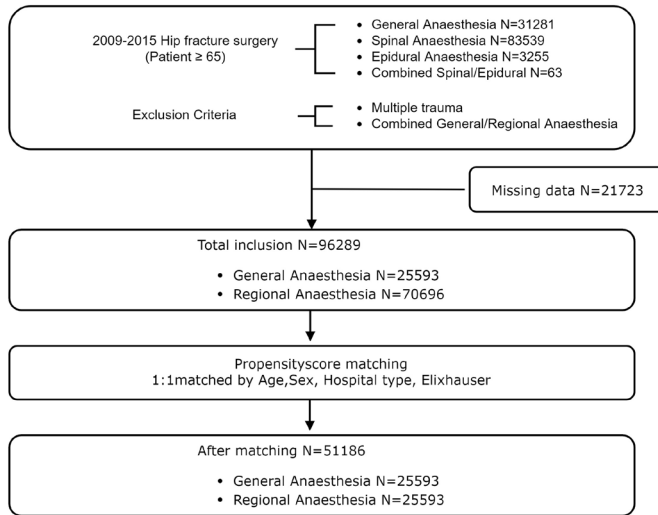


Figure 1 Flow diagram of included patient numbers.

Prior to PSM, patient characteristics were summarised using descriptive statistics. For continuous variables, data are presented as the median (range), and groups were compared using the Mann-Whitney U test. Descriptive variables were analysed using χ^2 analysis. Postmatching continuous variables are presented as the median (range); these were compared using Wilcoxon's signed rank-sum test. Categorical variables are presented as absolute numbers (percentages). Statistical differences between groups were tested with McNemar's tests. A p value < 0.05 was considered statistically significant. SAS V.9.3 was used for the analysis. All statistical testing was two sided at a significance level of 0.05.

RESULTS

We identified 118 012 patients undergoing hip fracture surgery, who were 65 years old or older and who were admitted to the hospital during 2009–2015; of these, 63 patients were excluded due to duplication of patient data, as they underwent combined spinal and epidural anaesthesia, and 21 723 patients were excluded due to missing data. Finally, 96 289 patients were included in our study. Among these, 25 593 patients were included in the GA group and 70 696 patients were included in the RA group (figure 1). Before PSM, baseline characteristics, including age, sex, comorbid conditions and hospital type, differed between the RA and GA groups (table 1). After performing 1:1 PSM, 25 593 patients were included in each group, with no significant difference between the two groups in terms of covariates, including age, sex, hospital type and comorbidities (table 1).

There were more female than male patients in this study. Prematching and postmatching results, including 30-day mortality and other complications, are reported in tables 2 and 3. The overall 30-day mortality was 2.45%, with no significant difference between the two groups before PSM. However, after propensity score analysis,

Table 1 Patient characteristics

	Prematching		Postmatching		P value
	Total (n=96289)	GA (n=25593)	RA (n=70696)	RA (n=25593)	
Age (years)	79 (74–84)	79 (74–84)	80 (75–85)	79 (74–84)	<0.0001*
Sex (male/female)	24 748/71 541	6764/18 829	17 984/52 712	6764/18 829	0.0019*
Hospital type (1/2/3)	69 814/25 320/1155	22 983/24 94/116	46 831/22 826/1039	22 983/2494/116	<0.0001*
Elixhauser (1/2/3)	18 401/43 433/34 455	4174/11 006/10 413	14 227/32 427/24 042	4174/11 006/10 413	<0.0001*

Hospital type 1: medical centre; hospital type 2: general hospital; hospital type 3: clinic. Elixhauser 1: Elixhauser comorbidity scores <5; Elixhauser 2: Elixhauser comorbidity scores 5–9; Elixhauser 3: Elixhauser comorbidity scores ≥10. Values are expressed as absolute numbers (percentages), median (25th–75th percentiles) or absolute numbers.

*P<0.05 between-group comparisons.

GA, general anaesthesia; RA, regional anaesthesia.

Table 2 Complications

	Prematching (n=96 289)			Postmatching (n=51 186)			
	GA (n=25 593)	RA (n=70 696)	P value	GA (n=25 593)	RA (n=25 593)	P value	95% CI
MI	393 (1.53)	1504 (2.13)	<0.0001*	393 (1.53)	424 (1.66)	0.27	0.001 to 0.036
Pulmonary embolism	1454 (5.68)	929 (1.31)	<0.0001*	1454 (5.68)	654 (2.55)	<0.0001*	-0.011 to 0.014
Cerebral haemorrhage	223 (0.87)	295 (0.42)	<0.0001*	223 (0.87)	123 (0.48)	<0.0001*	-0.011 to 0.021
ARDS	201 (0.78)	472 (0.67)	0.053	201 (0.78)	165 (0.64)	0.057	-0.0063 to 0.036
Pulmonary oedema	445 (1.74)	1244 (1.76)	0.83	445 (1.74)	451 (1.76)	0.84	-0.0089 to 0.019
AKI	655 (2.56)	1635 (2.31)	0.027*	655 (2.56)	655 (2.56)	>0.99	-0.0019 to 0.028
Hepatic failure	153 (0.59)	348 (0.49)	0.044	153 (0.59)	165 (0.64)	0.50	-0.012 to 0.012
Sepsis	273 (1.07)	637 (0.90)	0.019	273 (1.07)	263 (1.02)	0.66	-0.010 to 0.019

Values are expressed as absolute numbers (percentages) or absolute numbers.

*P<0.05 between-group comparisons.

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; GA, general anaesthesia; MI, myocardial infarction; RA, regional anaesthesia.

the mortality was higher in the GA than in the RA group (p=0.0208).

Postoperative complications, including sepsis, hepatic failure, acute kidney injury and myocardial infarction, were not significantly different between the two groups after PSM, although the difference between the two groups was significant before PSM (p=0.0189, 0.0443, 0.0265 and <0.0001, respectively). Other complications, including cerebral haemorrhage, pulmonary embolism, stay in the ICU, ventilator care, delirium and cost, differed significantly between the two groups before and after matching. These outcomes showed a higher incidence in the GA group than in the RA group. The overall cost of anaesthesia was also higher in the GA than in the RA group (prematching \$5389.51 vs \$4919.75, p<0.0001; postmatching \$5389.61 vs \$5213.24, p<0.0001)

DISCUSSION

This study of nationwide claims data of 96 289 patients confirmed that RA yielded a better outcome in terms of 30-day mortality than did GA for elderly patients undergoing surgery for hip fracture. Furthermore, delirium requiring pharmacological intervention was significantly

lower in patients who received RA. Moreover, patients who received RA had a lower incidence of ICU admission, ventilator care, hospital costs and complications, including pulmonary embolism and cerebral haemorrhage.

Several observational studies⁷⁻¹² have shown no benefit of RA compared with GA in patients with hip fractures. The meta-analyses performed by Mason *et al* and Guay showed that there was no significant difference between GA and RA regarding both postoperative delirium and long-term postoperative cognitive dysfunction.^{13 14} The recent meta-analysis performed by Patel *et al*¹⁵ found no evidence of the influence of type of anaesthesia on postoperative delirium or mortality. However, our findings were similar to those of another national claims database study.³ Compared with these previous studies, the strength our study was that it included more recent data, from 2009 to 2015, with a large sample size. A previous study using Taiwan's inpatient claims database of geriatric patients between 1997 and 2011 reported that neuraxial anaesthesia offered some advantages in terms of mortality, stroke, respiratory failure, renal failure, hospital stay, ICU admission, mechanical ventilator support and medical costs.³ In that study, the primary outcome of mortality

Table 3 Primary and secondary outcomes

	Prematching (n=96 289)			Postmatching (n=51 186)			
	GA (n=25 593)	RA (n=70 696)	P value	GA (n=25 593)	RA (n=25 593)	P value	95% CI
Mortality	654 (2.55)	1706 (2.41)	0.21	654 (2.55)	574 (2.24)	0.0047*	-0.099 to 0.016
Delirium	5828 (22.77)	12 733 (18.01)	<0.0001*	5828 (22.77)	5187 (20.27)	<0.0001*	0.019 to 0.045
ICU	8055 (31.47)	12 683 (17.94)	<0.0001*	8055 (31.47)	5838 (22.81)	<0.0001*	0.046 to 0.070
Ventilator care	1207 (4.72)	1095 (1.55)	<0.0001*	1207 (4.72)	459 (1.73)	<0.0001*	-0.0024 to 0.023

Values are expressed as absolute numbers (percentages), median (25th–75th percentile) or absolute numbers.

*P<0.05 between-group comparisons.

GA, general anaesthesia; RA, regional anaesthesia; ICU, intensive care unit.

was in-hospital mortality. However, we used a 30-day in or out of hospital mortality as a standard time frame that can directly reflect the level of hospital care.¹² Our study also showed a lower incidence of ICU admission, reduced need for ventilator care, lower hospital costs and fewer complications, including pulmonary embolism and cerebral haemorrhage. Thus, in elderly patients, RA has some advantages.

Several randomised controlled trials (RCTs) have been conducted in an attempt to confirm the association between hip fracture and anaesthesia techniques.^{16 17} According to O'Donnell's *et al* meta-analysis, 8200 patients per group would be required to achieve the minimum acceptable standard power (80%) for detecting a difference with respect to 30-day mortality.⁷ However, the number of patients in the two RCTs was only 45¹⁶ and 322, respectively.¹⁷ Although RCTs are not clinically or financially easy to perform, several pragmatic large RCTs assessing the effectiveness of GA and RA are underway. The RAGA-delirium trial is planned with 1000 randomised older patients undergoing hip fracture surgery.¹⁸ The REGAIN and iHope studies are international, multicentre, pragmatic RCTs including 1600 and 1032 patients, respectively.^{19 20} Moreover, the REGARD study comparing RA and GA and their effect on delirium in patients with hip fractures aiming to recruit 100 patients has been registered in the ISRCTN registry (ISRCTN1565914, <https://doi.org/10.1186/ISRCTN15165914>). A meta-analysis of their results may support our study findings and thus improve guideline development for enhanced outcome after hip fracture surgery.^{19 20}

Delirium is used as an indicator of healthcare quality for elderly patients. Identification of vulnerable patients and prevention of and intervention for delirium in hip fracture are of great public health concern.²¹ Delirium occurrence in the ICU is associated with a 2–4 fold increase in the mortality rates.^{22–25} Postoperative delirium is very common and has an impact on the length of stay in the postanaesthesia care unit and mortality and has been identified as an independent risk factor for in-hospital mortality and for mortality during 6 months of follow-up.²⁵ Several studies have identified GA as a risk factor for delirium. In contrast, Smith *et al*²⁶ have reported that intraoperative variables, including type of anaesthesia, were not associated with delirium. However, their study was a meta-analysis based on only 6704 patients. Therefore, our results may more reliably reflect the occurrence of delirium in elderly patients with hip fracture.

Delirium, an acute disorder of attention and cognition, is a clinical condition that is often unrecognised and overlooked and is difficult to evaluate.⁴ It comprises 23 ICD-10 codes, which represent the difficulty of the diagnosis, and the sensitivity for delirium is only approximately 3%.²⁷ In clinical settings, where screening instruments are not used systematically, diagnosis is missed in approximately 60%–80% of cases.²⁸ It has seldom been evaluated with nationwide claims data because of the lack of accuracy in

defining delirium in a wide-incidence range.⁷ Therefore, we needed to use a working definition to ensure the accuracy of diagnosis of postoperative delirium.

There are various methods to treat delirium, including ensuring patient safety with psychiatric, environmental and supportive management and identifying and treating the cause of delirium. Regarding pharmacological interventions, antipsychotic medication has been considered as the first-line pharmacotherapy of delirium except in cases of sedative or alcohol withdrawal.²⁹ Among the antipsychotic drugs, haloperidol is most frequently employed, while risperidone and quetiapine are increasingly being used. Haloperidol, risperidone and quetiapine have shown comparable efficacy and safety in the treatment of delirium.³⁰ Therefore, in our study, we defined 'delirium' based on a record of prescription of intravenous haloperidol, risperidone or quetiapine. This definition of delirium was established based on the delirium-treatment guideline of the American Psychiatric Association.³¹ However, according to our definition, the diagnosis of the hypoactive subtype of delirium may have been missed as the use of drugs in hypoactive delirium remains controversial.³² Although it remains unclear whether the hyperactive or mixed subtype of delirium could pose a more serious problem than the hypoactive subtype, patients with hyperactive delirium are more likely to experience falls,³³ intravenous line disconnection or incidental trauma in clinical settings. Hence, we used a definition of delirium that presents with symptoms requiring clinical interventions.

The strength of our study is that it was based on a large and representative national database that is widely used as a reliable research tool for identifying trends and demographics. A large-scale database can offer a vast amount of information, which can help improve the quality of medical care. Administrative claims databases are more useful for the evaluation of long-term complications, and patients can often be tracked within the time period of the databases for assessment of specific events. They are more representative of the general population.³⁴ We also used the Elixhauser Comorbidity Index, which is a more recent model that includes 31 conditions.³⁵ There are various risk stratification tools for predicting patient mortality and morbidity, such as the Charlson model and Nottingham Hip Fracture Score; therefore, future studies should focus on other risk scoring models.³⁶ We also used the ICD-10 codes that were introduced to enhance and expand the ICD-9-CM.³⁷ Furthermore, we used more recent data (2009–2015) to reflect improvements in anaesthetic drugs, perioperative haemodynamic monitoring and perioperative pain management.

Study limitations

This study had some limitations. First, this was a retrospective national claims data investigation, and thus, the patients' clinical data, such as body weight, perioperative blood loss and duration of surgery, were not included due to the nature of the database. To minimise heterogeneity,

we only included femoral neck fracture (S720) or trochanteric fracture (S721). Second, claims data can contain coding errors. Third, information on diagnosis and disease included in the healthcare utilisation 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. Fourth, as previously stated, the definition of delirium in our study has limitations. The initial treatment of delirium involves multidisciplinary non-pharmacological strategies such as reorientation, family presence and interaction, minimising disturbances in the sleep–wake cycle and addressing sensory impairment with hearing aids and eyeglasses, noise reduction and mobilisation.²⁸ Delirium not requiring pharmacological intervention may have missed detection in this study. Because of these limitations, we can only determine the association between the type of anaesthesia and mortality and not causal relationships. Therefore, the data and results require careful interpretation.

CONCLUSIONS

We conducted a retrospective analysis of the data of 96 289 elderly patients with hip fracture. RA was associated with better outcomes in terms of mortality and delirium than GA in elderly patients who underwent hip fracture surgery. Additionally, compared with GA, RA was associated with better outcomes in terms of ICU admission, ventilator care, hospital costs and complications, including pulmonary embolism and cerebral haemorrhage in elderly patients with hip fracture surgery.

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Competing interests The authors declare no conflict of interest with the NHIS.

Patient consent for publication Not required.

Ethics approval The study was reviewed and approved by the institutional review board of Seoul Paik Hospital (IRB No 2018-04-007).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available.

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