Anesthetic Management and Surgical Site Infections in Total Hip or Knee Replacement

A Population-based Study

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ABSTRACT

Background: Epidural or spinal anesthesia involves several mechanisms hypothesized to reduce risk of surgical site infections (SSIs) during this decisive period. This study aims to compare the risk of SSI within 30 days of surgery for patients receiving total hip or knee replacement under general anesthesia *versus* those under epidural or spinal anesthesia.

Methods: We used the Longitudinal Health Insurance Database of Taiwan. A total of 3,081 patients who underwent primary total hip or knee replacement from 2002 to 2006 were included in the study. Multivariate logistic regression and propensity score analyses were carried out to explore the relationship between method of surgical anesthesia and SSI occurring within 30 days of surgery.

Results: Of the 3,081 sampled patients, 56 patients (1.8%) had 30-day SSIs; 33 (2.8% of all under general anesthesia) of them had general anesthesia, and 23 (1.2% of all under epidural or spinal anesthesia) had epidural or spinal anesthesia ($P = 0.002$). The odds of SSI for patients receiving total hip or knee replacement under general anesthesia were 2.21 (95% CI = 1.25–3.90, $P = 0.007$) times higher than those who had the same procedure under epidural or spinal anesthesia, after adjusting for the patient's age, sex, the year of surgery, comorbidities, surgeon's age, and hospital teaching status.

Conclusions: Total hip or knee replacement under general anesthesia is associated with higher risk of SSI compared with epidural or spinal anesthesia. Our results support the evolving concept of long-term consequences of anesthesia and emphasize the anesthesiologist's role in preventing SSIs.

What We Already Know about This Topic

❖ Surgical site infections (SSIs) occur in nearly 5% of cases
❖ Epidural or spinal anesthesia, by increasing peripheral perfusion, might reduce SSIs

What This Article Tells Us That Is New

❖ In a retrospective review of more than 3,000 knee or hip replacement surgical patients in an administrative database, SSIs were less than half as likely if epidural or spinal anesthesia was used instead of general anesthesia

SURGICAL site infections (SSIs) are considered one of the most serious and common anesthetic and surgical complications.[1] SSIs are estimated to complicate an average of 5% of surgeries in the United States every year,[2] accounting for between four (in breast surgery) and 32.2 (in cardiothoracic surgery) additional days of hospitalization per infection,[3] doubling costs,[3] and increasing the hospital financial burden by $1,157 per incident.[4] Moreover, additional postdischarge costs are even higher.[1] The health and financial effects of SSIs are so serious that any further improvement would deserve attention.

Although SSIs are usually detected 5–10 days after a surgical procedure, they take hold during the first few hours of

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operation, a decisive period during which all surgical wounds are contaminated to some extent.[1,5] Therefore, techniques to promote resistance to SSIs are most likely to succeed if used during this period. Maintaining normothermia, which avoids hypothermic vasoconstriction[6,7] and preserves immune function, including antibody production by T cells[8] and neutrophil-mediated "nonspecific" oxidative bacterial killing,[9] is one of the most studied nonpharmacologic methods for preventing SSIs. Because inadequate tissue oxygen tension impairs tissue repair[10] and oxidative killing of surgical pathogens,[11] supplemental oxygen was once considered as another important mechanism for SSI prevention.[12,13] Other perioperative factors increasing the risk of SSI include smoking,[14,15] obesity,[16,17] duration of surgery,[18] and hyperglycemia.[19,20] Postoperative wound pain induces autonomic responses that noticeably increase sympathetic activity and plasma catecholamine, resulting in arteriolar vasoconstriction, reduced peripheral perfusion, and decreased tissue oxygen tension.[21] Postoperative pain control is thus considered as another potential, although still unverified, factor for decreasing risk of SSI.[1]

Compared with general anesthesia, epidural or spinal anesthesia has a sympathetic blocking effect that improves tissue perfusion and oxygenation.[22,23] Thus, it has been proposed that neuraxial anesthesia may diminish the risk of SSI. Therefore, we tested the hypothesis that epidural or spinal anesthesia is associated with lower incidence of SSI than general anesthesia in major surgeries.

Materials and Methods

Database
This study used the Longitudinal Health Insurance Database, which is provided to scientists in Taiwan for research purposes and contains registration files and original claims data for reimbursement for 1,000,000 enrollees under the National Health Insurance program. Taiwan began a National Health Insurance program in 1995 which has a unique combination of characteristics, specifically, universal coverage, a single-payer payment system with the government as the sole insurer, comprehensive benefits, and access to any medical institution of the patient's choice. As of 2007, of 22.96 million people of Taiwan, 22.60 million (> 98%) were enrolled in this program. The 1,000,000 enrollees contained in the Longitudinal Health Insurance Database were randomly selected from the entire set of enrollees. There were no statistically significant differences in age, gender, or healthcare costs between the patients in the Longitudinal Health Insurance Database, and all patients were covered under the program, as reported by the National Health Research Institutes, Taiwan. The Longitudinal Health Insurance Database offers a valuable opportunity to explore the effects of different types of anesthesia on the risk of SSIs for patients undergoing total hip or knee replacement.

Because the dataset used in this study consists of deidentified secondary data released to the public for research pur-

poses, this study was exempt from full review by the Institutional Review Board.

Study Sample
We identified 3,081 patients who underwent primary total hip or knee replacement from January 1, 2002, to December 31, 2006, based on the principal procedure code of 81.51 (total hip replacement; n = 951) or 81.54 (total knee replacement; n = 2,130). If a patient had more than one total hip or knee replacement during the study period, we only selected the first as the index hospitalization. Of these patients, 1,191 received general anesthesia and the other 1,890 received epidural (n = 609) or spinal anesthesia (n = 1,281).

Key Variables of Interest
The independent variable of interest was treated as a dichotomous category based on whether or not a patient received general anesthesia. The study outcome was whether a patient developed SSI during index hospitalization or was readmitted with a principal diagnosis of SSI within 30 days of the index hospitalization. In this study, the diagnosis of SSI included other cellulitis and abscess (International Classification of Diseases, Ninth Revision–Clinical Modification [ICD-9-CM] codes 682, 682.6, and 682.9); other specified local infections of skin and subcutaneous tissue (ICD-9-CM codes 686.8 and 686.9); postoperative infection (ICD-9-CM codes 998.5, 998.51, and 998.59); infection and inflammatory reaction due to unspecified internal prosthetic device, implant, and graft (ICD-9-CM code 996.60); infection and inflammatory reaction due to internal joint prosthesis (ICD-9-CM code 996.66); infection and inflammatory reaction due to other internal orthopedic device, implant, and graft (ICD-9-CM code 996.67); acute osteomyelitis (ICD-9-CM codes 730.0, 730.00, and 730.08); and chronic osteomyelitis (ICD-9-CM codes 730.1, 730.10, and 730.18).

We also took characteristics of patient, surgeon, and hospital into consideration in the regression modeling. Patient characteristics included age, sex, operation procedure (unilateral vs. bilateral), the year of surgery, and whether a patient had hypertension, diabetes, cerebrovascular disease, coronary heart disease (CHD), or hyperlipidemia. Surgeon characteristics consisted of the surgeon's age (as a surrogate for practice experience). Hospital characteristics included teaching status, which was treated as a dichotomous category based on whether a hospital was accredited in 2006 as a teaching hospital by the Department of Health in Taiwan.

Statistical Analysis
We used the SAS statistical package (SAS System for Windows, Version 8.2; SAS Institute Inc., Cary, NC) to perform all analyses in this study. Pearson chi-square tests were conducted to examine the differences between patients who received general anesthesia and those who received epidural or spinal anesthesia. Finally, logistic regression analyses were carried out to explore the relationship between 30-day post-

Table 1. Demographic Characteristics of Patients (n = 3,081) Who Underwent Total Knee Replacement or Total Hip Replacement According to Method of Anesthesia in Taiwan, 2002–2006

Variable	General Anesthesia, n = 1,191		Epidural or Spinal Anesthesia, n = 1,890		P Value
	Total n	Column %	Total n	Column %	
Patient characteristics					< 0.001
Gender					
Male	609	51.1	512	27.1	
Female	582	48.9	1,378	72.9	
Age (yr), mean (SD)	61.4 (8.2)		63.8 (9.1)		< 0.001
Hypertension					< 0.001
Yes	286	24.0	771	40.8	
No	905	76.0	1,119	59.2	
Diabetes					0.003
Yes	123	10.3	265	14.0	
No	1,068	89.7	1,625	86.0	
Coronary heart disease					0.031
Yes	85	7.1	177	9.4	
No	1,106	92.9	1,713	90.6	
Hyperlipidemia					< 0.001
Yes	48	4.0	134	7.1	
No	1,143	96.0	1,756	92.9	
Cerebrovascular disease					0.897
Yes	58	4.9	94	5.0	
No	1,133	95.1	1,796	95.0	
Surgical procedure					< 0.001
Unilateral	979	82.2	1,570	83.1	
Bilateral	212	17.8	320	16.2	
Year of surgery					0.008
2002	213	17.9	333	17.6	
2003	244	20.5	348	18.4	
2004	252	21.2	356	18.8	
2005	231	19.4	432	22.9	
2006	251	21.0	421	22.3	
Surgeon characteristics					
Age (yr), mean (SD)	44.6 (8.8)		45.6 (7.6)		0.003
Hospital characteristics					0.002
Teaching status					
Yes	943	79.2	1,046	74.4	
No	248	20.8	484	25.6	

operative infection and general anesthesia. We also used propensity score, which has been proposed as a better alternative in studies with rare events and multiple baseline characteristics (confounders),[24] as a tool for model adjustment. One study by Cepeda *et al.*[25] also showed that propensity score analysis performed better than logistic regression analysis alone in controlling for confounders, when there were seven or fewer events per baseline characteristic. In this study, the propensity score is obtained by using a logistic regression model, with exposure to general anesthesia or epidural or spinal anesthesia as the dependent variable, and all baseline characteristics as independent variables (patient's age, sex, operating procedure, the year of surgery, hypertension, diabetes, cerebrovascular disease, CHD, hyperlipidemia, surgeon's age, and hospital teaching status). The propensity score was then used as the only confounding variable, in association with exposure to general anesthesia or epidural or spinal anesthesia, to estimate the effect of mode of anesthesia

on the likelihood of SSI. A two-sided *P* value of less than 0.05 was considered statistically significant for this study.

Results

Table 1 presents the distribution of characteristics of patients, surgeons, and hospitals, according to the methods of anesthesia. The mean (±SD) age for the sampled patients was 62.6 (8.4) yr. The mean (±SD) age for patients who received general anesthesia was 61.4 (8.2) yr and for those who received epidural or spinal anesthesia was 63.8 (9.1) yr (*P* < 0.001). It also shows that patients who received epidural or spinal anesthesia were more likely to have comorbid hypertension (*P* < 0.001), diabetes (*P* = 0.003), hyperlipidemia (*P* < 0.001), and CHD (*P* = 0.031) than those receiving general anesthesia. Patients who received general anesthesia were more likely to be treated in a teaching hospital (*P* = 0.002) and by younger physicians (*P* = 0.003)

Table 2. Crude Odds Ratios (OR) for 30-day Surgical Site Infections (SSI) among Sampled Patients Who Underwent Total Knee Replacement or Total Hip Replacement in Taiwan, 2002–2006

Variable	Total Sample, n = 3,081		General Anesthesia, n = 1,191		Epidural or Spinal Anesthesia, n = 1,890	
	n	%	n	%	n	%
30-day SSI						
Yes	56	1.8	33	2.8	23	1.2
No	3,025	98.2	1,158	97.2	1,867	98.8
Crude OR (95% CI)			2.31 (1.35–3.96)		1.00	
Adjusted* OR (95% CI)			2.21 (1.25–3.90)		1.00	

* Adjustment for potential confounders (patient's age, sex, operating procedure, the year of surgery, hypertension, diabetes, cerebrovascular disease, coronary heart disease, hyperlipidemia, surgeon's age, and hospital teaching status) of the association between sampled patients who underwent total knee replacement or total hip replacement and 30-day SSI using propensity score analysis. Note that potential confounders are summarized in one single score (the propensity score).

CI = confidence interval.

compared with patients who received epidural or spinal anesthesia.

Table 2 shows the distribution of 30-day SSI according to the method of anesthesia. Patients who received general anesthesia had a higher 30-day rate of SSI than patients who received epidural or spinal anesthesia (2.8 *vs.* 1.2%, $P = 0.002$). The logistic regression analysis indicates that those patients who received general anesthesia were 2.31 (95% CI = 1.35–3.96, $P = 0.002$) times more likely to be rehospitalized for treatment of SSI within 30 days of the index hospitalization compared with their counterparts who received epidural or spinal anesthesia.

Table 2 also reveals that after adjusting for the patient's age, sex, operating procedure, the year of surgery, hypertension, diabetes, cerebrovascular disease, CHD, hyperlipidemia, surgeon's age, and hospital teaching status (these potential confounders were summarized in single propensity score), the odds ratio of SSI within 30 days of total hip or knee replacement was 2.21 (95% CI = 1.25–3.90, $P = 0.007$) for patients who received general anesthesia compared with those who received epidural or spinal anesthesia.

The appendix shows the ability of the regression model to balance the considered covariates. As the estimates (logarithm function of the odds ratio) approached zero, the considered covariates and patients with general anesthesia *versus* epidural or spinal anesthesia were not associated after the propensity score was adjusted. This induced a balance with respect to patients with general anesthesia *versus* those with epidural or spinal anesthesia. In addition, the propensity score model can easily distinguish differences between patients who received general anesthesia and those who received epidural or spinal anesthesia (the value of the C-index is 0.86).

Discussion

To our knowledge, this is the first study attempting to compare risk of SSI for patients receiving total hip or knee replacement under general anesthesia and those having the

procedure under epidural or spinal anesthesia. Our study shows for the first time that the odds of SSI within 30 days of surgery for patients who received total hip or knee replacement under general anesthesia were 2.21 times higher (95% CI = 1.25–3.90, $P = 0.007$) than those who had epidural or spinal anesthesia, after adjusting for the patient's age, sex, operation procedure, hypertension, diabetes, cerebrovascular disease, CHD, hyperlipidemia, surgeon's age, and hospital teaching status.

Several studies compared clinical outcomes for surgeries under general anesthesia with those under epidural or spinal anesthesia. In a most recent meta-analysis of 18 independent studies involving 1,239 patients receiving total hip arthroplasty, there was no sufficient evidence to show that epidural or spinal anesthesia decreased mortality, cardiovascular morbidity, or the incidence of deep vein thrombosis and pulmonary embolism compared with general anesthesia.[26] However, when combined with general anesthesia in patients undergoing elective major upper abdominal surgery, epidural anesthesia did contribute an additional effect of increasing tissue oxygen tension,[23] which was associated with lower incidences of SSI.[26]

Plausible mechanisms by which epidural or spinal anesthesia carries lower risk of SSI than general anesthesia remain to be explored. General anesthesia does not block afferent inputs and autonomic responses completely and thus would result in a higher level of stress responses.[27] The resulting vasoconstriction impairs tissue perfusion and decreases tissue oxygen tension.[28] Volatile anesthetics and opioids *per se* impair neutrophil, macrophage, dendritic cell, T-cell, and natural killer cell immune functions,[29] diminishing host defense mechanisms. On the other hand, epidural or spinal anesthesia provides a sympathetic blockade, and greater vasodilatation could result in improved tissue oxygenation,[22,23] increased polymorphonuclear cells at surgical sites,[30] and can better maintain regional normothermia.[31] Although a recent study denied the preventive effects of supplemental oxygen and perhaps tissue oxygenation on SSIs,[32] regional

normothermia and the absence of volatile anesthetic and opioid use in epidural or spinal anesthesia could still contribute to an environment strengthening the host defense against surgical pathogens. What makes the factors more powerful is that all of these potential benefits occur on induction of anesthesia, well before surgical incision and the decisive period of surgery, reducing the likelihood that contamination will progress to clinical infection. Together, these provide plausible mechanisms to explain our observation.

It is hardly self-evident that the effects of anesthetic management could last more than days or even hours after surgery because current anesthetics are uniformly short acting. In fact, long-term consequences of anesthesia were only critically considered in recent years as increasing evidence of the long-lasting effects of intraoperative anesthetic decisions emerge.[5] Our results lend support to the evolving concept of long-term consequences of anesthesia. Clinical implications are that anesthesia decisions might be incorporated into strategies for deterring SSI, intensifying the anesthesiologist's role in preventing SSI.[30]

Although our population-based dataset enables us to trace all SSIs, this study still suffers from a few limitations that should be addressed. First, the database did not contain information regarding patient characteristics such as tobacco use and body mass index, which would not be identified in this administrative database if not undergoing active medical management. Nor did our database contain anesthesia and surgical parameters, including the fraction of inspired oxygen in the anesthetic gas mixture (FIO_2), body temperature, duration of the surgical procedure, blood transfusions, postoperative antibiotic use, and status of postoperative pain control, all of which might relate to the risk of SSI. We assumed that effects of all of these factors were evenly distributed between groups and the estimated odds ratio would not be biased in a study with such a large sample size. We did not have information about whether patients who received general anesthesia had it combined with neuroaxial anesthesia. Nevertheless, we assumed that these rare cases, if there were any, would not bias the odds ratio estimation to any statistical significance. On the other hand, for our study, SSIs were defined as whether a patient was readmitted with a principal diagnosis of SSI within 30 days of the index hospitalization. Patients with the same diagnosis whose conditions were not serious enough to justify readmission were not included in this study. This could lead to an underestimation of the overall SSI rates. However, there is no reason for differential distribution, and an unbiased odds ratio could be expected. Finally, the use of retrospective data did not guarantee randomized allocation between groups. Although we have adjusted for some major determinants of anesthetic management, this nonrandomization might have some residual influence on the estimations and deserves further exploration.

Conclusions

We have found that the overall risk of SSI after total hip or knee replacement in Taiwan is 1.8% and that the odds for patients receiving total hip or knee replacement under general anesthesia are about 2.21 times higher than those who received epidural or spinal anesthesia. This finding seems to support previously proposed mechanisms for decreasing SSIs, including improved tissue oxygenation and maintained normothermia. Our results support the evolving concept of long-term consequences of anesthesia and emphasize the anesthesiologist's role in preventing SSIs.[30]

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Appendix

Appendix. Balance with Respect to Treatment

Variable	Log (Odds Ratio)	95% Confidence Interval	P Value
Patient characteristics			
Gender			
Female	0		
Male	−0.018	−0.215 to 0.179	0.982
Age	−0.024	−0.202 to 0.154	0.792
Hypertension	−0.051	−0.235 to 0.133	0.587
Coronary heart disease	−0.008	−0.298 to 0.281	0.955
Diabetes	−0.011	−0.256 to 0.233	0.929
Hyperlipidemia	−0.047	−0.401 to 0.307	0.794
Cerebrovascular disease	0.000	−0.368 to 0.369	0.999
Surgical procedure			
Unilateral	0		
Bilateral	−0.216	−0.522 to 0.100	0.170
Year of surgery			
2002	0		
2003	−0.006	−0.186 to 0.178	0.952
2004	−0.003	−0.191 to 0.182	0.973
2005	−0.002	−0.186 to 0.182	0.986
2006	0.000	−0.181 to 0.183	0.997
Surgeon characteristics			
Age (yr)	0.000	−0.200 to 0.198	0.998
Hospital characteristics			
Teaching status			
Yes	0.003	−0.186 to 0.191	0.973
No	0		

Each row corresponds to the logarithm function of odds ratio for the association between a covariate and patients with general anesthesia *vs.* those with epidural or spinal anesthesia after adjusting for propensity score.