General anaesthesia is associated with increased risk of surgical site infection after Caesarean delivery compared with neuraxial anaesthesia: a population-based study

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Background. This study compared the odds ratio (OR) of surgical site infection (SSI) within 30 days after operation with general anaesthesia (GA) or neuraxial anaesthesia (NA) in Taiwanese women undergoing Caesarean delivery (CD).

Methods. An epidemiologic design was used. The study population was based on the records of all deliveries in hospitals or obstetric clinics between January 2002 and December 2006 in Taiwan. Anonymized claim data from the Taiwan National Health Insurance Research Database (NHIRD) were analysed. Women who received CD were identified from the NHIRD by Diagnosis-Related Group codes. The mode of anaesthesia was defined by order codes. Multivariate logistic regression was used to estimate the OR and associated 95% confidence interval (CI) of post-CD SSIs for GA when compared with NA. The outcome was whether a woman had been diagnosed as having an SSI during the hospitalization or was re-hospitalized within 30 days after CD for the treatment of SSIs using five or 81 International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes.

Results. Among the 303 834 Taiwanese women who underwent CD during the 5 yr observation period, the 30 day post-CD SSI rate was 0.3% or 0.9% based on five or 81 ICD-9-CM codes. The multivariate-adjusted OR of having post-CD SSIs in the GA group was 3.73 (95% CI, 3.07–4.53) compared with the NA group (P<0.001) using five ICD-9-CM codes for the definition of SSI.

Conclusions. GA for CD was associated with a higher risk of SSI when compared with neuraxial anaesthesia.

Keywords: anaesthesia; Caesarean section; general anaesthesia; neuraxial anaesthesia; surgical site infection

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Despite a decline in birth rate, the rate of Caesarean delivery (CD) is increasing worldwide.1 The rate of CD in Taiwan was 34.59% in 2009,2 which is one of the highest in the world. CD is frequently complicated by surgical site infection (SSI),3,4 which increases maternal morbidity, mortality,5 and medical costs.6 With the increase in CD rates, SSI associated with CD may become a significant health and economic burden. Factors frequently thought to be associated with SSI after CD include numbers of prenatal consultations, obesity, premature rupture of membranes, diabetes, hypertension, history of previous CD, duration of surgery, and the use of prophylactic antibiotics.3,4,7–9 However, previous findings on predicting factors of SSI after CD have been inconsistent across studies.

General anaesthesia (GA) was reported to be associated with increased risk of SSI in individuals receiving total hip

Editor’s key points

• This is an important large study of the influence of anaesthetic technique on surgical site infection after Caesarean delivery.
• More than 300 000 notes were examined.
• Incidence of post-surgical infection within 30 days after surgery was 0.9%.
• The odds ratio of having infection was 3.7 when general anaesthesia was compared with neuraxial block.
or knee replacement, when compared with neuraxial anaesthesia (NA).\textsuperscript{10} To the best of our knowledge, the effects of different modes of anaesthesia on SSI have never been taken into consideration when examining predicting factors of SSI after CD. Compared with GA, NA for CD decreased blood loss\textsuperscript{11} and the duration of hospital stay,\textsuperscript{12} which, in turn, may decrease the risk of SSI.

In this study, we used a population-based, epidemiologic approach to examine the association of different modes of anaesthesia on the risk of SSI after CD. In particular, we compared the odds ratio (OR) of SSI within 30 days after operation between GA and NA [i.e. epidural anaesthesia (EA) or spinal anaesthesia (SA)] in Taiwanese women who underwent CD during a 5 yr period. We hypothesized that GA is associated with a higher odds of acquiring an SSI in women after CD when compared with NA.

**Methods**

**Data source**

The study used 2002–7 publicly available, anonymized data from the Taiwan National Health Insurance Research Database (NHIRD) provided by the National Health Research Institutes. The National Health Insurance programme provides a comprehensive benefit package covering preventive, dental, and medical services to all citizens in Taiwan. From the NHIRD, we obtained registries of medical institutions that contract with the Bureau of the National Health Insurance in Taiwan and monthly collect summaries for all claims with a principal International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and up to four secondary diagnoses being listed for each patient.

The study population was based on the records of all deliveries in hospitals or obstetric clinics between January 2002 and December 2006. Women who received CDs were identified from the database by Diagnosis-Related Group (DRG) codes 0371A (CD) and 0373B (maternally requested CD). For those women with multiple CDs during the observation period, only the first CD was counted. There were a total of 305,330 women who received CD during the observation period. The case notes were carefully inspected to screen for outliers. Subjects with an extremely short (<1 day, \(n=180\)) or long (>1000 days, \(n=2\)) hospital stay for the CD were identified and subsequently excluded. Women with extreme values of maternal age (i.e. younger than 16 yr or older than 50 yr, \(n=151\)) and women with missing data (\(n=1163\)) were further excluded, resulting in a total of 303,834 case notes.

**Definition of variables**

The independent variable of interest was the mode of anaesthesia, which was defined by the order codes for GA and for SA and EA. The primary outcome under investigation in this study was whether a woman had been diagnosed as having an SSI during the surgical hospitalization (i.e. CD) or re-hospitalized within 30 days after operation for the treatment of SSIs using five or 81 ICD-9-CM codes according to previous studies. One group of investigators defined post-CD SSI using five ICD-9-CM codes.\textsuperscript{7} Another group showed that identification of SSI could be enhanced by the use of 81 diagnosis codes.\textsuperscript{13}

We also extracted variables frequently associated with post-CD SSIs and variables that might influence an anaesthesiologist’s choice of mode of anaesthesia for women undergoing CD. These included the woman’s age in years, length of stay (LOS) in days, diabetes mellitus, chronic hypertension, pregnancy-related hypertension, premature rupture of membranes, fetal distress, previous CD, antepartum haemorrhage, preeclampsia/eclampsia, and CD by maternal request.

**Statistical analysis**

The SPSS statistics software, version 16.0 (SPSS Statistics, IBM Corporation, Somers, NY, USA), was used to perform the statistical analyses in this study. Continuous data were presented as mean (SD). Categorical data were presented as numbers and percentage. The Mann–Whitney \(U\)-tests, \(\chi^2\) tests, and the Kruskal–Wallis \(H\) tests were used to examine the differences among modes of anaesthesia. Univariable logistic regression was performed to estimate the OR and 95\% confidence interval (CI) of SSI for GA when compared with NA in women undergoing CD with SSI as a binary variable. Multivariable logistic regression was used to estimate the OR and associated 95\% CI of post-CD SSIs for GA when compared with NA in women undergoing CD after adjusting for various potential confounding variables. The analyses were performed with SSI defined by five ICD-9-CM codes and with SSI defined by 81 ICD-9-CM codes, respectively. As aforementioned, variables were selected for inclusion in the model based on the clinical plausibility that they would have an effect on an anaesthesiologist’s choice of the mode of anaesthesia for women undergoing CD or variables frequently associated with post-CD SSIs and therefore may explain the differences in the incidence of SSI between modes of anaesthesia. These variables included age, diabetes mellitus, chronic hypertension, pregnancy-related hypertension, premature rupture of membranes, fetal distress, previous CD, CD by maternal request, antepartum haemorrhage, and preeclampsia/eclampsia. As all variables are of clinical relevance and were significantly different between modes of anaesthesia, they were forced into the first multivariable logistic regression model. Because LOS was found to be significantly different between modes of anaesthesia, in the second model, we adjusted all the above-mentioned variables and LOS as well.

**Results**

Among the 303,834 women who underwent CD during the 5 yr observation period, 12,531 (4.1\%) women received GA whereas 95.9\% of the parturients under study received SA or EA. The GA group was slightly older, had longer LOS, had more parturients with a history of diabetes or hypertension, had more parturients with fetal distress, antepartum...
haemorrhage, premature rupture of membranes, or preeclampsia, had less CDs by maternal request, and less previous CDs than the NA group (all \( P < 0.001 \); Table 1). A comparison of the sample characteristics among the GA, EA, and SA groups also revealed significant group differences in all variables compared (all \( P < 0.001 \); Table 1). These potentially confounding variables were later adjusted in the multivariable logistic regression models.

The overall 30 day SSI rate was 0.3% in women who underwent CDs using five-code methodology. The GA group had a significantly higher SSI rate than the NA group (\( P < 0.001 \); Table 2). Using the 81 additional diagnosis codes that constitute indicators for SSI after CD, the overall 30 day SSI rate was 0.9%. The post-CD 30 day SSI rates for GA, EA, and SA were 1.9%, 1.0%, and 0.7%, respectively (Table 2).

The unadjusted ORs of SSI were 4.51 and 2.61 for the GA group when compared with the SA group (both \( P < 0.001 \); Table 3). The ORs of having SSIs were 4.21 (95% CI, 3.45–5.14) and 2.35 (2.04–2.70), respectively, using the two definitions for SSI, for the GA group when compared with the SA group (both \( P < 0.001 \)) after adjusting for age, diabetes mellitus, hypertension, fetal distress, antepartum haemorrhage, premature rupture of membranes, CD by maternal request, preeclampsia/eclampsia, and a history of previous CD depending on the definitions for SSI (data not shown). The likelihood of having SSIs was not significantly different between the EA and the SA groups using the five ICD-9 codes for the definition of SSI. However, the likelihood of having SSIs was significantly higher for the EA group when compared with the SA group using the five ICD-9 codes for the definition of SSI (data not shown). After adjusting the multivariate regression models for LOS, the results were largely unchanged (Table 3).

Because the ORs of SSI were not significantly different between the EA and SA groups using the five ICD-9 codes for the definition of SSI, the two groups were combined in subsequent analyses. Examined by univariable logistic regression, the OR of having post-CD SSIs was 4.37 times as high in the GA group compared with the NA group (\( P < 0.001 \); data not shown). After adjusting the multivariable regression models for LOS, the results were largely unchanged (Table 3).

### Discussion

The observed 30 day SSI rate after CD in Taiwan, 0.3%, defined by five ICD codes suggested by Olsen and colleagues,\(^7\) is lower than those reported in the literature\(^3\) \(^4\).
and the pooled mean rate of 3.15% (2.71–7.53%) reported by the Centre for Disease Control and Prevention’s National Nosocomial Infections Surveillance System in the USA.14 By including disease codes that constitute SSI indicators suggested by another group,13 we found a 30 day SSI rate after CD of 0.9%. Taiwanese women’s high utilization of free prenatal care covered by the Taiwan’s National Health Insurance programme could partially explain for the low SSI rate after CD. However, the 30 day SSI rate for CD reported in the current study was probably underestimated because only inpatient claim data were used for data analysis. There could be superficial incisional infections that were treated in the outpatient settings and hence were not accounted for. On the other hand, the use of 81 ICD-9-CM codes to extract SSI cases could also result in an overestimation of the SSI rate as in a previous study only 68% of CD claims, and thus data on prenatal and maternal characteristics addressing. First, this study analysed data from insurance claims, and thus data on prenatal and maternal characteristics may very likely be associated with SSI were generally lacking. For example, factors that could have an effect on SSI including maternal obesity,7 type of skin closure,7 duration of surgery,8 and prenatal visits8 were not available for analysis and thus were not accounted for when examining the relationship between the mode of anaesthesia and SSI. Secondly, GA is much more likely to be used for emergency CD which is thought to be a risk factor for post-CD SSI. As we were unable to differentiate emergency from elective procedures, ‘maternal requested CD’ was extracted and controlled for in the multivariable regression models instead. Nevertheless, there was evidence indicating no significant difference in the SSI rate between elective and emergency CD.21 Thirdly, as aforementioned, only inpatient claim data were analysed, and therefore, the 30 day SSI rate might be underestimated. Finally, in this study, list-wise deletion was performed to handle missing data instead of imputing missing data. Of the

<table>
<thead>
<tr>
<th>Mode of anaesthesia</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 day SSI based on five ICD-9-CM codes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Unadjusted</td>
<td>4.51</td>
<td>3.71–5.48</td>
<td>&lt;0.001</td>
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<tr>
<td>General Multivariate adjusted1</td>
<td>3.82</td>
<td>3.12–4.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epidural Unadjusted</td>
<td>1.10</td>
<td>0.94–1.28</td>
<td>0.24</td>
</tr>
<tr>
<td>Epidural Multivariate adjusted1</td>
<td>1.08</td>
<td>0.92–1.26</td>
<td>0.37</td>
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<tr>
<td>Spinal General</td>
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<tr>
<td>General Unadjusted</td>
<td>4.37</td>
<td>3.62–5.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>General Multivariate adjusted1</td>
<td>3.73</td>
<td>3.07–4.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Spinal Unadjusted</td>
<td>1.38</td>
<td>1.27–1.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Spinal Multivariate adjusted1</td>
<td>1.36</td>
<td>1.25–1.48</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Prolonged hospital stay has been identified as a risk factor for SSI and nosocomial infections. Alternatively, prolonged hospital stay may be a result of SSI. When duration of hospital stay was added into the regression model, the risk of SSI associated with GA was only slightly reduced, suggesting that other mechanisms were involved.

Mechanisms underlying the differential impact of the modes of anaesthesia on post-CD SSIs are largely unknown. Previously, it has been argued that GA is associated with greater immunosuppression and host defence impairment compared with SA or EA.15 16 However, a recent study found that differences in the mode of anaesthesia did not affect the concentrations of serum cytokines (interleukin-6 or tumour necrosis factor-alpha) in parturients undergoing elective CD.17 Another plausible mechanism by which NA could reduce SSIs is by providing sympathetic block18 19 and thereby vasodilatation and greater surgical site tissue oxygenation. CD has become one of the most common surgical procedures. Given the risk associated with surgery and anaesthesia, clinical decisions on deliveries should be guided by best-practice guidelines. However, the choice of anaesthesia modes has not always been based on medical indications and clinical practice guidelines. There are instances where anaesthesiologists’ and/or obstetricians’ individual preferences outweigh clinical indications. The strength of the study was that a population-based epidemiologic approach was used to elucidate the association of modes of anaesthesia with the 30 day SSI rate after CD. Clinicians and future parturients should be informed by findings of this study, so that informed decisions can be made.

Recent publications demonstrated that GA increased the odds of stroke in preeclamptic women after CD20 and that of SSI in individuals receiving total hip or knee replacements,10 when compared with NA. Our data also support that GA may be associated with long-term consequences and warrant further investigations.

There are certain limitations in this study that need to be addressed. First, this study analysed data from insurance claims, and thus data on prenatal and maternal characteristics that may very likely be associated with SSI were generally lacking. For example, factors that could have an effect on SSI including maternal obesity,7 type of skin closure,7 duration of surgery,8 and prenatal visits8 were not available for analysis and thus were not accounted for when examining the relationship between the mode of anaesthesia and SSI. Secondly, GA is much more likely to be used for emergency CD which is thought to be a risk factor for post-CD SSI. As we were unable to differentiate emergency from elective procedures, ‘maternal requested CD’ was extracted and controlled for in the multivariable regression models instead. Nevertheless, there was evidence indicating no significant difference in the SSI rate between elective and emergency CD.21 Thirdly, as aforementioned, only inpatient claim data were analysed, and therefore, the 30 day SSI rate might be underestimated. Finally, in this study, list-wise deletion was performed to handle missing data instead of imputing missing data. Of the

Table 3 Mode of anaesthesia in predicting 30 day SSI. *Tested by logistic regression. †30 day SSI refers to SSIs occur during the surgical hospitalization or re-hospitalization within 30 days after operation identified using five ICD-9-CM codes. ‡Adjusted for age, diabetes mellitus, hypertension, fetal distress, antepartum haemorrhage, premature rupture of membranes, Caesarean section by maternal request, preeclampsia/eclampsia, previous Caesarean section, and length of hospital stay. 30 day SSI refers to SSIs occur during the surgical hospitalization or re-hospitalization within 30 days after operation identified using 81 SSI indicators. OR, odds ratio; CI, confidence interval.
1163 cases with missing data, 870 had missing data on the date of discharge from the hospital (necessary for the calculation of LOS), 290 had missing data on the mode of anaesthesia, and three had missing data on both variables. Because imputation might not be suitable for these two variables, we decided to perform list-wise deletion instead. The 30 day SSI rates of the 1163 cases were 0.3% based on five ICD-9-CM codes and 1.5% based on 81 ICD-9-CM codes, which were similar to those of the study sample (data not shown).

In conclusion, the incidence of SSI was about 0.3–0.9% in Taiwanese women undergoing CD, with an observation period of 30 days after operation. About four in 100 women who underwent CD received GA for the delivery. GA for CD was associated with a higher risk of SSI when compared with NA.

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Conflict of interest
None declared.

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