

OBSTETRICS

Differential impacts of modes of anaesthesia on the risk of stroke among preeclamptic women who undergo Caesarean delivery: a population-based study

C.-J. Huang^{1,2,3}, Y.-C. Fan¹ and P.-S. Tsai^{4,5,6*}

¹ Department of Anaesthesiology, Buddhist Tzu Chi General Hospital, Taipei Branch, 289, Jianguo Rd, Sindian City, Taipei County 231, Taipei, Taiwan

² School of Medicine, Tzu Chi University, 701, Zhongyang Rd, Sec. 3, Hualien 970, Taiwan

³ Department of Pharmacology, College of Medicine and ⁴ Graduate Institute of Nursing, College of Nursing, Taipei Medical University, 250 Wu Hsing St., Taipei 110, Taiwan

⁵ Department of Nursing, Taipei Medical University-Wan Fang Hospital, 111, Section 3, Hsing-Long Rd, Taipei 116, Taiwan

⁶ Sleep Science Center, Taipei Medical University Hospital, 252 Wu-Hsing St., Taipei 110, Taiwan

* Corresponding author. E-mail: ptsai@tmu.edu.tw

Key points

- General anaesthesia for Caesarean section (CS) was associated with decreased stroke-free survival rate in preeclamptic women, compared with neuraxial anaesthesia.
- The post-partum stroke rate was not significantly different between spinal and epidural anaesthesia in preeclamptic women undergoing CS.
- Among preeclamptic women, the risk of stroke after general compared with neuraxial anaesthesia over a 1–6 yr follow-up period was 2.38 times after adjustment for confounders.

Background. This study compared the stroke-free survival rates and hazard ratios (HRs) for stroke between preeclamptic women who received general anaesthesia and those who received neuraxial anaesthesia for Caesarean section (CS).

Methods. This study used 2002–7 data from the Taiwan National Health Insurance Research Database. The stroke-free survival rate was estimated by the Kaplan–Meier method. The log-rank test was used to examine the difference in the stroke-free survival rates between general, spinal, and epidural anaesthesia. The Cox proportional hazard regression was used to estimate the HR for general anaesthesia.

Results. A total of 303 862 women underwent CS of which 8567 had preeclampsia (75 stroke cases) and 295 295 did not (303 stroke cases). The stroke-free survival rate was significantly lower in the preeclamptic women who received general anaesthesia when compared with those who received epidural ($P=0.008$) or spinal anaesthesia ($P<0.001$) within the 6 yr period after the index delivery. There was no statistically significant difference between spinal and epidural anaesthesia in terms of stroke rate ($P=0.143$). The unadjusted HR of stroke for general anaesthesia was 2.81 [95% confidence interval (CI), 1.69–4.64; $P<0.001$]. After adjusting for potential confounders, the adjusted HR for general anaesthesia was 2.38 (95% CI, 1.33–4.28; $P=0.004$) compared with neuraxial anaesthesia over a 1–6 yr follow-up period.

Conclusions. In this study, general anaesthesia for CS delivery was associated with increased risk of stroke when compared with neuraxial anaesthesia in preeclamptic women.

Keywords: anaesthesia; Caesarean section; preeclampsia; stroke

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Preeclampsia is characterized by the onset of hypertension (i.e. systolic arterial pressure ≥ 140 mm Hg or diastolic arterial pressure ≥ 90 mm Hg for two readings at least 4 h apart) after 20 weeks gestation accompanied by renal (e.g. proteinuria) or haematological and liver involvement.¹ Proteinuria is confirmed by the presence of a 24 h urinary protein excretion in excess of 0.3 g dl^{-1} . Preeclampsia remains one of the leading causes of maternal mortality worldwide.²

Anaesthesiologists use their judgement in selecting the appropriate anaesthesia for the severely preeclamptic women requiring Caesarean section (CS). Neuraxial

anaesthesia for CS is preferable to general anaesthesia given the risks of aspiration, failed intubation, and unstable haemodynamics associated with general anaesthesia in the preeclamptic parturient.^{3–4} Although epidural anaesthesia can be used,^{5–7} the recommended technique in the haemodynamically stable parturient with preeclampsia is spinal anaesthesia.^{8–10} There are also instances in which neuraxial anaesthesia is relatively or absolutely contraindicated and therefore general anaesthesia may be required.^{3–4} Moreover, evidence suggests that general and regional anaesthetic methods are equally acceptable for CS in pregnancies

complicated by severe preeclampsia, provided a careful approach is adopted.¹¹

Preeclampsia is associated with increased risk of stroke in later life.¹² In addition, data from a population-based study in Taiwan revealed that women with preeclampsia have increased risk of stroke during pregnancy and the first postpartum year.¹³ Caesarean delivery has also been demonstrated to be a strong and significant predictor of post-partum stroke over a 12 month period in a population-based study in Taiwan.¹⁴ The long-term effects of different modes of anaesthesia in terms of the incidence of maternal postoperative complications are largely unknown. We investigated the impact of general, spinal, and epidural anaesthesia on the risk of stroke, including cerebrovascular complications of the puerperium and stroke in later life, in preeclamptic patients who undergo CS delivery in Taiwan. Because general anaesthesia has been associated with unstable haemodynamic and increased neuroendocrine stress responses to Caesarean delivery in women with severe preeclampsia,¹⁵ it was hypothesized that general anaesthesia is associated with a greater risk of stroke when compared with neuraxial anaesthesia (i.e. epidural and spinal anaesthesia) in preeclamptic women who undergo Caesarean delivery.

Methods

Data sources

The study used 2002–7 anonymized data from the Taiwan National Health Insurance Research Database (NHIRD) that was published by the National Health Research Institutes and released for public access for research purposes.

Initiated in March 1995, the National Health Insurance (NHI) program, in which the government is the sole insurer, provides a comprehensive benefit package covering preventive, dental, and medical services to all citizens in Taiwan. The NHI program provides universal coverage and access to any medical institution of the individual patient's choice. The NHIRD provides registries of medical institutions that contract with the Bureau of the NHI in Taiwan and monthly claim summaries for all inpatient 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.

Study sample

The study sample was based on the records of deliveries in hospitals or obstetric clinics between January 2002 and December 2006. CS delivery cases were identified from the database by drug-related group (DRG) codes 0371A (CS delivery) and 0373B (maternally requested CS delivery). For those women with multiple Caesarean deliveries during the observation period, only the first CS was counted. There were a total of 305 330 cases of CS. These CSs were carefully inspected to screen for outliers. Two subjects with a peculiarly long hospital stay for the Caesarean delivery (>1000 days) were identified and subsequently excluded. To ease comparison between our study and a previous

study,¹³ subjects with extreme values (i.e. younger than 16 yr or older than 49 yr, $n=155$) of maternal age were excluded as in the previous study. Subjects with a history of stroke ($n=150$) and subjects with missing data ($n=1161$) were further excluded, resulting in a total of 303 862 CSs.

Individuals diagnosed with preeclampsia were identified from the database by ICD-9-CM codes 642.4–642.7. A total of 8567 cases (2.82%) were identified.

Definition of variables

The independent variable of interest was the mode of anaesthetic procedure, which was defined by the order codes (96020C–96022C for general anaesthesia; 96007C and 96008C for spinal anaesthesia; 96005C and 96006C for epidural anaesthesia). The endpoint under investigation in this study was whether an individual had been hospitalized for the treatment of any type of stroke (ICD-9-CM codes 430–438, 671.50–671.54, and 674.0–674.04). To identify all stroke cases, each case was tracked from the index date (admission date for the delivery) until the end of 2007. For those who suffered from multiple stroke events, only the first stroke event after delivery was included. The stroke-free survival time was defined as the period between the index delivery and admission for any type of stroke.

To determine the impact of mode of anaesthesia on the risk of stroke, it is important to take into consideration the influences of possible confounding variables. We thus extracted variables frequently associated with peri- and postpartum stroke.^{13 14 16} These included the patient's age in years, multiple gestation (ICD-9-CM code 651), comorbidities [diabetes mellitus (ICD-9-CM codes 648.0, 250), chronic hypertension (ICD-9-CM codes 401–405), pregnancy-related hypertension (ICD-9-CM codes 642.0–642.3, 642.9, 760.0), antepartum haemorrhage (ICD-9-CM codes 641, 640.9), postpartum haemorrhage (ICD-9-CM codes 666, 667, 669.1), hyperlipidaemia (ICD-9-CM code 272), disorders of fluid/electrolytes/acid–base balance (ICD-9-CM code 276), heart disease (ICD-9-CM codes 393–398, 424), and thrombophilia (ICD-9-CM codes 273.8, 286.9, V12.51, 286.5, 289.8, 289.9, 795.79)], and history of CS (ICD-9-CM code 654.2).

The length of hospital stay for the delivery in days, whether a patient had been admitted to the intensive care unit (ICU; order codes 03010E, 03011F, 03012G, and 03013H), and the severity of preeclampsia were also extracted. To classify the severity of preeclampsia, all preeclampsia cases were recoded into two categories: mild (ICD-9-CM 642.4: mild preeclampsia) and severe (ICD-9-CM 642.5: severe preeclampsia; ICD-9-CM 642.6: eclampsia and ICD-9-CM 642.7: preeclampsia or eclampsia with complications).

Statistical analysis

The Statistical Package for the Social Sciences, version 16.0 (SPSS Inc., Chicago, IL, USA) was used to perform the statistical analyses in this study. The Mann–Whitney U -tests and χ^2 tests were used to examine the differences between modes of anaesthesia. The stroke-free survival rate was estimated by

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