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Research paper

Perioperative risk factors for postpartum pulmonary embolism in Taiwanese Cesarean section women

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ABSTRACT

Objective: To explore the perioperative risk factors for predicting postpartum pulmonary embolism (PE) in Taiwanese women with Cesarean section (CS) delivery.
Methods: Data from Taiwan Longitudinal Health Insurance Database were analyzed. All CS women (2002–2007) in Taiwan, according to Diagnosis-Related Group codes, were included. Women having postpartum PE were identified by the diagnosis codes of PE from the medical records within 40 days after CS. Risk factors were analyzed using multivariate logistic regression.
Results: A total of 285,043 women who received CS between 2002 and 2007 were analyzed. Among them, 44 women were diagnosed as having postpartum PE. The overall incidence of postpartum PE was 0.154 per 1000 CS women. Analysis revealed that the perioperative risk factors for predicting postpartum PE in CS women included chronic heart disease (adjusted odds ratio [OR] = 89.92, 95% confidence intervals [CI] = 41.34–195.60, $P < 0.001$), systemic lupus erythematosus (adjusted OR = 45.05, 95% CI = 7.56–268.40, $P < 0.001$), postpartum hemorrhage (adjusted OR = 3.20, 95% CI = 1.10–9.31, $P = 0.033$), postpartum blood transfusion (adjusted OR = 8.92, 95% CI = 4.17–19.09, $P < 0.001$) and postpartum infection (adjusted OR = 7.13, 95% CI = 2.93–17.38, $P < 0.001$). Of note, anesthetic mode was not a risk factor for predicting postpartum PE in CS women, as women receiving general anesthesia for CS delivery were not associated with an increased risk of developing postpartum PE comparing to those who received neuraxial anesthesia (adjusted OR = 1.28, 95% CI = 0.52–3.14, $P = 0.591$).
Conclusions: Chronic heart disease, systemic lupus erythematosus, postpartum hemorrhage, postpartum blood transfusion and postpartum infection, but not anesthetic mode, were strong perioperative risk factors for predicting postpartum PE in Taiwanese CS women.

1. Introduction

Pulmonary embolism (PE), a severe form of venous thromboembolism and a rare but potentially fatal disorder, remains a major cause of maternal mortality despite the tremendous progresses in modern obstetrical practices.[1,2] The risk of PE in pregnant women is four to five times higher than those who are not pregnant.[3,4] The risk of PE further increased during the postpartum period.[3,4] What's more, the incidence of postpartum PE is much higher with Cesarean section (CS) delivery than with vaginal delivery.[5,6] Many risk factors for PE have been identified for women during pregnancy and the puerperium period.[7] However, PE was thought to be relatively uncommon for Asian population and very few data are available regarding the perioperative risk factors of postpartum PE in Asian women undergoing CS delivery.

The etiology of PE during pregnancy is multifactorial. Crucial mechanisms include gradual activation of the hemostatic system, progressive development of hormonally-induced regional stasis of blood flow and pelvic venous compression from the enlarging uterus.[8,9] The impacts of these mechanisms reach a peak in late pregnancy.[10] For women undergoing CS delivery, surgery can further enhance hypercoagulability, as tissue damage,

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catecholamine release and systemic inflammatory responses resultant from surgery synergistically activate coagulation factors and platelets.[11–13] Surgery can also decrease deep vein blood flow in legs and aggravate regional stasis.[14] These mechanisms provide rational explanations for the clinical observation of higher incidences of postpartum PE in CS women.

Identification of high risk patients and provision of timely therapeutic interventions is the key element for successful management of PE.[10] Therefore, we conducted this large, comprehensive population-based study aimed at identifying the perioperative risk factors for predicting postpartum PE in Taiwanese CS women.

2. Materials and methods

2.1. Ethics

Ethical approval for this study (Protocol Number: 02-X11-025) was provided by the Institutional Review Board of Taipei Tzu Chi Hospital, Taipei, Taiwan. This study complies with "Personal Information Protection Act" in Taiwan and was exempt from full review by the Institutional Review Board of Taipei Tzu Chi Hospital.

2.2. Data source

This study used anonymized data from the Taiwan National Health Insurance Research Database (NHIRD) that was published by the National Health Research Institutes (NHRI) and released for public access for research purposes. The National Health Insurance (NHI) program in Taiwan is a single-payer payment system with the government as the sole insurer. The NHI program provides a comprehensive benefit package covering preventive, dental and medical services to all the 23 million residents of Taiwan. The NHI program provides universal coverage and access to any medical institution of the individual patient's choice. According to the NHRI, all data that could be used to identify the patients or the care providers or medical institutions were encrypted before entry into the NHIRD, and were further encrypted by the NHRI before being released to researchers.

2.3. Study sample

In this analysis, the CS cohort was defined from medical records, between January 2002 and December 2007, as all women ascribed to Diagnosis-Related Group (DRG) codes of CS (0371A) and maternally requested CS (0373B). Those who aged under 16 or over 50 years were excluded from the data set. Previous data indicated that the risk for postpartum venous thromboembolism remains high for up to 6 weeks after delivery.[4] Thus, the follow-up for CS cohort was conducted up to 40 days after CS or until their withdrawal from the NHI program.

2.4. Definition of variables

The diagnosis of PE was identified from the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes (Table 1). CS women with the PE diagnostic code on their discharge with CS history within 40 days were identified as the PE CS cohort and those without the PE diagnostic code were identified as the non-PE CS cohort. Based upon previous studies reporting the risk factors of PE or venous thromboembolism,[5,6] we also extracted and factored into the analysis information regarding CS women's demographic characteristics, medical comorbidities, pregnancy characteristics, delivery complications and anesthetic mode from NHIRD by using the ICD-9-CM diagnosis and order codes (Table 1). For factors regarding pregnancy characteristics and delivery complications, we only extracted those at the time of the index pregnancy or the index CS. Postpartum blood transfusion and postpartum infection (including urinary tract infection) were recognized as the related diagnosis codes on the discharge records from the index CS or within 40 days after the index CS.

2.5. Statistical analyses

We performed Chi-square test to compare the differences in sample characteristic distributions, including baseline demographic characteristics, medical comorbidities, pregnancy characteristics, anesthetic mode and delivery complications, between the PE CS cohort and the non-PE CS cohort. All variables with a P value of less than 0.2 in univariate logistic regression were subsequently included in the multivariate logistic regression models to identify the predicting factors for postpartum PE in CS cohort. The Statistical Package for the Social Sciences, version 16.0, for windows (SPSS, Inc., Chicago, IL, USA) was used for statistical analyses.

3. Results

A total of 44 patients were identified as the PE CS cohort and 284,999 were identified as the non-PE CS cohort (Fig. 1). The overall incidence rate of postpartum PE was 0.154 per 1000 CS women.

The differences in baseline demographic characteristics, medical comorbidities, pregnancy characteristics, anesthetic mode and delivery complications between the PE and non-PE CS cohorts were summarized in Table 2. Compared to the non-PE CS cohort, the PE CS cohort had significantly higher incidences of chronic heart disease (including rheumatic heart disease, chronic rheumatic pericarditis, endocarditis and diseases of aortic valve, mitral valve, tricuspid valve or other endocardial structure) ($P < 0.001$), systemic lupus erythematosus ($P < 0.001$), preeclampsia ($P = 0.004$), early or threatened labor ($P = 0.003$), postpartum hemorrhage ($P < 0.001$), postpartum blood transfusion ($P < 0.001$), postpartum infection (including urinary tract infection) ($P < 0.001$) and receiving general anesthesia ($P < 0.001$).

All variables that presented in Table 2 with a P value of less than 0.2 in univariate logistic regression were further analyzed to elucidate the risk factors for predicting postpartum PE in CS cohort (Table 3). Analysis revealed that the crucial risk factors for predicting postpartum PE in CS women included chronic heart disease chronic heart disease (adjusted odds ratio [OR] = 89.92, 95% confidence intervals [CI] = 41.34–195.60, $P < 0.001$), systemic lupus erythematosus (adjusted OR = 45.05, 95% CI = 7.56–268.40, $P < 0.001$), postpartum hemorrhage (adjusted OR = 3.20, 95% CI = 1.10–9.31, $P = 0.033$), postpartum blood transfusion (adjusted OR = 8.92, 95% CI = 4.17–19.09, $P < 0.001$) and postpartum infection (adjusted OR = 7.13, 95% CI = 2.93–17.38, $P < 0.001$). Of note, preeclampsia, early or threatened labor and general anesthesia were not significant risk factors for predicting postpartum PE in CS women (all $P > 0.05$, Table 3).

4. Discussion

Impacts of a wide range of potential risk factors, including demographic characteristics, medical comorbidities, pregnancy characteristics, delivery complications, and anesthetic mode, were comprehensively investigated in this population-based study. Data from this large, national cohort study of nearly 300,000 CS deliveries over a 6-year period revealed that the overall incidence rate of postpartum PE was 0.154 per 1000 CS deliveries in Taiwan. This study further demonstrated that chronic heart disease, systemic

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