学位論文の要旨

Anesthesia for cesarean section and postpartum cardiovascular events in congenital heart disease: a retrospective cohort study

（先天性心疾患合併妊娠帝王切開の麻酔方法と分娩後母体心血管イベントの関係に関する後ろ向き観察研究）

June, 2022

（ 2022 年 6 月 ）

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https://doi.org/10.1053/j.jvca.2020.11.042

1. Introduction

Given the advances in the management of congenital heart disease during the last few decades, it has become common for women with congenital heart disease to become pregnant (van der Linde et al., 2011; Whittemore et al., 1982). Pregnancy causes tremendous changes in hemodynamics (Sanghavi and Rutherford, 2014) and could result in decreased cardiac function, particularly in women with congenital heart disease. Compared with the general population, a higher proportion of women with congenital heart disease undergo cesarean section for cardiac indications (Hayward et al., 2017; Hrycyk et al., 2016).

In pregnant women without heart disease, neuraxial anesthesia is the preferred technique for cesarean section due to difficulties in airway management and the desire to minimize the use of systemic medications that can be transferred to the fetus (Bucklin et al., 2005; Djabatey and Barclay, 2009; Kodali et al., 2008). For pregnant women with heart disease or congenital heart disease, neuraxial anesthesia is usually favored over general anesthesia (Goldszmidt et al., 2010; Hidano et al., 2011; Maxwell et al., 2013; Warrick et al., 2015). However, there have been no randomized controlled studies to determine which anesthetic technique is superior in parturients with high cardiac risk. Moreover, some parturients with congenital heart disease cannot avoid general anesthesia because of contraindications to neuraxial anesthesia, emergent surgery, or the need for invasive monitoring. Therefore, clarifying the effect of these anesthetic techniques might help reduce maternal and neonatal complications after cesarean section.

The aim of the study was to compare the incidence of postpartum cardiovascular events in parturients with congenital heart disease who received general *versus* neuraxial anesthesia. We also investigated the association between the anesthetic technique and neonatal condition after delivery.

2. Methods:

The institutional research and ethics committee waived the requirement for patient consent due to its retrospective design and approved the study before medical record review began (Study No. R19094).

This retrospective cohort study included parturients with congenital heart disease who underwent cesarean section between 1994 and 2019. We compared maternal and neonatal outcomes by the anesthetic technique (general *versus* neuraxial anesthesia). The primary outcome was a composite postpartum cardiovascular event including all-cause death and new-onset or worsening heart failure, pulmonary hypertension, sustained or non-sustained arrhythmia, and thromboembolic complications that required treatment with intravenous or oral medication or electrical defibrillation. Secondary outcomes consisted of maternal respiratory events, neonatal all-cause death, neonatal intubation, Apgar score, and umbilical arterial pH. Composite neonatal outcomes included neonatal intubation and low Apgar score. Primary or secondary outcomes could include events that occurred up to 1 week after cesarean section. The association between the anesthetic technique, composite postpartum cardiovascular events, and neonatal outcome was analyzed using generalized linear mixed models, assuming a binomial distribution (i.e., mixed-effects logistic regression) with a random intercept for each modified World Health Organization (WHO) classification for maternal cardiovascular risk (Regitz-Zagrosek et al., 2018).

3. Results

Among 263 cesarean sections, general anesthesia and neuraxial anesthesia was performed in 47 (17.9%) and 214 (81.3%) parturients, respectively. Cardiovascular events were more common in the general anesthesia group (n=7; 14.9%) than in the neuraxial anesthesia group (n=17; 7.9%) (Table 1). Generalized linear mixed models assuming a binomial distribution with a random intercept for each modified WHO classification for maternal cardiovascular risk revealed that general anesthesia is not significantly associated with cardiovascular events (odds ratio [OR], 1.00; 95% confidence interval [CI], 0.30–3.29) (Table 2). In addition, general anesthesia was associated with composite neonatal outcomes (Apgar score <7 at 1 or 5 minutes or need for neonatal intubation; OR, 13.3; 95% CI, 5.52–32.0).

4. Discussion

Our main results are not consistent with a prior systematic review of case reports that suggest higher maternal mortality with general anesthesia and improved outcomes with neuraxial anesthesia; however, this systematic review could not exclude selection bias due to sicker parturients receiving general anesthesia (Bédard et al., 2009). The mixed-effects logistic regression models adjusted for major confounders make the present study more reliable.

Regarding neonatal outcomes, the OR for the association between general anesthesia and adverse composite neonatal outcomes was high. This result was not consistent with a previous systematic review that showed no significant difference between the two anesthetic techniques in terms of neonatal outcomes (Afolabi and Lesi, 2012). The differences may be attributed to the manner of general anesthesia induction in parturients with congenital heart disease. Induction of general anesthesia in parturients with high cardiac risk took more time than in the general population. Blunting the hemodynamic response at intubation and during surgery is crucial for maintaining hemodynamic stability in parturients with cardiac disease. Especially during induction, titration of anesthetics and analgesics can achieve hemodynamic stability more easily than rapid sequence induction. Adequate doses of anesthetics and analgesics to prevent noxious responses during intubation in parturients often cause neonatal depression. Therefore, neonatal outcomes were worse in the general anesthesia group. However, an adequate dose for a parturient might outweigh the risk of neonatal depression because fetal well-being depends on the maintenance of maternal hemodynamic stability and the effects of anesthetics and opioid analgesics on the fetus could be reversible (Moir, 1970).

The choice of neuraxial or general anesthesia should be tailored for each parturient to maintain hemodynamic stability after considering the risks and benefits of both anesthetic techniques (Bishop L, 2018). Since we did not find significant associations between increased maternal risk and the anesthetic technique, both anesthetic techniques may be acceptable, especially general anesthesia when there are contraindications to neuraxial anesthesia, emergency surgery, or the need for invasive monitoring. Moreover, the choice of anesthetic technique should be made with the consideration that general anesthesia is associated with a higher risk of neonatal intubation or lower Apgar scores based on our results.

In conclusion, we showed that the anesthetic technique is not significantly associated with postpartum composite cardiovascular events and that general anesthesia is significantly associated with an increased need for intubation and lower Apgar scores in neonates.

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List of the published papers

I Main paper

Anesthesia for cesarean section and postpartum cardiovascular events in congenital heart disease: a retrospective cohort study

Tsukinaga, A., Yoshitani, K., Kubota, Y., Kanemaru, E., Nishimura, K., Ogata, S., Nakai, M., Tsukinaga, R., Kamiya, C., A., Yoshimatsu, J., Ohnishi, Y.: Journal of Cardiothoracic and Vascular Anesthesia, 35(7), 2108–2114, 2021

II Sub-paper

None

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