

# 学位論文の要約

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 )

Akito Tsukinaga

月永 晶人

Department of Anesthesiology,

Yokohama City University Graduate School of Medicine

横浜市立大学 大学院医学研究科 生体制御・麻酔科学

( Research Supervisor: Kenji Yoshitani )

( Department of Anesthesiology, National Cerebral and Cardiovascular Center )

( 研究指導教員: 吉谷 健司 先生 )

( Doctoral Supervisor Advisor: Takahisa Goto, Professor )

( 指導教員: 後藤 隆久 教授 )

# 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)

<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.

Table 1. Postpartum outcomes in patients receiving neuraxial anesthesia or general anesthesia.

	Neuraxial anesthesia (n=214)	General anesthesia (n=47)	P value
All-cause death	0	0	

Cardiovascular event	17 (7.9%)	7 (14.9%)	0.16
Heart failure	7	5	
Pulmonary hypertension	3	2	
Arrhythmia	7	0	
Thromboembolic complication	0	0	
Respiratory event	0	0	
Other*	3 (1.4%)	4 (8.5%)	

Values are number (proportion).

\*Other included transfusion (n=4), depression (n=1), and pregnancy-induced hypertension (n=2).

Table 2. Association between cardiovascular events after cesarean section with an anesthetic technique based on mixed-effects logistic regression models with random intercepts for each modified WHO classification for maternal cardiovascular risk.

	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
General anesthesia relative to neuraxial anesthesia	1.31 (0.43–4.04)	0.64	1.00 (0.30–3.29)	0.99

Abbreviations: WHO, World Health Organization; OR, odds ratio; CI, confidence interval.

## References

- Afolabi, B. B., and Lesi, F. E. (2012), Regional versus general anaesthesia for caesarean section. *Cochrane Database Syst Rev*, 10, CD004350.
- Bédard, E., Dimopoulos, K., and Gatzoulis, M. A. (2009), Has there been any progress made on pregnancy outcomes among women with pulmonary arterial hypertension? *Eur Heart J*, 30, 256-265.
- Bishop L, L. A., English K. (2018), Adult congenital heart disease and pregnancy. *BJA Educ*, 18, 23-29.
- Bucklin, B. A., Hawkins, J. L., Anderson, J. R., and Ullrich, F. A. (2005), Obstetric anesthesia workforce survey: twenty-year update. *Anesthesiology*, 103, 645-653.
- Djabatey, E. A., and Barclay, P. M. (2009), Difficult and failed intubation in 3430 obstetric general anaesthetics. *Anaesthesia*, 64, 1168-1171.
- Goldszmidt, E., Macarthur, A., Silversides, C., Colman, J., Sermer, M., and Siu, S. (2010), Anesthetic management of a consecutive cohort of women with heart disease for labor and delivery. *Int J Obstet Anesth*, 19, 266-272.
- Hayward, R. M., Foster, E., and Tseng, Z. H. (2017), Maternal and Fetal Outcomes of Admission for Delivery in Women With Congenital Heart Disease. *JAMA Cardiol*, 2, 664-671.
- Hidano, G., Uezono, S., and Terui, K. (2011), A retrospective survey of adverse maternal and neonatal outcomes for parturients with congenital heart disease. *Int J Obstet Anesth*, 20, 229-235.
- Hrycyk, J., Kaemmerer, H., Nagdyman, N., Hamann, M., Schneider, K., and Kuschel, B. (2016), Mode of Delivery and Pregnancy Outcome in Women with Congenital Heart Disease. *PLoS One*, 11, e0167820.
- Kodali, B. S., Chandrasekhar, S., Bulich, L. N., Topulos, G. P., and Datta, S. (2008), Airway changes during labor and delivery. *Anesthesiology*, 108, 357-362.
- Maxwell, B. G., El-Sayed, Y. Y., Riley, E. T., and Carvalho, B. (2013), Peripartum outcomes and

anaesthetic management of parturients with moderate to complex congenital heart disease or pulmonary hypertension\*. *Anaesthesia*, 68, 52-59.

Moir, D. D. (1970), Anaesthesia for Caesarean section. An evaluation of a method using low concentrations of halothane and 50 per cent of oxygen. *Br J Anaesth*, 42, 136-142.

Sanghavi, M., and Rutherford, J. D. (2014), Cardiovascular physiology of pregnancy. *Circulation*, 130, 1003-1008.

van der Linde, D., Konings, E. E., Slager, M. A., Witsenburg, M., Helbing, W. A., Takkenberg, J. J., and Roos-Hesselink, J. W. (2011), Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol*, 58, 2241-2247.

Warrick, C. M., Hart, J. E., Lynch, A. M., Hawkins, J. A., and Bucklin, B. A. (2015), Prevalence and descriptive analysis of congenital heart disease in parturients: obstetric, neonatal, and anesthetic outcomes. *J Clin Anesth*, 27, 492-498.

Whittemore, R., Hobbins, J. C., and Engle, M. A. (1982), Pregnancy and its outcome in women with and without surgical treatment of congenital heart disease. *Am J Cardiol*, 50, 641-651.

## 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

### III Bibliography

1. Relationship Between FFP/RBC Transfusion Ratio and Mortality in Cardiovascular Surgery  
Tsukinaga, A., Maeda, T., Takaki, S., Michikata, N., Ohnishi, Y:  
*Journal of Anesthesia* 32(4), 539-546, 2018
2. Measurement of the Aortic Annulus Area and Diameter by Three-Dimensional Transesophageal Echocardiography in Transcatheter Aortic Valve Replacement  
Ebuchi, K., Yoshitani, K., Kanemaru, E., Fujii, T., Tsukinaga, A., Shimahara, Y., Ohnishi, Y.:  
*Journal of Cardiothoracic and Vascular Anesthesia* 33(9), 2387-2393, 2019
3. Low Hematocrit Levels: A Risk Factor for Long-Term Outcomes in Patients Requiring Prolonged Mechanical Ventilation After Cardiovascular Surgery. A Retrospective Study  
Tsukinaga, A., Takaki, S., Mihara, T., Okamura, K., Isoda, S., Kurahashi, K., Goto T.:  
*Journal of Investigative Medicine* 68(2), 392-396, 2020
4. Pitfalls of Anesthetic Management With the Impella® 5.0 Device: A Case Series  
Hotta, N., Tsukinaga, A., Yoshitani, K., Ohnishi, Y.:  
*Journal of Anesthesia Clinical Reports* 6(1), 21, 2020
5. Comparison of Right Ventricular Function Between Patients With and Without Pulmonary Hypertension Owing to Left-Sided Heart Disease Assessment Based on Right Ventricular Pressure-Volume Curves  
Kanemaru, E., Yoshitani, K., Kato, S., Fujii, T., Tsukinaga, A., Ohnishi, Y.:



Journal of Cardiothoracic and Vascular Anesthesia 34(1), 143-150, 2020

6. Transient Neurological Events After Surgery for Pediatric Moyamoya Disease: A Retrospective Study of Postoperative Sedation Practices  
Matsuura, H., Yoshitani, K., Nakamori, Y., Tsukinaga, A., Takahashi, J., C., Nakai, M., Ohnishi, Y.:  
Journal of Neurosurgical Anesthesiology 32(2), 182-185, 2020
7. Transfusion Characteristics and Hemostatic Conditions in Octogenarians Undergoing Emergency Surgery for Acute Aortic Dissection: A Retrospective Study  
Masubuchi, T., Yoshitani, K., Minami, K., Yokoyama, C., Tsukinaga, A., Goto, T., Ohnishi, Y.:  
Journal of Anesthesia Clinical Reports 6(1), 52, 2020
8. Accuracy and Trending Ability of Cardiac Index Measured By the CNAP System in Patients Undergoing Abdominal Aortic Aneurysm Surgery  
Miyazaki, E., Maeda, T., Ito, S., Oi, A., Hotta, N., Tsukinaga, A., Kanazawa, H., Ohnishi, Y.:  
Journal of Cardiothoracic and Vascular Anesthesia 35(5):1439-1446.
9. Effect of Melatonin and Melatonin Agonists on Postoperative Sleep Quality in Adult Patients: A Protocol for Systematic Review and Meta-Analysis With Trial Sequential Analysis  
Tsukinaga, A., Mihara, T., Takeshima, T., Tomita, M., Goto, T., Yamanaka T.:  
BMJ Open 11, e047858, 2021