Taiwanese Journal of Obstetrics & Gynecology 60 (2021) 41–44

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Risk factors for intraoperative hemorrhage during cesarean myomectomy

Ji Young Kwon, Ji Hea Byun, Inhye Shin, Subeen Hong, Rayon Kim, In Yang Park*

Department of Obstetrics and Gynecology, The Catholic University of Korea, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Accepted 17 September 2020

Keywords:
Cesarean myomectomy
Operative hemorrhage
Leiomyoma

ABSTRACT

Objective: We intended to identify the risk factors of intraoperative hemorrhage on occasions of a combined operation of myomectomy with cesarean section for patients with uterine leiomyoma.
Materials and methods: A retrospective cohort study was done of all patients who underwent cesarean myomectomy for intramural leiomyoma at a single university hospital. Cases identified with subserosal leiomyoma, placental disorder, and comorbid conditions related to coagulopathy were excluded. All the included cases were classified into intraoperative hemorrhage and non-hemorrhage group. Obstetric and demographic factors and parameters of leiomyoma were compared between two groups.
Results: A total of 302 women underwent cesarean myomectomy during the study period. Among these women, 212 pregnant women met the inclusion criteria. Intraoperative hemorrhage occurred in 43 women (20.3%). There was no significant intergroup difference in the number of removed leiomyomas. Multiple logistic regression analysis demonstrated that lower segmental location (odds ratio [OR], 2.827; 95% confidence interval [CI], 1.033–7.734, $P = 0.043$) and the diameter (OR, 1.167; 95% CI, 1.044–1.305, $P = 0.006$) were significant independent risk factors for hemorrhage during cesarean myomectomy. The combination of $\geq$ 8 cm diameter or lower segmental position of the leiomyoma yielded a specificity of 79.3% for operative hemorrhage during cesarean myomectomy. The negative predictive value of this combination was 88.7% for operative hemorrhage with a prevalence of 20%.
Conclusion: The large size and lower segmental position of the leiomyoma are significantly risk factors for intraoperative hemorrhage during cesarean myomectomy. If the leiomyoma is located in the uterine fundus or body and its diameter is less than 8 cm, the removal of leiomyoma may be considered at the time of cesarean section.

Introduction

Uterine leiomyoma is a benign tumor most frequently observed in about 10–20% of fertile women [1]. It has been reported as accompanying several complications, such as bleeding, pain, and consequential subfertility [2]. For a uterine leiomyoma found during pregnancy, the potential inducement of rapid growth in size with pains and relevance to premature labor have been reported [3,4]. The prevalence of uterine leiomyoma increases with increasing age of women [5]. Recently, the frequency of observations of uterine leiomyoma during pregnancy has been increasing along with advancing age of pregnant women [3]; so leiomyomas found in the course of antenatal care placed additional burdens on obstetricians.

For patients planning cesarean section, obstetrician may consider doing a simultaneous operation for myomectomy. Co-execution of a cesarean section with simultaneous myomectomy has an advantage of avoiding complications that might result from re-operation for future leiomyoma removal. However, in terms of the safety of a combined execution of cesarean section and myomectomy, further definite clarifications are yet to be reported. In the past, a combined operation was not recommended for a leiomyoma found during pregnancy, because of increased complications [6]. Recently, studies reported the feasibility of a combined operation [7–10]. The reasons behind the reluctance to do a combined operation in the past are based on judgments about increasing postpartum complications, such as increased hemorrhage, fever, and reduced bowel movements,

* Corresponding author. Department of Obstetrics and Gynecology, Maternal Fetal Medicine, The Catholic University of Korea, 222 Banpodaero, Sechogu, Seoul St. Mary's Hospital, 06591, Seoul, Republic of Korea.
E-mail address: ooooobbbbb@catholic.ac.kr (I.Y. Park).

https://doi.org/10.1016/j.tjog.2020.11.007

including the ileus [11,12]. However, leaving the leiomyoma diagnosed during a cesarean section to avoid perinatal complications would necessitate doing an operation under general anesthesia a few months later; so the decision making about the appropriate time for a combined operation of a cesarean section with myomectomy seems necessary. In contrast, the possible complications accompanying a combined operation, such as hemorrhage or infection, need to be considered sufficiently before doing a combined operation. For this reason, the discernment of which complications such as a hemorrhage could arise in which pregnant women seems necessary.

Thus, we participated in this study in order to examine the cases of increasing risk of hemorrhage in the combined operation of cesarean section and myomectomy for pregnant women found with leiomyoma in the course of prenatal diagnosis before the cesarean section was performed; so we were searching for the conditions supporting myomectomy at the time of cesarean section.

Material and methods

A retrospective cohort study was done of all patients who had undergone a myomectomy for intramural leiomyoma during a cesarean section at a single university hospital from January 2015 to August 2016. Cases of subserosal leiomyomas in which > 50% of the leiomyoma protruded out of the serosal surface of the uterus on antenatal sonography were excluded. In addition, women who had a placental disorder or comorbid conditions related to coagulopathy were excluded. All types of cesarean section were included: scheduled or emergency and primary or repeat. This study was approved by the institutional Review Board (IRB) of the Catholic University of Korea. The patient records were accessed anonymously, and the IRB waived the need for informed consent.

All patients diagnosed with leiomyoma during pregnancy and scheduled for cesarean section because of maternal or fetal indications had been preoperatively counseled about the possibility of cesarean myomectomy, which was undertaken for all the women who consented to the operation. Main indications for cesarean myomectomy were the patient's desire followed by symptomatic leiomyoma. The operative technique followed usual practices, including perioperative prophylactic antibiotics. Diluted vasopressin (20 IU in 200 ml normal saline) was infused before incision of the leiomyoma to minimize bleeding. For the operation technique, we exploited the cold-knife surgery employing a scalpel solely without using the monopolar or bipolar electrocautery machine in order to avoid electronic burns on the uterus. During operation, we inserted the hemovac into the abdominal cavity and removed it if the amount of drainage fluid was below 50 cc in a day.

Data regarding patient's characteristics, such as age, previous delivery history, gestational age at delivery, and birthweight, and the parameters of the removed leiomyoma, including size, number, pathology report, and location, were recorded. The size of leiomyoma was defined as its largest diameter. For multiple leiomyomas, the factors of the largest leiomyoma were recorded. In addition, data about operative outcomes, including operation time, duration of postoperative hospital stay, intraoperative blood loss, hemoglobin concentration on the preoperative day and at 24 h postoperative, need for transfusion, need for re-procedure for hemostasis, and postoperative fever or ileus were recorded from the chart. Postoperative fever was defined as a temperature above 38 °C on 2 consecutive days. The definition of intraoperative hemorrhage was modified based on the previous studies [10,13,14]: Estimated blood loss exceeding 1000 ml or requiring a 24-h postoperative hemoglobin drop greater than 3 g/dl.

Statistical methods

All maternal characteristics and operative outcomes were summarized using descriptive statistics. The demographic characteristics, parameters of the leiomyoma, operative outcomes between the operative hemorrhage and non-hemorrhage groups were compared using a Mann–Whitney *U*-test, a chi-square test, or Fisher's exact test, as appropriate. We then entered factors found to be significantly associated with intraoperative hemorrhage into multivariate logistic regression analysis to identify risk factors for hemorrhage. For significant continuous variables, the optimized cut-off values were assessed by means of receiver operating characteristic (ROC) analysis. We calculated the screening performance for the combination of significant variables. A $P < 0.05$ was considered statistically significant. We used SPSS (version 12.0; SPSS Inc., Chicago, IL, USA) for statistical analysis.

Results

A total of 302 women underwent cesarean myomectomy during the study period. Among these women, 212 pregnant women met the inclusion criteria. Table 1 shows the demographic characteristics and operative outcomes of the study population. The proportion of women without any history of uterine surgery was 84.5%. Removal of a single leiomyoma was done in 68.2% of included women. Mean size of the leiomyoma was 5.8 ± 3.0 cm. There was no case of re-laparotomy or uterine embolization. The proportion of women requiring transfusion was 6.6%. Postoperative ileus or fever occurred in 6 women (2.8%).

Operative hemorrhage occurred in 43 women (20.3%). Other operative outcomes in cases with and without hemorrhage are shown in Table 2. Women in the hemorrhage group had significantly more estimated blood loss, more hemoglobin drop, longer operative time, and longer postoperative stay in hospital than women in the non-hemorrhage group ($P < 0.001$, < 0.001, 0.007, and 0.011, respectively). There was no significant difference in the occurrence of postoperative fever and ileus.

Patient characteristics, including parity, multifetal pregnancy, gestational age, previous uterine operation, or emergency operation showed no significant differences between the operative

Table 1
Demographics and operating outcomes of study population.

Variable	N = 212
Age (years)	34.7 ± 3.3
Gestational age (week)	36.6 ± 3.3
Baby weight (kg)	2.8 ± 0.7
Nullipara	186 (87.7)
Multifetal pregnancy	15 (7.1)
Previous cesarean delivery	17 (8.0)
Previous myomectomy	19 (9.0)
Preterm delivery (<37 weeks)	61 (28.8)
Emergent cesarean section	76 (35.8)
Removed leiomyoma	
Diameter (cm)	5.8 ± 3.0
Number	1.5 ± 0.9
Hb at preoperative day (mg/dl)	12.0 ± 1.3
Hb at postoperative 24- hour (mg/dl)	10.8 ± 1.5
24- hour postoperative Hb drop (mg/dl)	1.2 ± 1.0
Estimated blood loss (ml)	594.5 ± 297.1
Operative time (min)	45.9 ± 17.8
Postoperative hospital stay (day)	3.4 ± 1.6
Need for transfusion	16 (7.5)
Postoperative ileus	3 (1.4)
Postoperative fever	3 (1.4)

All values are expressed as mean (±standard deviation) or number (%).
Hb, hemoglobin.

Table 2
Comparison of operative outcomes in the hemorrhage and non-hemorrhage group.

Parameters	Hemorrhage (N = 43)	Non-hemorrhage (N = 169)	*P* value
Hb at preoperative day (mg/dl)	12.3 (11.2–13.0)	12.0 (11.1–12.6)	0.359
Hb at postoperative 24- hour (mg/dl)	9.9 (8.6–11.1)	11.2 (10.2–12.1)	<0.001
24- hour postoperative Hb drop (mg/dl)	2.0 (1.2–3.2)	0.8 (0.2–1.5)	<0.001
Estimated blood loss (ml)	1000 (800–1200)	500 (300–600)	<0.001
Operative time (min)	48 (38–57)	42 (33–51)	0.007
Postoperative hospitalization (≥4 days)	21 (48.8)	47 (27.8)	0.011
Amount of PRC transfusion ([a]pack)	2 (0–2)	0 (0–0)	<0.001
Postoperative ileus	1 (2.3)	2 (1.2)	0.571
Postoperative fever	1 (2.3)	2 (1.2)	0.571

All values are expressed as median (interquartile range) or number (%).
Mann–Whitney *U*-test or Fisher's exact test was used as appropriate.
Hb, hemoglobin; PRC, packed red blood cell.
[a] 1pack = 400 ml.

hemorrhage and non-hemorrhage groups (Table 3). Removed leiomyomas in the operative hemorrhage group showed significantly larger diameters ($P = 0.002$) and lower segmental location than those in the control group ($P = 0.001$). There was no significant intergroup difference in the number of removed leiomyomas (Table 3). Multiple logistic regression analysis demonstrated that the parameters of leiomyomas, including low segmental location (odds ratio [OR], 2.827; 95% confidence interval [CI], 1.033–7.734, $P = 0.043$) and the diameter (OR, 1.167; 95% CI, 1.044–1.305, $P = 0.006$) were significant independent predictors of hemorrhage after cesarean myomectomy (Table 4).

The ROC curves analysis showed that the area under the curve for the prediction of operative hemorrhage by diameter of leiomyoma was 0.635 (95% CI, 0.566–0.700, $P = 0.008$). The optimal cut-off value was 8 cm with a sensitivity of 46.5% and a specificity of 79.3%. The combination of ≥ 8 cm diameter or low segmental position of the leiomyoma yielded a specificity of 88.7% for hemorrhage after cesarean myomectomy. The positive and negative predictive value of this combination was 41.8% and 84.0% for operative hemorrhage with a prevalence of 20%.

Table 4
Multiple logistic regression analysis for the prediction of operative hemorrhage.

Parameter of leiomyoma	OR (95% CI)	*P* value
Lower segmental location	2.827 (1.033–7.734)	0.043
Diameter (cm)	1.167 (1.044–1.305)	0.001

OR, Odds ratio; 95% CI, 95% confidence interval.

Discussion

The removal of leiomyoma at the time of cesarean section is still considered as a controversial issue. Traditionally, cesarean myomectomy has not been supported due to the risk of hemorrhage. However, this procedure has its own advantages for both pregnant women and surgeons. For patients, myomectomy during cesarean delivery could eliminate the symptoms related with leiomyoma and prevent repeated anesthesia and surgery [15]. Further fertility after cesarean myomectomy seems not to be impaired [16]. For surgeons, leiomyoma could be easily removed because the psuedocapsule of leiomyoma is likely to be larger during pregnancy compared to that during non-pregnancy [17].

The major concern about cesarean myomectomy is that it may give rise to heavy hemorrhage the risk of massive hemorrhage which could result in postoperative morbidity and obstetric hysterectomy. However, to date the evidences to support this concern seems to be sparse. Previous several studies demonstrated that cesarean myomectomy were not associated with significant hemorrhage or other postoperative morbidity, although there were increased operative time and hemoglobin drop [7–10]. Therefore, cesarean myomectomy can be considered in selected cases.

Table 3
Comparison of demographic characteristics and parameters of leiomyoma in the hemorrhage and non-hemorrhage group.

Parameters	Hemorrhage (N = 43)	Non-hemorrhage (N = 169)	*P* value
Age (years)	34 (32–37)	34 (32–37)	0.349
Newborn weight (kg)	2.91 (2.45–3.32)	2.96 (2.59–3.32)	0.652
Nullipara	41 (95.3)	145 (85.8)	0.088
Multifetal pregnancy	1 (2.3)	14 (8.3)	0.315
Previous cesarean delivery	2 (4.7)	15 (8.9)	0.534
Previous myomectomy	3 (7.0)	16 (9.5)	0.610
Preterm delivery	11 (25.6)	50 (29.6)	0.605
Emergent cesarean section	10 (33.3)	66 (36.3)	0.839
Removed leiomyoma			
Multiple (≥2)	9 (30.0)	54 (29.7)	0.971
Diameter (cm)	7 (4–10)	5 (3–7)	0.006
Degenerative changes and/or necrosis	20 (46.5)	91 (54.2)	0.370
Location (I)			0.578
Anterior	36 (83.7)	147 (87.0)	
Posterior	7 (16.3)	22 (13.0)	
Location (II)			0.006
Fundus	4 (9.3)	28 (16.6)	
Body	30 (69.8)	131 (77.5)	
Lower segment	9 (20.9)	10 (5.9)	

All values are expressed as median (interquartile range) or number (%).
Mann–Whitney *U*- test, Chi-squared test or Fisher's exact test was used as appropriate.

The present study revealed that the diameter of leiomyoma and low segmental location were significant risk factors for intraoperative hemorrhage of cesarean myomectomy. In terms of postoperative ileus and fever exhibited no significant differences according to operative hemorrhage.

The combination of $\geq$ 8 cm diameter or low segmental position of the leiomyoma yielded a specificity of 79.4% for significant hemorrhage during cesarean myomectomy. In particular, the negative predictive value of this combination was 84.0% for operative hemorrhage. If the leiomyoma is located in the uterine fundus or body and its diameter is less than 8 cm, the removal of leiomyoma may be considered at the time of cesarean section.

The distinct decrease in the level of hemoglobin accompanied the relatively large sized leiomyoma, probably because of the hemorrhage resulting from the large uterine incision needed to perform the myomectomy. Dedes et al. [18] reported the significant increase in hemorrhage for removal of leiomyoma exceeding 5 cm during cesarean section. In this study, leiomyoma exceeding 8 cm was significantly associated with intraoperative hemorrhage. In addition, Intraoperative hemorrhage was more significantly occurred in cases of removal of leiomyomas located in low segment of the uterus compared with leiomyoma located in uterine fundus or body, probably because there was less postpartum uterine contraction in a uterine low segment than in the uterine fundus.

The average age of the subjects was 34.7 $\pm$ 3.3 years and mean gestational age at the time of delivery was 36.6 $\pm$ 3.3 weeks. High proportion of women with advanced maternal age and preterm delivery might be due to characteristic of high-risk pregnancy unit in university hospital. The incidence of leiomyoma increases with age with an incidence of 40–60% by age 35 [1]. Women with advanced maternal age may be more likely to have leiomyoma during pregnancy. Leiomyoma was known to be associated with preterm labor [2]. As this study was conducted for cases of cesarean myomectomy, it is not possible to determine whether a high rate of advanced maternal age and preterm birth are characteristics of pregnant women with leiomyoma.

We did not include cases of removal of pedunculated or subserosal leiomyoma at the time of cesarean section. Such cases revealed postoperative complications, such as hemorrhage, similar to those in cases of general cesarean section [15]. According to Rong Zhao et al. [19], the cesarean myomectomy provided to patients with pedunculated or subserosal leiomyoma and the cases that were solely provided with cesarean section were reported as bearing no significant differences in hemorrhage to each other [19]. Thus, our scope was limited to cases of intramural leiomyoma wherein estimating the safety of cesarean myomectomy was not established.

The cases of leiomyoma located at the anterior side of the uterus appeared dominantly in this study, which might be attributable to the difficulty in follow-up of leiomyoma located at the posterior side of the uterus along with the progression of pregnancy embracing cases of found leiomyoma during pregnancy, thereby resulted in incomplete counseling with pregnant women about having the myomectomy before taking the cesarean section.

In terms of surgical technique, the reason for selecting cold-knife surgery is associated with the increasing possibility of uterine rupture at the next pregnancy caused by an electronic burn on the uterus [16,20]. In the group of subjects participating in the present study, none of the subjects underwent uterine artery embolization, re-operation, or hysterectomy except for cases of blood transfusion because of a relatively large hemorrhage upon completion of the cesarean myomectomy. The dosage of uterotonics was identical to that of the same kind of drug used for usual cesarean section.

The group of subjects who had relatively large hemorrhages also had a longer time of operation and extended postoperative stays in hospital as well, probably because the discharge of subjects belonging to the group exhibited large hemorrhage after stabilization of the level of hemoglobin and vital sign. For the generation of postoperative fever and postoperative ileus, the subjects in the two groups showed no significant differences.

In conclusion, this study suggested that removal of leiomyoma exceeding 8 cm or leiomyomas located in a uterine low segment at the time of cesarean section was significantly associated with intraoperative hemorrhage. This finding will provide useful information for the assessment and counseling of pregnant women who had leiomyoma and plan to get cesarean delivery. It appeared that cases with leiomyoma less than 8 cm and located elsewhere than in a uterine low segment during pregnancy would be relatively safe if provided with a cesarean myomectomy, given the results of our analysis of risk.

Declaration of competing interest

The researcher claims no conflict of interest.

References

[1] Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of uterine myomas: a review. Int J Fertil Steril 2016;9:424–35.
[2] Parazzini F, Tozzi L, Bianchi S. Pregnancy outcome and uterine fibroids. Best Pract Res Clin Obstet Gynaecol 2016;34:74–84.
[3] Kellal I, Haddouchi N, Lecuyer A, Body G, Perrotin F, Marret H. Leiomyoma during pregnancy: which complications? Gynecol Obstet Fertil 2010;38:569–75.
[4] Rice JP, Kay HH, Mahony BS. The clinical significance of uterine leiomyomas in pregnancy. Am J Obstet Gynecol 1989;160:1212–6.
[5] Lurie S, Piper I, Woliovitch I, Glezerman M. Age-related prevalence of sonographicaly confirmed uterine myomas. J Obstet Gynaecol 2005;25:42–4.
[6] Dashe JS, Bloom SL, Spong CY, Hoffman BL. Williams obstetrics. 25th ed. New York: McGraw Hill; 2018. p. 1195–7.
[7] Huang Y-P, Hsu M-C, Lee C-N, Fan S-Z, Chen L-K. Myomectomy of a massive uterine myoma during cesarean section under regional anesthesia. Taiwan J Obstet Gynecol 2015;54:196–7.
[8] Song D, Zhang W, Chames MC, Guo J. Myomectomy during cesarean delivery. Int J Gynaecol Obstet 2013;121:208–13.
[9] Ramesh Kumar R, Patil M, Shruthi S. The utility of caesarean myomectomy as a safe procedure: a retrospective analysis of 21 cases with review of literature. J Clin Diagn Res 2014;8:OC05.
[10] Pergialiotis V, Sinanidis I, Louloudis I-E, Vichos T, Perrea DN, Doumouchtsis SK. Perioperative complications of cesarean delivery myomectomy: a meta-analysis. Obstet Gynecol 2017;130:1295–303.
[11] Sheiner E, Sarid L, Levy A, Seidman DS, Hallak M. Obstetric risk factors and outcome of pregnancies complicated with early postpartum hemorrhage: a population-based study. J Matern Fetal Neonatal Med 2005;18:149–54.
[12] Kim YS, Choi SD, Bae DH. Risk factors for complications in patients undergoing myomectomy at the time of cesarean section. J Obstet Gynaecol Res 2010;36:550–4.
[13] Sei K, Masui K, Sasa H, Furuya K. Size of uterine leiomyoma is a predictor for massive haemorrhage during caesarean delivery. Eur J Obstet Gynecol Reprod Biol 2018;223:60–3.
[14] Sparić R, Papoutsis D, Bukumirić Z, Kadija S, Spremović Radjenović S, Malvasi A, et al. The incidence of and risk factors for complications when removing a single uterine fibroid during cesarean section: a retrospective study with use of two comparison groups. J Matern Fetal Neonatal Med 2020;33:3258–65.
[15] Sparic R, Kadija S, Malvasi A, Babovic I, Nejkovic L, Tinelli A. Cesarean myomectomy trends and controversies: an appraisal. J Matern Fetal Neonatal Med 2017;30:1114–23.
[16] Tian Y, Long T, Dai Y. Pregnancy outcomes following different surgical approaches of myomectomy. J Obstet Gynaecol Res 2015;41:350–7.
[17] Incebiyik A, Hilali NG, Camuzcuoglu A, Vural M, Camuzcuoglu H. Myomectomy during caesarean: a retrospective evaluation of 16 cases. Arch Gynecol Obstet 2014;289:569–73.
[18] Dedes I, Schäffer L, Zimmermann R, Burkhardt T, Haslinger C. Outcome and risk factors of cesarean delivery with and without cesarean myomectomy in women with uterine myomatas. Arch Gynecol Obstet 2017;295:27–32.
[19] Zhao R, Wang X, Zou L, Zhang W. Outcomes of myomectomy at the time of cesarean section among pregnant women with uterine fibroids: a retrospective cohort study. BioMed Res Int 2019;2019:7576934.
[20] Yazawa H, Takiguchi K, Ito F, Fujimori K. Uterine rupture at 33rd week of gestation after laparoscopic myomectomy with signs of fetal distress. A case report and review of literature. T Taiwan J Obstet Gynecol 2018;57:304–10.