Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Nationwide population-based cohort study of adverse obstetric outcomes in pregnancies with myoma or following myomectomy: Retrospective cohort study

Se Jin Lee
Kangwon National University Hospital https://orcid.org/0000-0002-8626-6250
Hyun Sun Ko
Seoul Saint Mary's Hospital
Sunghun Na
Kangwon National University Hospital
Jin Young Bae
Catholic University of Daegu
Won Joon Seong
Kyungpook National University Hospital
Jong Woon Kim
Chonnam National University Hospital
Jaeeun Shin
Catholic University of Korea
Hae Joong Cho
Wonkwang University College of Medicine
Gyu Yeon Choi
Soonchunhyang University Hospital
Jinsil Kim
Korea University Guro Hospital
Geum Joon Cho (geumjoon@korea.ac.kr)
Korea University College of Medicine
In Yang Park
Seoul Saint Mary's Hospital

Research article

Keywords: Myoma, Myomectomy, Pregnancy outcome, Uterine rupture

Posted Date: September 16th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-27382/v3

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Version of Record: A version of this preprint was published on November 23rd, 2020. See the published version at https://doi.org/10.1186/s12884-020-03406-9.

Abstract

Background: Our objective was to evaluate risks of adverse obstetric outcomes in pregnancies with myoma(s) or in pregnancies following myomectomy.

Methods: We analyzed the national health insurance database, which covers almost the entire Korean population, between 2004 and 2015. The risks of adverse pregnancy outcomes in pregnancies with myoma(s) or in pregnancies following myomectomy, compared to those in women without a diagnosed myoma, were analyzed in multivariate logistic regression analysis.

Results: During the study period, 38,402 women with diagnosed myoma(s), 9,890 women with a history of myomectomy, and 740,675 women without a diagnosed myoma gave birth. Women with a history of diagnosed myoma(s) and women with a history of myomectomy had significantly higher risks of cesarean section (aOR 1.13, 95% CI 1.1-1.16 and aOR 7.46, 95% CI 6.97-7.98, respectively) and placenta previa (aOR 1.41, 95% CI 1.29-1.54 and aOR 1.58, 95% CI 1.35-1.83, respectively), compared to women without a diagnosed myoma. And the risk of uterine rupture was significantly higher in women with previous myomectomy (aOR 12.78, 95% CI 6.5-25.13), compared to women without a diagnosed myoma, which was much increased (aOR 41.35, 95% CI 16.18-105.69) in nulliparous women. The incidence of uterine rupture was the highest at delivery within one year after myomectomy and decreased over time after myomectomy.

Conclusions: Women with a history of myomectomy had significantly higher risks of cesarean section and placenta previa compared to women without a diagnosed myoma.

Background

Uterine myomas (leiomyomata, fibroids) are the most common tumor of the reproductive tract, with a prevalence of 20–25%[1] and a cumulative incidence of 70% in women of reproductive age.[2]

It has been reported that the presence of fibroids is associated with infertility, spontaneous abortion, fetal malpresentation, placenta previa, preterm birth, cesarean section, and peripartum hemorrhage.[3] Although surgical interventions such as myomectomy have been tried in infertile women without specific causes, it is unclear whether the treatment of uterine fibroids can improve pregnancy outcomes, except for cavity-distorting myomas (submucosal, or intramural with a submucosal component).[4] The most serious concern in pregnancies after myomectomy is the risk of uterine rupture, which can result in significant increased morbidity and mortality for both the mother and the fetus. The incidence of uterine rupture after prior myomectomy has been reported to range from 0.2 to 3.7% in women with prior myomectomy.[5] There is no consensus on the optimal interval between myomectomy and conception.

Because there is insufficient evidence that myomectomy improves pregnancy outcomes, a practice committee of the American Society for Reproductive Medicine (ASRM) and the Society of Obstetricians and Gynaecologists of Canada (SOGC) are against myomectomy in asymptomatic women with non-

cavity-distorting myomas.[6, 7] However, in US Census Bureau population projections, it was estimated that myomectomies are predicted to increase 31% between 2007 and 2050.[8] In Korea, the number of women who underwent myomectomy have increased 37.3% between 2006 and 2010.[9] Women in their 30s and 40s, who are a major population for pregnancy, have been major candidates for myomectomy. There have been poor evidences about obstetric outcomes in women with myoma and previous myomectomy.[10]

The purpose of this study was to evaluate adverse pregnancy outcomes in women with a history of diagnosed myoma or myomectomy, including prevalence of uterine rupture in women with myomectomy, according to the time interval after myomectomy.

Methods

The characteristics of the dataset

In Korea, 97% of the population is enrolled in the Korea National Health Insurance (KNHI) program. All claims information for these individuals is contained within the KNHI claims database. Nearly all information about the prevalence of different diseases and procedures can be obtained from this centralized database, with the exception of procedures not covered by insurance. As part of the KNHI system, children aged 4–80 months are eligible for a National Health Screening Program for Infants and Children (NHSP-IC).[11] An NHSP-IC is composed of seven consecutive health examinations based on age groupings. The first to the seventh health examinations are performed at ages 4–9, 9–18, 18–30, 30–42, 42–54, 54–66, and 66–80 months. An NHSP-IC consists of history taking, physical examination, anthropometric examination, developmental screening, and visual acuity testing based on the child's age. Women's data in the KNHI claims database were linked to the data of their offspring contained within the NHSP-IC database.

Data on women's health conditions including obstetric diagnosis were obtained from the KNHI claims database using ICD-10 codes. ICD-10 codes for uterine myomas were D25. Surgery codes for myomectomy were JR4123, JR4124, JR4127, JR4128 and JR4129. To evaluate the effects of myomectomy according to types of myomas on pregnancy outcomes, myometomy groups were divided to submucosal (D25.0) or intramural (D25.1) myomas, and subserosal myomas (D25.2) or unspecified myomas (D25.9), by ICD codes.

Data on preterm birth and birth weight were corrected from the NHSP-IC database.

Outcomes

We analyzed the KNHI claims database, between 2004 and 2015. Using the database, we identified all women who had given birth between January 1, 2014, and December 31, 2015. We also identified whether these women had a diagnosis of uterine myoma based on ICD-10 codes before pregnancy and

whether these women had a myomectomy using procedure codes from the Health Insurance Medical Care Expenses.

The flow chart of study participants' enrollment is presented in Figure 1. For pregnancy outcomes, we extracted information on delivery mode, nulliparity, multiple pregnancy, preeclampsia, PPH, placental abruption, placenta previa, and uterine rupture using the KNHI claims database (dataset 1). For the other outcomes, the KNHI claims database and the NHSP-IC database were merged. Because data on preterm birth and birth weight were corrected from the NHSP-IC database, women were excluded from analysis if their offspring did not undergo at least one of the seven consecutive NHSP-IC examinations or had missing data (dataset 2). Data on preterm birth, low birth weight (LBW), and large for gestational age (LGA) were extracted from dataset 2. Preterm birth was defined as gestational age < 37 weeks. LBW was defined as birth weight < 2.5 kg. LGA was defined as birth weight > 4.0 kg.

Statistical analysis

Continuous and categorical variables are expressed as the mean ± standard deviation and percentages, respectively. Clinical characteristics were compared using the Kruskal-wallis test for continuous variables and the chi-square test for categorical variables. Multivariate logistic regression analysis was used to estimate the adjusted odd ratio (aOR) and the 95% confidence interval (CI)s for the association of a presence of leiomyoma and myomectomy with adverse pregnancy outcomes. For multivariate analyses, a fixed set of known risk factors for adverse pregnancy outcomes was adjusted for potential confounding: maternal age (categorical variable; < 35 or ≥35 years old), and nulliparity (categorical variable). Statistical analyses were done using SAS for Windows v9.4 (SAS, Inc., Cary, NC).

Results

From 2014 to 2015, 789,482 women delivered in Korea. After excluding women with missing data (*n* = 515), 788,967 remaining women were included in dataset 1. Among them, 740,675 (93.88%) women had no diagnosed myoma, 38,402 (4.88%) had diagnosed myoma(s) but no history of myomectomy, and 9,890 (1.25%) women had a history of myomectomy before pregnancy. Dataset 2[11] included 534,259 women, excluding women whose infants did not receive infant screening (*n* = 254,693) or showed missing values (*n* = 15). There were 502,209 (94.00%) women who had never been diagnosed with myoma, 25,408 (4.76%) women who had diagnosed myoma(s) but no history of myomectomy, and 6,642 (1.24%) women who had a history of myomectomy, in dataset 2.

Maternal characteristics and adverse pregnancy outcomes of the study population in dataset 1 as described in Table 1. There were differences in maternal age, rates of nulliparity, multiple pregnancy, cesarean section, and complications of preeclampsia, postpartum hemorrhage, placenta previa, and uterine rupture, between the groups. However, there was no significant difference in placental abruption between the three groups.

Obstetric characteristics in dataset 2 are presented in Table 2. There were significant differences in neonatal birth weight and sex, and rates of preterm birth, LBW, and LGA.

Multivariate logistic regression analysis for adverse obstetric outcomes in pregnancies with myoma or following myomectomy

Both groups of women with a history of diagnosed myoma(s) and women with a history of myomectomy had significantly higher risks of cesarean section (aOR 1.13, 95% CI 1.1-1.16 and aOR 7.46, 95% CI 6.97-7.98, respectively) and placenta previa (aOR 1.41, 95% CI 1.29-1.54 and aOR 1.58, 95% CI 1.35-1.83, respectively), compared to women without a diagnosed myoma (Table 3). However, women with a history of myomectomy had a significantly higher risk of uterine rupture (aOR 12.78, 95% CI 6.5-25.13). We evaluated incidences of uterine rupture in women with myomectomy, according to the time interval after myomectomy (Figure 2). The incidence of uterine rupture was significantly higher at delivery within one year after myomectomy (0.71%) compared to any longer delivery interval after myomectomy.

We compared obstetric outcomes in dataset 2 (Table 4). Both groups of women with a history of diagnosed myoma or myomectomy had significantly higher risks of preterm birth and LBW than did women without a diagnosed myoma. However, women with diagnosed myoma(s) and women with a history of myomectomy had a significantly lower risk of LGA.

When the myomectomy group was divided to two groups based on the types of myomas, the results were similar in women with submucosal or intramural myomas and subserosal or unspecified myomas (suppl 1&2).

Multivariate logistic regression analysis for adverse obstetric outcomes in pregnancies with myoma or following myomectomy, in nulliparous women

In nulliparous women, both groups of women with a history of diagnosed myoma(s) and women with a history of myomectomy had significantly higher risks of cesarean section (aOR 1.13, 95% CI 1.1-1.17 and aOR 6.38, 95% CI 5.84-6.97, respectively), placenta previa (aOR 1.5, 95% CI 1.34-1.67 and aOR 1.78, 95% CI 1.49-2.13, respectively), and uterine rupture (aOR 4.14, 95% CI 1.14-15.06 and aOR 41.35, 95% CI 16.18-105.69, respectively), compared to women without a diagnosed myoma (Table 5). Risk of preeclampsia was slightly increased in women with a history of diagnosed myoma(s) (aOR 1.15, 95% CI 1.05-1.27), compared to women without a diagnosed myoma. In obstetric outcomes of dataset 2, among nulliparous women, both groups of women with a history of diagnosed myoma(s) and women with a history of myomectomy had significantly higher risks of preterm birth (aOR 1.45, 95% CI 1.33-1.57 and aOR 1.79, 95% CI 1.57-2.05, respectively), and LBW (aOR 1.31, 95% CI 1.23-1.41 and aOR 1.55, 95% CI 1.38-1.74, respectively), compared to women without a diagnosed myoma (Table 6). In nulliparous women, women with a history of myomectomy had a significantly lower risk of LGA (aOR 0.66, 95% CI 0.53-0.82), compared to women without a diagnosed myoma.

Discussion

Main Findings

The principal findings of this study are as follows, if myomectomy was performed within 10 to 11 years before delivery: (1) In the study population (dataset 2), 25,408 (4.76%) women had a history of diagnosed myoma(s) but no myomectomy, and 6,642 (1.24%) women received myomectomy before pregnancy.; (2) Women who have had a myomectomy had higher risks of cesarean section, placenta previa, preterm birth, LBW, and uterine rupture, but a lower risk of LGA, than did women without a history of diagnosed myoma.; (3) The incidence of uterine rupture was higher at delivery within one year after myomectomy (0.71%) than during any longer delivery interval after myomectomy.; (4) Women with a history of diagnosed myoma had higher risks of cesarean section and placenta previa, but no increased risks of preterm birth, LBW, or uterine rupture, compared to women without a history of diagnosed myoma. (5) In nulliparous women, both groups of women with a history of diagnosed myoma(s) and women with a history of myomectomy had higher risks of cesarean section, placenta previa, uterine rupture, preterm birth, and LBW, compared to women without a diagnoses myoma. Especially, aORs for uterine rupure in women with diagnosed myoma and women who have had a myomectomy were 4.14 and 41.35, respectively, in nulliparous women.

Interpretation

Previous studies have also reported increased adverse pregnancy outcomes, including abnormal placentation, such as placenta previa or placenta accreta,[10,12,13] preterm delivery, cesarean delivery, uterine rupture, and postpartum bleeding, in women with a history of myomectomy.[14-17] The true incidence of uterine rupture during subsequent pregnancy following myomectomy is difficult to establish, because most of the studies have been cases, case series, or small retrospective cohort studies that do not account for the total number of pregnancies achieved after myomectomy and their consequent outcomes. The incidences of preterm birth and uterine rupture after myomectomy have been variously reported to range from 3.1% to 35% and from 0.2 to 3.7%, respectively.[18,19] The previous systematic review including all cohort studies with at least five cases demonstrated that the overall incidence of uterine rupture after myomectomy was 0.93% (0.45–1.92%) (*n* = 7/756); specifically, it was 0.47% (0.13–1.70%) (*n* = 2/426) in women undergoing a trial of labor after myomectomy, and 1.52% (0.65–3.51%) (*n* = 5/330) in women before the onset of labor.[5] However, the number of pregnancies and viable deliveries after prior myomectomy were 2,367 and 1,284, respectively, from a total of 23 studies. In our study, pregnancy outcomes were available for 9,890 women with a history of myomectomy, which was the largest population. In the previous studies, although uterine rupture occurred at various gestation, it occurred more often before the onset of labor, with a high rate of fetal loss.[5,19] In this study, the incidence of uterine rupture in women with a history of myomectomy was 0.22%, which is less than the reported incidence of uterine rupture (0.4-0.7%) in a trial of labor after cesarean section.[20,21] Possible reasons can be a missing diagnosis when uterine rupture or dehiscence was combined with placental abruption or antepartum/postpartum bleeding in the middle of pregnancy. However, in this study, women with a history of myomectomy had more than a 12-fold risk of uterine rupture over that of women without a

diagnosed myoma. In nulliparous women, women with a history of diagnosed myoma(s) and women with a history of myomectomy had 4.14-fold and 41.35-fold higher risks of uterine rupture, compared to it of women without a diagnoses myoma. Therefore, counseling for myomectomy in women who desire a pregnancy in the future should discuss the risk of adverse pregnancy outcomes, especially uterine rupture during pregnancy, which can be associated with fetal loss.

In a previous comparison study about delivery outcomes between pregnancies following myomectomy and myoma-complicated pregnancies, the latter showed better outcomes, including fewer cesarean sections, preterm births, and less blood loss, than outcomes of pregnancies after myomectomy, which were similar to the results of this study[22] A recent retrospective cohort study[23] revealed that women with a history of myomectomy were associated with increased risks of intraoperative transfusion, bowel injury, and a cesarean hysterectomy.

Previously, ACOG stated that myomectomy should be considered for a woman with uterine leiomyomas who has undergone several unsuccessful IVF cycles despite appropriate ovarian response and good-quality embryos.[24] SOGC, ASRM, and French guidelines also stated that intramural myomas may have a negative effect on fertility, but treating them does not improve fertility, and myomectomy is therefore indicated only for symptomatic myomas,[6,24,25] They emphasized that information should be provided about the risk of uterine rupture during a future pregnancy, before planning a myomectomy in women who might become pregnant later on.

Strengths and Limitations

A limitation of this study was our lack of data on number, size, or type of myomas, type of closure after myomectomy, number of suture layers, surgical techniques such as uterine artery clamps before myomectomy, and use of vasopression or electrocauterization, which may have important clinical significance. However, we divided myomectomy group to submucosal or intramural myomas and subserosal or unspecified myomas, based on diagnostic codes. The results were not different according to types of myomas, although it is difficult to define the unspecified myomas. The second limitation was that there was no information on the type of myomectomy (laparoscopic, open, hysteroscopic, or robot-assisted) or type of conception (natural, OS, OS-IUI, or IVF). And data about gestational age at uterine rupture or rupture site were not available. Lastly, this study did not have data if myomectomy or cesarean section was performed before the study period (2004-2015).

However, this study included the largest population in the group with a history of diagnosed myoma(s) with and without myomectomy. In addition, the nationwide design of the original database can provide more generalized outcomes in pregnancies with diagnosed myoma(s) and with previous myomectomy. To our knowledge, this is the first study about incidence of uterine rupture in women with myomectomy, according to delivery time interval after myomectomy. The incidence of uterine rupture was highest within one year after surgery, in this study. A previous study has reported that incision healing after a caesarean section took at least 6 months for the complete involution and recovery of uterine zonal anatomy by

magnetic resonance imaging.[26] The other study also reported that risk of uterine rupture was 3.12 fold in pregnant women less than <12 months since their last caesarean delivery, compared to it in women more than 24 months since their last caesarean delivery, with the odds of rupture appearing to plateau for intervals beyond 12 months.[27] Lastly, we had subgroup analysis for adverse obstetric outcomes in nulliparous women, because it can clearly eliminate the effects of previous cesarean section, which could be performed before the study period. In nulliparous women, both groups of women with a history of diagnosed myoma(s) and women with a history of myomectomy had higher risks of cesarean section, placenta previa, uterine rupture, preterm birth, and LBW compare to women without a diagnoses myoma. However, the risk of uterine rupture was much higher in women with a history of myomectomy. These results might be useful in counseling when a woman, who might become pregnant later on, is diagnosed with uterine myoma.

Conclusion

Women with a history of myomectomy had significantly higher risks of cesarean section and placenta previa compared to women without a diagnosed myoma. And the risks of uterine rupture, preterm birth, and low birth weight were significantly higher in women with previous myomectomy, compared to women without a diagnosed myoma. In nulliparous women, the risk of uterine rupture was much increased in women with a history myomectomy, compared to women without a diagnosed myoma. In addition, the incidence of uterine rupture was significantly higher at delivery within one year after myomectomy. When a woman is diagnosed as having myoma(s) before pregnancy, counseling should include information about the risks of pregnancies with myoma(s) and after myomectomy. Especially, if myomectomy is considered before pregnancy, a woman should be counseled that her risk of uterine rupture, during pregnancies after myomectomy can be increased.

Abbreviations

ASRM, American Society for Reproductive Medicine

SOGC, Society of Obstetricians and Gynaecologists of Canada

KNHI, Korea National Health Insurance

NHSP-IC, National Health Screening Program for Infants and Children

LBW, Low birth weight

LGA, Large for gestational age

ART, Assisted reproductive treatment

PPH, Postpartum hemorrhage

Declarations

Ethics approval and consent to participate

The institutional review board of Korea University Guro Hospital approved the collection and use of clinical information for research purposes (No. 2020GR0012; Approval date, January 9, 2020). This study is in compliance with the 2013 Helsinki World Medical Association Declaration.

Consent for publication

Not applicable..

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

Funding

This research was supported by the Korean society of Maternal Fetal Medicine Research Fund. (grant no. KSMFM-2019-001). The Korean society of Maternal Fetal Medicine had no role in the design of the study and collection, analysis, and interpretation of data.

Authors' contributions

SJL, HSK, GJC and IYP conceived the study and designed the experiment. SJL, HSK, SHN, JYB, WJS, JWK, JES, HJC, KYC, GJC and IYP contributed the collection of data and performed the experiment. HSK, GJC and IYP analyzed the data and contributed to the statistical analysis. SJL, HSK, GJC and IYP wrote the article. All authors critically revised the article and gave approval of the version to be published.

Acknowledgments

We are grateful to the patients in the study. We thank our medical staffs for their assistance. This research was supported by the Korean society of Maternal Fetal Medicine Research Fund. (grant no. KSMFM-2019-001)

References

1. Practice Committee of the American Society for Reproductive Medicine. Myomas and reproductive function. Fertil Steril. 2004;82 Suppl 1:S111-6
2. Practice Committee of the American Society for Reproductive Medicine. Myomas and reproductive function. Fertil Steril. 2006; 86(5 Suppl 1): S194-9

3. Klatsky PC, Tran ND, Caughey AB, Fujimoto VY. Fibroids and reproductive outcomes: a systematic literature review from conception to delivery. Am J Obstet Gynecol 2008; 198(4): 357-66. doi: 10.1016/j.ajog.2007.12.039.
4. Whynott RM, Vaught KCC, Segars JH. The effect of uterine fibroids on infertility: A systematic review. Semin Reprod Med. 2017; 35(6): 523-32. doi: 10.1055/s-0037-1607295.
5. Gambacorti-Passerini Z, Gimovsky AC, Locatelli A, Berghella V. Trial of labor after myomectomy and uterine rupture: a systematic review. Acta Obstet Gynecol Scand 2016; 95(7): 724-34. doi: 10.1111/aogs.12920.
6. Practice Committee of the American Society for Reproductive Medicine. Removal of myomas in asymptomatic patients to improve fertility and/or reduce miscarriage rate: a guideline. Fertil Steril. 2017; 108(3): 416-25. doi: 10.1016/j.fertnstert.2017.06.034.
7. Carranza-Mamane B, Havelock J, Hemmings R, REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY COMMITTEE; SPECIAL CONTRIBUTOR. The management of uterine fibroids in women with otherwise unexplained infertility. J Obstet Gynaecol Can. 2015; 37(3): 277-85. doi: 10.1016/S1701-2163(15)30318-2.
8. Wechter ME, Stewart EA, Myers ER, Kho RM, Wu JM. Leiomyoma-related hospitalization and surgery: prevalence and predicted growth based on population trends. Am J Obstet Gynecol 2011; 205(5): 492. e1-. e5. doi: 10.1016/j.ajog.2011.07.008.
9. Yuk JS, Lee JH. Six-year survival of patients with unsuspected uterine malignancy after laparoscopic versus laparotomic myomectomy: An 11-year national retrospective cohort study. Gynecol Oncol 2018; 151(1): 91-5. doi: 10.1016/j.ygyno.2018.08.026.
10. Milazzo GN, Catalano A, Badia V, Mallozzi M, Caserta D. Myoma and myomectomy: Poor evidence concern in pregnancy. J Obstet Gynaecol Res. 2017; 43(12): 1789-804. doi: 10.1111/jog.13437.
11. National Health Screening Program for Infants and Children. http://hi.nhis.or.kr/aa/ggpaa001/ggpaa004_m01.do. Accessed 6 September 2020.
12. Miller DA, Chollet JA, Goodwin TM. Clinical risk factors for placenta previa–placenta accreta. Am J Obstet Gynecol 1997; 177(1): 210-4.
13. Khong TY. The pathology of placenta accreta, a worldwide epidemic. J Clin Pathol 2008; 61(12): 1243-6. doi: 10.1136/jcp.2008.055202. Epub 2008 Jul 19.
14. Fukuda M, Tanaka T, Kamada M, Hayashi A, Yamashita Y, Terai Y, et al. Comparison of the perinatal outcomes after laparoscopic myomectomy versus abdominal myomectomy. Gynecol Obstet Invest 2013; 76(4): 203-8. doi: 10.1159/000355098.
15. Fagherazzi S, Borgato S, Bertin M, Vitagliano A, Tommasi L, Conte L. Pregnancy outcome after laparoscopic myomectomy. Clin Exp Obstet Gynecol 2014; 41(4): 375-9.
16. Seracchioli R, Manuzzi L, Vianello F, Gualerzi B, Savelli L, Paradisi R, et al. Obstetric and delivery outcome of pregnancies achieved after laparoscopic myomectomy. Fertil Steril. 2006; 86(1): 159-65.
17. Flyckt R, Soto E, Nutter B, Falcone T. Comparison of long-term fertility and bleeding outcomes after robotic-assisted, laparoscopic, and abdominal myomectomy. Obstet Gynecol Int 2016;

2016:2789201. doi: 10.1155/2016/2789201.

18. Palomba S, Zupi E, Falbo A, Russo T, Marconi D, Tolino A, et al. A multicenter randomized, controlled study comparing laparoscopic versus minilaparotomic myomectomy: reproductive outcomes. Fertil Steril. 2007; 88(4): 933-41.
19. Pop L, Suciu ID, Oprescu D, Micu R, Stoicescu S, Foroughi E, et al. Patency of uterine wall in pregnancies following assisted and spontaneous conception with antecedent laparoscopic and abdominal myomectomies–a difficult case and systematic review. J Matern Fetal Neonatal Med. 2019; 32(13): 2241-8. doi: 10.1080/14767058.2018.1427060.
20. Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, et al. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. N Engl J Med 2004; 351(25): 2581-9.
21. Guise JM, Denman MA, Emeis C, Marshall N, Walker M, Fu R, et al. Vaginal birth after cesarean: new insights on maternal and neonatal outcomes. Obstet Gynecol 2010; 115(6): 1267-78. doi: 10.1097/AOG.0b013e3181df925f.
22. Kinugasa-Taniguchi Y, Ueda Y, Hara-Ohyagi C, Enomoto T, Kanagawa T, Kimura T. Impaired delivery outcomes in pregnancies following myomectomy compared to myoma-complicated pregnancies. J Reprod Med 2011; 56(3-4): 142-8.
23. Gimovsky AC, Frangieh M, Phillips J, Vargas MV, Quinlan S, Macri C, et al. Perinatal outcomes of women undergoing cesarean delivery after prior myomectomy. J Matern Fetal Neonatal Med 2018: 1-6. doi: 10.1080/14767058.2018.1542680.
24. American College of Obstetricians and Gynecologists. ACOG practice bulletin. Alternatives to hysterectomy in the management of leiomyomas. Obstet Gynecol. 2008; 112(2 Pt 1): 387-400. doi: 10.1097/AOG.0b013e318183fbab.
25. Marret H, Fritel X, Ouldamer L, Bendifallah S, Brun JL, De Jesus I, et al. Therapeutic management of uterine fibroid tumors: updated French guidelines. Eur J Obstet Gynecol Reprod Biol. 2012; 165(2): 156-64. doi: 10.1016/j.ejogrb.2012.07.030.
26. Dicle O, Küçükler C, Pirnar T, Erata Y, Posaci C. Magnetic resonance imaging evaluation of incision healing after cesarean sections. Eur Radiol. 1997;7(1):31-34. doi:10.1007/s003300050103
27. Fitzpatrick KE, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M. Uterine rupture by intended mode of delivery in the UK: a national case-control study. PLoS Med. 2012;9(3):e1001184. doi:10.1371/journal.pmed.1001184

Tables

Table 1. Demographics and birth outcomes of study population (Dataset 1)

*Group A, Women who had never been diagnosed with myoma; Group B, Women who had diagnosed myoma(s) but no history of myomectomy; Group C, Women who had a history of

	Group A* (N = 740,675)	Group B* (N = 38,402)	Group C* (N = 9,890)	*p*-value
Age	31.62 ± 3.96	33.87 ± 3.50	34.63 ± 3.42	<.0001
Nulliparity	385,663 (52.07)	19,541 (50.89)	5,380 (54.40)	<.0001
Multiple pregnancy	12,495 (1.69)	1,074 (2.80)	432 (4.37)	<.0001
Cesarean section	286,946 (38.74)	17,547 (45.69)	8,447 (85.41)	<.0001
Preeclampsia	16,033 (2.16)	1,063 (2.77)	327 (3.31)	<.0001
PPH	72,501 (9.79)	3,946 (10.28)	1,007 (10.18)	0.0035
Placental abruption	2,728 (0.37)	170 (0.44)	40 (0.40)	0.0572
Placenta previa	9,365 (1.26)	848 (2.21)	289 (2.92)	<.0001
Uterine rupture	107 (0.01)	12 (0.03)	22 (0.22)	<.0001

*Group A, Women who had never been diagnosed with myoma; Group B, Women who had diagnosed myoma(s) but no history of myomectomy; Group C, Women who had a history of myomectomy

PPH, Postpartum hemorrhage

Values are given as mean ± standard deviation or number (%).

Table 2. Demographics and birth outcomes of study population (Dataset 2)

	Group A* (N = 502,209)	Group B* (N = 25,408)	Group C* (N = 6,642)	*p*-value
Preterm birth	13,470 (2.68)	1,018 (4.01)	327 (4.92)	<.0001
Neonatal sex–male	258,518 (51.48)	13,066 (51.42)	3,430 (51.64)	<.0001
Birth weight (kg)	3.20 ± 0.46	3.17 ± 0.50	3.11 ± 0.50	<.0001
LBW	20,203 (4.02)	1,452 (5.71)	459 (6.91)	<.0001
LGA	17,390 (3.46)	885 (3.48)	165 (2.48)	<.0001

*Group A, Women who had never been diagnosed with myoma; Group B, Women who had diagnosed myoma(s) but no history of myomectomy; Group C, Women who had a history of myomectomy

LBW, Low birth weight; LGA, Large for gestational age

Values are given as mean ± standard deviation or number (%).

Table 3. The obstetric outcomes in women with diagnosed myoma(s) or a history of myomectomy (Dataset 1)

Obstetric outcomes	Odds ratio (95% confidence interval)	
	Unadjusted	Adjusted [a]
Cesarean section		
Group A	1	1
Group B	1.312 (1.279 – 1.346)	1.193 (1.163 – 1.224)
Group C	8.992 (8.408 – 9.617)	7.985 (7.463 – 8.544)
Preeclampsia		
Group A	1	1
Group B	1.326 (1.227 – 1.433)	1.124 (1.123 – 1.313)
Group C	1.360 (1.175 – 1.574)	1.159 (1.000 – 1.343)
PPH		
Group A	1	1
Group B	1.048 (1.005 – 1.092)	1.049 (1.006 – 1.094)
Group C	1.064 (0.983 – 1.152)	1.062 (0.981 – 1.151)
Placental abruption		
Group A	1	1
Group B	1.185 (0.970 – 1.448)	1.118 (0.914 – 1.368)
Group C	1.156 (0.784 – 1.704)	1.037 (0.703 – 1.532)
Placenta previa		
Group A	1	1
Group B	1.797 (1.646 – 1.962)	1.549 (1.418 – 1.692)
Group C	2.223 (1.912 – 2.584)	1.772 (1.523 – 2.063)
Uterine rupture		
Group A	1	1
Group B	2.421 (1.037 – 5.651)	2.032 (0.865 – 4.777)
Group C	17.00 (8.836 – 32.708)	13.674 (6.986 – 26.765)

*Group A, Women who had never been diagnosed with myoma; Group B, Women who had diagnosed myoma(s) but no history of myomectomy; Group C, Women who had a history of myomectomy

PPH, Postpartum hemorrhage

[a] Adjusted for age and parity

Table 4. The obstetric outcomes in women with diagnosed myoma(s) or a history of myomectomy (Dataset 2)

Obstetric outcomes	Odds ratio (95% confidence interval)	
	Unadjusted	Adjusted [a]
Preterm birth		
Group A	1	1
Group B	1.514 (1.419 – 1.616)	1.426 (1.336 – 1.523)
Group C	1.879 (1.679 – 2.103)	1.698 (1.517 – 1.902)
LBW		
Group A	1	1
Group B	1.446 (1.369 – 1.528)	1.355 (1.282 – 1.432)
Group C	1.771 (1.609 – 1.949)	1.580 (1.435 – 1.741)
LGA		
Group A	1	1
Group B	1.006 (0.939 – 1.078)	0.981 (0.916 – 1.051)
Group C	0.711 (0.609 – 0.830)	0.688 (0.589 – 0.803)

*Group A, Women who had never been diagnosed with myoma; Group B, Women who had diagnosed myoma(s) but no history of myomectomy; Group C, Women who had a history of myomectomy

LBW, Low birth weight; LGA, Large for gestational age

[a] Adjusted for age and parity

Table 5. The obstetric outcomes in nulliparous women with diagnosed myoma(s) or a history of myomectomy (Dataset 1)

Obstetric outcomes	Odds ratio (95% confidence interval)	
	Unadjusted	Adjusted [a]
Cesarean section		
Group A	1	1
Group B	1.386(1.339 – 1.435)	1.210(1.168 – 1.253)
Group C	8.194(7.502 – 8.949)	6.908(6.320 – 7.551)
Preeclampsia		
Group A	1	1
Group B	1.289(1.173 – 1.418)	1.180(1.072 – 1.298)
Group C	1.353(1.139 – 1.607)	1.180(0.992 – 1.403)
PPH		
Group A	1	1
Group B	1.045(0.988 – 1.105)	1.050(0.993 – 1.111)
Group C	1.037(0.934 – 1.151)	1.046(0.942 – 1.162)
Placental abruption		
Group A	1	1
Group B	1.113(0.863 – 1.435)	1.054(0.816 – 1.361)
Group C	1.015(0.619 – 1.664)	0.933(0.567 – 1.533)
Placenta previa		
Group A	1	1
Group B	2.008(1.798 – 2.242)	1.689(1.510 – 1.890)
Group C	2.672(2.236 – 3.193)	2.059(1.720 – 2.466)
Uterine rupture		
Group A	1	1
Group B	5.071(1.431 – 17.972)	4.667(1.295 – 16.816)
Group C	54.783(23.070 – 130.090)	48.206(19.239 – 120.789)

*Group A, Women who had never been diagnosed with myoma; Group B, Women who had diagnosed myoma(s) but no history of myomectomy; Group C, %) women who had a history of myomectomy

PPH, Postpartum hemorrhage

a Adjusted for age

Table 6. The obstetric outcomes in nulliparous women with diagnosed myoma(s) or a history of myomectomy (Dataset 2)

Obstetric outcomes	Odds ratio (95% confidence interval)	
	Unadjusted	Adjusted [a]
Preterm birth		
Group A	1	1
Group B	1.649(1.520 – 1.788)	1.510(1.390 – 1.639)
Group C	2.145(1.876 – 2.452)	1.874(1.636 – 2.145)
LBW		
Group A	1	1
Group B	1.512(1.412 – 1.620)	1.377(1.285 – 1.476)
Group C	1.883(1.678 – 2.114)	1.631(1.451 – 1.833)
LGA		
Group A	1	1
Group B	1.030(0.937 – 1.132)	1.021(0.928 – 1.123)
Group C	0.676(0.546 – 0.838)	0.667(0.538 – 0.827)

*Group A, Women who had never been diagnosed with myoma; Group B, Women who had diagnosed myoma(s) but no history of myomectomy; Group C, %) women who had a history of myomectomy

LBW, Low birth weight; LGA, Large for gestational age

Figures

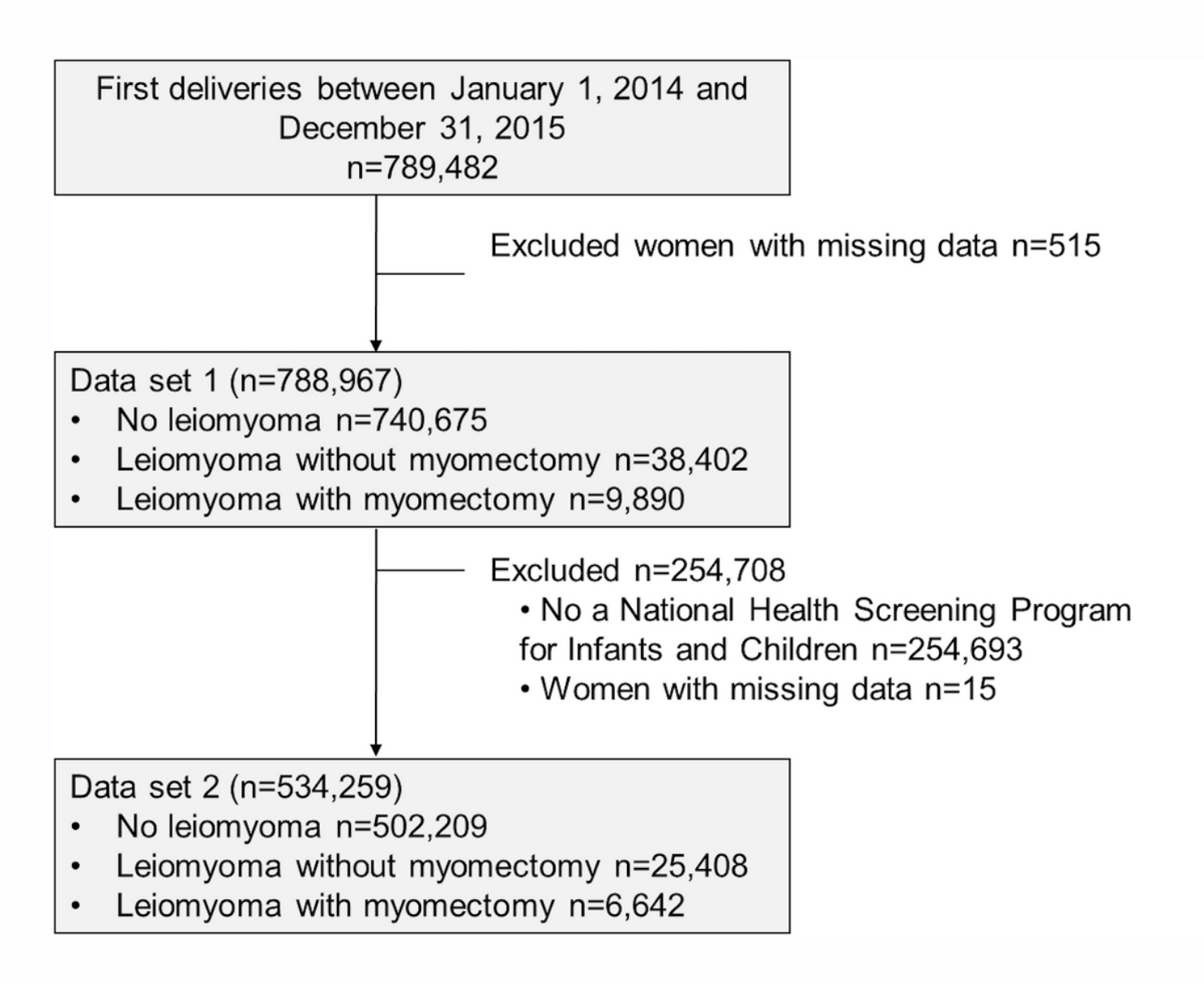

Figure 1

Flow chart of study participants' enrollment

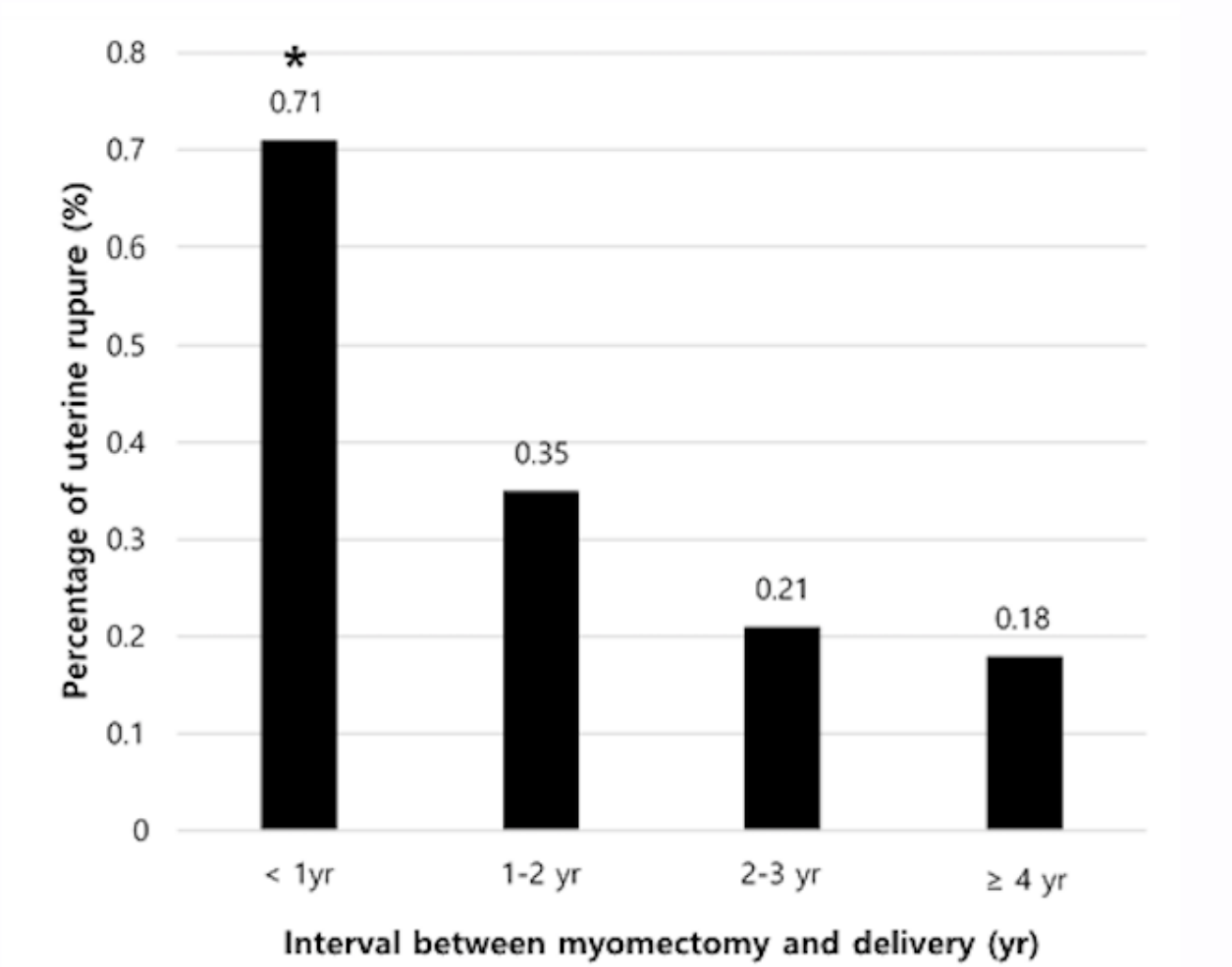

Figure 2

Incidence of uterine rupture in women with myomectomy, according to time interval after myomectomy.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarytable.docx