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ORIGINAL RESEARCH

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Comparison of open and laparoscopic appendectomy according to the trimester of pregnancy: A nationwide observational study

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Abstract

Objective: To compare the outcomes of open appendectomy (OA) and laparoscopic appendectomy (LA) for acute appendicitis during pregnancy by trimester.

Methods: We conducted a nationwide retrospective cohort study using the Diagnosis Procedure Combination database in Japan. We identified pregnant women diagnosed with appendicitis who underwent OA or LA from 2010 to 2022. Pathological confirmation of appendicitis was not required for inclusion. The patients were categorized by the trimester of pregnancy. Outcomes were compared using multivariate analysis with generalized estimating equations.

Results: A total of 1624 patients were included. In the first trimester, 64.2% patients underwent OA, whereas 35.8% patients underwent LA; in the second trimester, 59.1% patients had OA and 40.9% patients had LA; and in the third trimester, 72.8% patients had OA and 27.2% patients had LA. LA was associated with a higher rate of preterm labor, preterm delivery, or abortion in the second (odds ratio, 3.37; 95% confidence interval, 1.76–6.47; and $p < 0.001$) and third trimesters (odds ratio, 2.57; 95% confidence interval, 1.15–5.70; and $p = 0.021$) but not in the first trimester. The duration of surgery was longer across all trimesters in patients who underwent LA. Additionally, the postoperative hospital stay was shorter in patients who had LA than in those who had OA in the second trimester.

Conclusions: In-hospital outcomes vary by trimester, and our results suggest that LA does not consistently lead to better outcomes than OA. Based on our findings, treatment options for appendicitis during pregnancy must be carefully selected.

KEYWORDS
abortion, acute appendicitis, appendectomy, complication, pregnancy, premature birth

1 | INTRODUCTION

Acute appendicitis during pregnancy is the most common nonobstetric surgical condition, with an incidence reported as 101 cases/100,000 births.[1] Although open appendectomy (OA) has been widely performed in the past, laparoscopic appendectomy (LA) is increasingly becoming the standard treatment for appendectomy.[2] LA has a lower risk of complications, such as preterm labor, antepartum hemorrhage, and intrauterine infections, than OA.[3,4] Furthermore, the Society of American Gastrointestinal Endoscopic Surgeons recommends LA in all trimesters.[3,5]

However, some previous studies demonstrated an increased incidence of fetal loss linked to LA.[6–8] Furthermore, previous large-scale studies have been criticized for evaluating outcomes without taking gestational age into consideration.[1,3,4,9] In laparoscopic surgery during pregnancy, outcomes vary by gestational age suggesting that including gestational age in the analysis might be appropriate.[10]

This study aimed to address the discrepancies reported in the outcomes of OA and LA across various studies, particularly regarding not taking gestational age into account. We used a national inpatient database from Japan to compare the outcomes of OA and LA during pregnancy. In our analysis, we stratified gestational age by trimester to evaluate the associations between surgical methods and peripartum complications.

2 | METHODS

2.1 | Study design and data source

A retrospective nationwide cohort analysis was conducted using the Diagnostic Procedure Combination database from July 2010 to March 2022. This database includes discharge summaries and administrative claims data from more than 1500 acute-care hospitals and it encompasses approximately 90% of all tertiary-care emergency hospitals in Japan.[11,12] This database includes the following data for all hospitalizations: dates of admission and discharge, patient's age and sex, body weight and height, main diagnosis, admission-precipitating diagnosis, most and second most resource-consuming diagnoses, comorbidities present on admission and complications arising after admission, procedures performed, medications and devices used, in-hospital mortality, pregnancy status (pregnant or not), gestational age at admission, and delivery during hospitalization. Diagnoses, comorbidities, and complications are recorded using the international classification of diseases, 10th Revision (ICD-10) codes and text in Japanese. Attending physicians are encouraged to record diagnoses accurately by linking data entries with reimbursement for healthcare costs. The details of this database have been described previously [11] and its reliability has been demonstrated. In this database, the diagnostic data accuracy ranges from 50% to 80% for sensitivity and reaches up to 96% for specificity.[13] The accuracy of recorded procedures is also high, with specificity and sensitivity exceeding 90%.[13]

The study was approved by the Institutional Review Board of the University of Tokyo (approval number: 3501) and complied with the Declaration of Helsinki's ethical standards. The requirement for informed consent was waived because of the anonymization and deidentification of data.

2.2 | Study population

We included individuals who were pregnant and were diagnosed with acute appendicitis. Acute appendicitis was defined using ICD-10 codes coded in the main diagnosis, admission-precipitating diagnosis, or two resource-consuming diagnoses (Supplementary Table 1 in Supporting Information S1). Acute appendicitis was classified into complicated and uncomplicated appendicitis. Complicated appendicitis, based on the ICD-10 codes, included acute appendicitis with generalized peritonitis and acute appendicitis with peritoneal abscess, whereas uncomplicated appendicitis included all other cases of acute appendicitis (Supplementary Table 1 in Supporting Information S1). Appendectomy was classified into LA (K7182) and OA (K718) based on Japanese medical procedure codes. The exclusion criteria were unknown gestational age, multiple gestations, and receiving neither LA nor OA.

2.3 | Variables and outcomes

The primary outcome was preterm delivery, preterm labor, or abortion. Here, abortion refers exclusively to spontaneous abortion. These outcomes were based on previous studies.[3,9] The secondary outcomes included premature rupture of membranes, amniotic fluid infection, sepsis, surgical complications, operative time, and postoperative hospital stay. Surgical complications included thrombosis, intestinal injury, ileus, and wound infection. We defined the outcomes using ICD-10 codes (Supplementary Table 1 in Supporting Information S1).

Other studied variables included age, body mass index, ambulance use, teaching hospital, gestational age at admission, severity of appendicitis, number of days from admission to surgery, and anesthesia method during surgery.

2.4 | Statistical analysis

According to the gestational age at admission, we categorized pregnant women with acute appendicitis into those in the first trimester (<14 weeks), second trimester (≥14 weeks and <28 weeks), and third trimester (≥28 weeks). Continuous variables are presented as the median and interquartile range (IQR), whereas categorical variables are presented as the number and percentage. We compared the outcomes of OA and LA using the Mann–Whitney *U* test for continuous variables and Fisher's exact test for categorical data. To adjust for individual-level and hospital-level factors when comparing outcomes, we used a multivariable regression with generalized estimating equations. Clinically important factors were preferentially selected as confounders. A logistic regression was conducted for binary outcomes and a multivariable linear regression was conducted for continuous outcomes. All statistical analyses were conducted using Stata/SE17 (StataCorp, College Station, TX) and *R* version 4.3.0 (The *R* Foundation, Vienna, Austria). All tests were two-tailed, with a threshold for statistical significance set at $p < 0.05$.

3 | RESULTS

A flowchart of the patients' selection is shown in Figure 1. After the inclusion and exclusion criteria were applied, 1624 pregnant women with acute appendicitis from 470 facilities were eligible for the present study. Among the eligible patients, the selection of surgeries varied by trimester. In the first trimester, 337 (64.2%) patients had OA and 188 (35.8%) patients had LA. In the second trimester, 506 (59.1%) patients had OA and 350 (40.9%) patients had LA. In the third trimester, 177 (72.8%) patients had OA and 66 (27.2%) patients had LA. The annual trend of the percentage of LA during the observation period is shown in Figure 2. From 2010 to 2022, the percentage of LA increased by 6.43% (95% confidence interval [CI], 5.86–7.00; and $p < 0.001$) annually and rose from 0.0% to 81.3%.

Table 1 shows the characteristics of the patients stratified by trimester. Age, body mass index, gestational age at admission, and the proportion of complicated appendicitis were similar across the trimesters. Although surgeries on the day of admission were common in all trimesters, the LA group showed a slightly longer time between admission and surgery than the OA group in the third trimester.

Table 2 shows the in-hospital outcomes stratified by trimesters. The percentage of preterm delivery, preterm labor, or abortion was significantly higher in the LA group than in the OA group in the second trimester (3.6% vs. 10.6% and $p < 0.001$) and in the third trimester (11.3% vs. 24.2% and $p = 0.015$). Premature rupture of membranes, amniotic fluid infection, sepsis, and surgical complications were similar between the groups across all trimesters. The operative time was significantly longer in the LA group than in the OA group across all trimesters. Additionally, the number of days of the postoperative hospital stay was significantly shorter in the LA group than in the OA group in the second and third trimesters. However, in the first trimester, the hospital stay was similar between the groups.

Table 3 shows the results of the multivariable regression. The LA group showed significantly higher odds for preterm delivery, preterm labor, or abortion than the reference group (OA group) in the second (OR, 3.37; 95% CI, 1.76–6.47; and $p < 0.001$) and third (OR, 2.57; 95% CI, 1.15–5.70; and $p = 0.021$) trimesters. The LA group showed a significantly longer operative time across all trimesters. The LA group showed a significantly shorter postoperative hospital stay only in the second trimester (−2.26 days; 95% CI, −3.84 to −0.69 days; and $p = 0.005$).

4 | DISCUSSION

Our study showed several key findings. The incidence of LA has increased over time. However, patients in the LA group showed higher odds for preterm delivery, preterm labor, or abortion in the second and third trimesters. The operative time was longer in the LA group than in the OA group in all trimesters. Furthermore, the length of the postoperative hospital stay was shorter in the LA group in the second trimester. Our findings suggest that physicians should be aware that outcomes of pregnant women with acute appendicitis vary by the trimester.

In our cohort, we observed a clear increasing trend in LA during the observation period. This observation is consistent with the current guideline, which states that laparoscopic surgery can be safely performed at any stage of pregnancy.[5] However, the existing research supporting these guidelines is not robust and is often constrained by limited data on gestational ages and small cohort sizes.[14,15]

A recent study reported that LA was associated with significantly lower percentages of preterm delivery and preterm labor than OA, which is in contrast with our findings.[3] However, the percentage of preterm abortion was similar in both groups in the previous study, which appears to be consistent with our results.[3] The previous study and our study both used national hospital data. However, the differences between the studies may be due to variations in the patients' demographics or disparities in the quality and care of medical services across different regions and countries. Additionally, the previous study lacked data on gestational age, which might have resulted in a distribution of cases by

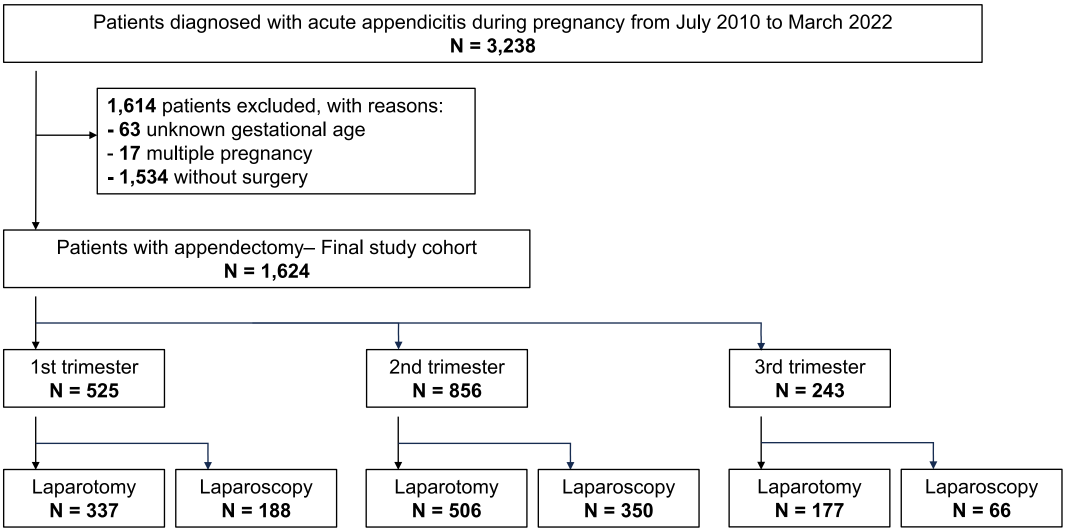

FIGURE 1 Flowchart of the study participants. A total of 3238 cases of acute appendicitis in pregnancy were identified in the database, of which 1624 met the eligibility criteria and formed the final study cohort. The cohort included 525 (32.3%) in the first trimester, 856 (52.7%) in the second trimester, and 243 (15.0%) in the third trimester. [Colour figure can be viewed at wileyonlinelibrary.com]

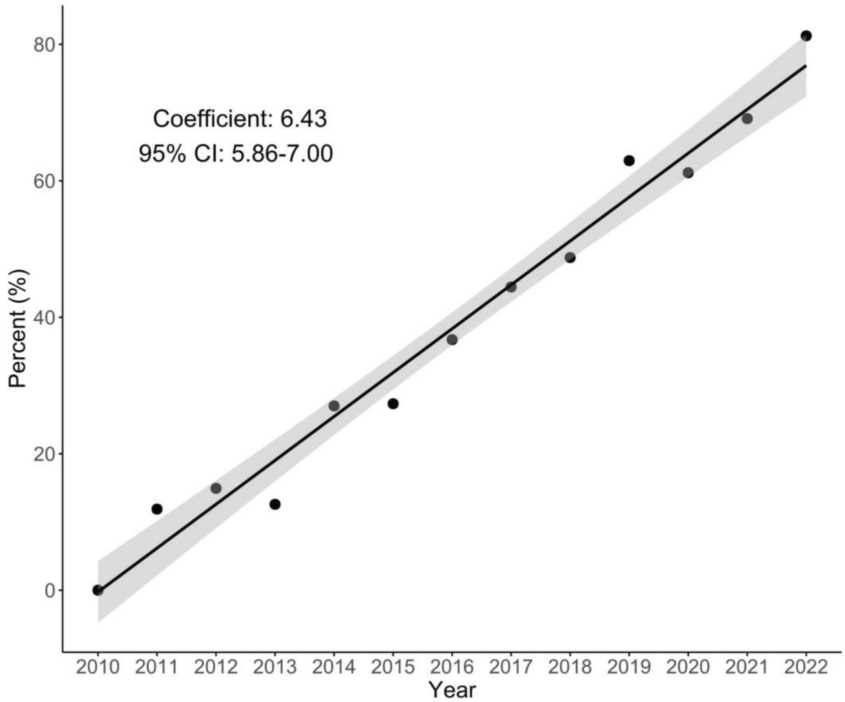

FIGURE 2 Annual trends in laparoscopic appendectomy during pregnancy. The numerator represents the number of laparoscopic appendectomies and the denominator shows the total number of all appendectomies during pregnancy. From 2010 to 2022, the rate of laparoscopic appendectomy increased by 6.43% (95% confidence interval, 5.86–7.00 and $p < 0.001$) annually rising from 0.0% to 81.3%.

trimester that was different to that in our cohort.[3,7] In studies during pregnancy, data should be analyzed taking into account the gestational age.

The operative time in the LA group was approximately 20 min longer than that in the OA group across all trimesters. This trend is consistent with the comparison between laparoscopic and open surgeries in nonpregnant patients.[16] To what extent an extended duration of surgery affects the mother and fetus is unclear. Pneumoperitoneum associated with laparoscopic surgery can increase intra-abdominal pressure and potentially affect the blood circulation.[17] Additionally, uterine irritability associated with surgery may be associated with preterm labor. Taking these factors into

TABLE 1 Comparison of clinical characteristics of patients who underwent open appendectomy and those who underwent laparoscopic appendectomy.

Characteristics	1st trimester Open appendectomy (*N* = 337)	1st trimester Laparoscopic appendectomy (*N* = 188)	*p*-value	2nd trimester Open appendectomy (*N* = 506)	2nd trimester Laparoscopic appendectomy (*N* = 350)	*p*-value	3rd trimester Open appendectomy (*N* = 177)	3rd trimester Laparoscopic appendectomy (*N* = 66)	*p*-value
Age (years)	30 (26–34)	30 (26–35)	0.244	30 (26–34)	31 (27–34)	0.598	32 (28–35)	32 (27–35)	0.859
Body mass index (kg/m^2)			1.000			0.950			0.765
<18.5	57 (16.9)	31 (16.5)		52 (10.3)	35 (10.0)		9 (5.1)	1 (1.5)	
18.5–24.9	225 (66.8)	123 (65.4)		373 (73.7)	255 (72.9)		114 (64.4)	46 (69.7)	
25.0–29.9	26 (7.7)	14 (7.4)		47 (9.3)	38 (10.9)		40 (22.6)	13 (19.7)	
≥30.0	7 (2.1)	4 (2.1)		8 (1.6)	6 (1.7)		9 (5.1)	4 (6.1)	
Missing	22 (6.5)	16 (8.5)		26 (5.1)	16 (4.6)		5 (2.8)	2 (3.0)	
Gestational age (weeks)	9 (7–12)	10 (7–12)	0.501	20 (16–23)	19 (16–23)	0.364	32 (29–34)	31 (29–35)	0.792
Ambulance use	64 (19.0)	46 (24.5)	0.146	119 (23.5)	113 (32.3)	0.005	67 (37.9)	25 (37.9)	1.000
Teaching hospital	318 (94.4)	185 (98.4)	0.038	476 (94.1)	346 (98.9)	<0.001	166 (93.8)	59 (89.4)	0.273
Length of hospital stay before surgery (days)	0 (0–1)	0 (0–1)	0.900	0 (0–1)	0 (0–1)	0.750	0 (0–1)	0.5 (0–1)	0.047
General anesthesia during surgery	47 (13.9)	163 (86.7)	<0.001	101 (20.0)	297 (84.9)	<0.001	54 (30.5)	54 (81.8)	<0.001
Complicated appendicitis	64 (19.0)	41 (21.8)	0.495	100 (19.8)	79 (22.6)	0.347	55 (31.1)	22 (33.3)	0.758

Note: Data are presented as the median (interquartile range) or number (percentage).

TABLE 2 In-hospital outcomes: open versus laparoscopic appendectomy.

Characteristics	1st trimester Open appendectomy (N = 337)	1st trimester Laparoscopic appendectomy (N = 188)	p-value	2nd trimester Open appendectomy (N = 506)	2nd trimester Laparoscopic appendectomy (N = 350)	p-value	3rd trimester Open appendectomy (N = 177)	3rd trimester Laparoscopic appendectomy (N = 66)	p-value
Preterm delivery, preterm labor, or abortion	8 (2.4)	3 (1.6)	0.754	18 (3.6)	37 (10.6)	<0.001	20 (11.3)	16 (24.2)	0.015
Premature rupture of membrane	0 (0.0)	0 (0.0)	-	1 (0.2)	0 (0.0)	1.000	3 (1.7)	1 (1.5)	1.000
Amniotic fluid infection	0 (0.0)	0 (0.0)	-	12 (2.4)	2 (0.6)	0.053	8 (4.5)	2 (3.0)	0.733
Sepsis	1 (0.3)	0 (0.0)	1.000	6 (1.2)	0 (0.0)	0.087	2 (1.1)	1 (1.5)	1.000
Surgical complications[a]	4 (1.2)	4 (2.1)	0.466	11 (2.2)	6 (1.7)	0.804	10 (5.6)	3 (4.5)	1.000
Operative time (min)	75 (60–99)	102 (85–129)	<0.001	89 (69–115)	105 (86–125.5)	<0.001	106 (84–129)	132.5 (103–156)	<0.001
Postoperative hospital stay (days)	5 (4–7)	5 (4–7)	0.851	7 (5–11)	6 (4–9)	<0.001	10 (8–15)	8 (6–14)	0.025

Note: Data are presented as the median (interquartile range) or number (percentage).

[a]Surgical complications included deep vein thrombosis/pulmonary embolism, bowel injury, bowel obstruction, and wound infection.

consideration, a shorter operative time is believed to be safer for the fetus.[18] This difference between LA and OA may influence the primary outcome. In this study, a shorter postoperative hospital stay was only observed in the LA group during the second trimester. The length of hospital stay is considerably affected by a country's healthcare system. Japanese medical care focuses on closely monitoring uterine contractions, genital bleeding, and the fetal condition after surgery. Therefore, careful management observed in the LA group may explain why there was no difference in the postoperative hospital stay in the first or third trimester.

Our study has several strengths. Most cases were likely to have been managed in facilities participating in the Diagnostic Procedure Combination database because of the unique context of acute appendicitis during pregnancy. This likelihood suggests that the population of our study is a representative cohort in Japan. Unlike prior large database studies, we were able to ascertain the gestational age, which enabled us to assess clinical information by the trimester. Furthermore, our use of a multivariate analysis with generalized estimating equations allowed us to adjust not only for individual-level factors but also for facility-level factors.

However, our study also has several limitations. First, we identified acute appendicitis and primary outcomes using ICD-10 codes. Although various medical records in the Diagnostic Procedure Combination database have been rigorously validated, validation studies have not specifically focused on these populations. Therefore, the diagnoses for acute appendicitis or primary outcomes may not have been accurate. Second, segmenting data by trimester reduced the number of cases in each group. Therefore, the reduction in outcomes for each group prevented the inclusion of sufficient confounding factors in the logistic regression analysis. Third, the absence of pathological results in the database means that postappendectomy histological confirmation was not available, potentially leading to misclassification of appendicitis, which could affect maternal and fetal outcomes. Fourth, this database lacks detailed clinical information such as symptoms, vital signs, and laboratory data. Finally, the Diagnostic Procedure Combination database does not provide data on postdischarge outcomes, and thus the final obstetric outcomes are unknown.

5 | CONCLUSION

Although the use of LA is increasing, it may not always yield favorable outcomes particularly in the unique context of pregnancy. Furthermore, the effect of LA on the mother and fetus might vary depending on the gestational age, which should be considered when planning treatment.

TABLE 3 Multivariable regression analysis of outcomes: open versus laparoscopic appendectomy.

	1st trimester		2nd trimester		3rd trimester	
Outcomes	Odds ratio (95% CI)	*p*-value	Odds ratio (95% CI)	*p*-value	Odds ratio (95% CI)	*p*-value
Preterm delivery, preterm labor, or abortion[a]	0.62 (0.16–2.44)	0.498	3.37 (1.76–6.47)	<0.001	2.57 (1.15–5.70)	0.021
	Effect (95% CI)	*p*-value	Effect (95% CI)	*p*-value	Effect (95% CI)	*p*-value
Operative time (min)[b]	25.5 (19.1–31.9)	<0.001	14.3 (8.81–19.8)	<0.001	23.1 (13.3–32.9)	<0.001
Postoperative hospital stay (days)[b]	−0.26 (−1.23–0.72)	0.606	−2.26 (−3.84 to −0.69)	0.005	−2.3 (−4.6 to 0.06)	0.056

Note: The reference group was the open appendectomy group.

Abbreviation: CI, confidence interval.

[a]Adjusted for complicated appendicitis.

[b]Adjusted for complicated appendicitis, age, body mass index, ambulance use, admission to teaching hospital, and length of hospital stay before surgery.

AUTHOR CONTRIBUTIONS

Shunya Sugai: Conceptualization; data curation; formal analysis; investigation; methodology; writing—original draft; writing—review & editing. **Yusuke Sasabuchi**: Conceptualization; data curation; formal analysis; writing—review & editing. **Hideo Yasunaga**: Data curation; funding acquisition; supervision; writing—review & editing. **Shotaro Aso**: Data curation; writing—review & editing. **Hiroki Matsui**: Data curation; writing—review & editing. **Kiyohide Fushimi**: Data curation; writing—review & editing. **Kosuke Yoshihara**: Conceptualization; funding acquisition; supervision; writing—review & editing. **Koji Nishijima**: Conceptualization; supervision; writing—review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data used for the present study are not publicly available owing to contracts with hospitals that provide data to the Diagnostic Procedure Combination database.

ETHICS STATEMENT

This study was approved by the Institutional Review Board of the University of Tokyo (approval number: 3501-(5) on May 19, 2021).

INFORMED CONSENT

The requirement for informed consent was waived due to the anonymous nature of the data.

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SUPPORTING INFORMATION

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