





Safety of appendectomy during pregnancy in the totally laparoscopic age

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Purpose: Acute appendicitis is the most common nonobstetric indication for surgical intervention during pregnancy. In the argument of the optimal surgical approach to acute appendicitis in pregnancy, laparoscopy seems to be won with a similar complication rate and shorter postoperative recovery than open. We aimed to compare perioperative outcomes of appendectomy in pregnant and nonpregnant women in the totally laparoscopic age.

Methods: We retrospectively analyzed 556 nonincidental appendectomies performed in women (aged 18–45 years) between January 2014 and December 2018. To reduce the confounding effects, we used propensity score considering the variables age, American Society of Anesthesiologists physical status classification, and the operative finding; whether the appendicitis was simple or complicated. After propensity score matching, the outcomes of 15 pregnant women were compared with those of the 30 nonpregnant women.

Results: All the operations were performed with laparoscopy. Most of the pregnant cases were in their first and second trimester. The postoperative morbidity rate was significantly higher in the pregnant group before propensity score matching; however, the significance disappeared after matching. Operative outcomes and the parameters related to the postoperative recovery were not different between the two groups. Two patients in their first trimester decided to terminate the pregnancy after appendectomy. One patient in her second trimester experienced preterm labor which was resolved spontaneously. There was no other obstetric adverse outcome.

Conclusion: In the laparoscopy age, appendectomy during pregnancy is safe and not associated with a significantly increased risk of postoperative complication.

Keywords: Laparoscopy, Emergencies, Appendectomy, Pregnancy

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INTRODUCTION

Acute appendicitis is the most common nonobstetric indication for surgical intervention during pregnancy [1] and has a variable incidence of 0.05% to 0.13% among pregnant women [1,2]. The diagnosis of acute appendicitis during pregnancy may be challenging because of the nonspecific abdominal symptoms of pregnancy itself, physiological leukocytosis, transposition of the appendix, and the limitations of imaging modalities such as the risk of radiation and poor contrast. Acute appendicitis during pregnancy is known to be associated with an increased rate of adverse effects, including poor obstetric outcomes and maternal complications, due to the pregnant body's anatomic and physiologic changes. Difficulties in diagnosis and consequent delay in treatment often make it worse.

Laparoscopic appendectomy has become a standard procedure

for acute appendicitis since it was first performed in 1983 [3]. Given its obvious advantages, including reduced postoperative pain, faster recovery, and less postoperative morbidity [4], patients are generally advised to undergo laparoscopic surgery instead of an open procedure. However, the same confidence about the benefits of laparoscopic appendectomy does not seem to apply to pregnant patients. The possibility of incidental injury to the obstetric organs, as well as the unproven effects of pneumoperitoneum and increased abdominal pressure on the fetus and gravid uterus, have hampered the rapid uptake of laparoscopic appendectomy during pregnancy.

With the recent evolution of technology and increased experience, many studies, including several meta-analyses, have demonstrated that laparoscopic procedures carry no additional risk of maternal and obstetric complications. In the debate about the optimal surgical approach to acute appendicitis during pregnancy, it appears that laparoscopy is now the preferred procedure. Previous studies have focused on the modality of appendectomy in pregnant patients and have mainly compared laparoscopic with open appendectomies during pregnant women [5–9]. By contrast, the risk of morbidity after laparoscopic appendectomy has not been compared between pregnant women and the general population.

In the totally laparoscopic age, most of the appendectomies are now performed using laparoscopic techniques. We aimed to assess the safety of laparoscopic appendectomy in pregnant women and compare them with that of the general population. We also investigated the obstetric outcomes of the pregnant women in this study.

MATERIALS AND METHODS

Patients and data collection

This study retrospectively analyzed a consecutive series of nonincidental appendectomy patients who were treated with surgery at a single tertiary referral center between January 2014 and December 2018. Emergency appendectomies performed in women aged 18 to 45 years at the time of surgery were included in the analysis. Patient demographics and perioperative clinical parameters were collected from an electronic medical record system. Complicated appendicitis was defined in the pathology reports as a gangrenous or perforated appendix, or by the presence of periappendiceal abscess. Leukocytosis was defined as an elevated total white blood cell count greater than 10,000 cells/mm³. If there was any deviation from the ideal intraoperative course, it was counted as an intraoperative complication, except when the deviation was an inevitable consequence of the patients' underlying disease (such as intraoperative sepsis due to purulent peritonitis associated with perforated appendicitis). Postoperative complication and mortality within 30 days following surgery were investigated. Postoperative complication was defined as complications that required any additional treatment, prolonged hospital stay, or frequent outpatient clinic visits. The first, second, and third trimesters were defined according to gestational age as weeks 1 to 14, 15 to 28, and 29 to 42, respectively. Preterm labor was defined as regular contractions of the uterus before 37 weeks of gestation. Preterm delivery was defined as birth before 37 weeks.

Laparoscopic technique

All appendectomies were performed in the department of surgery. Surgical staff specialized in laparoscopy, and novice trainees participated in the operation according to their duties without distinction. All the cases in the pregnancy group were led by surgical staff. On the contrary, about one-fifth of the nonpregnant group cases were led by novice trainees. However, even when the trainee started the operation, surgical staff or fellow supervised it. If there was any difficulty in proceeding with the operation, the supervisor took over the operation.

The patient was placed on the table in the supine position with her head tilted down by 15° to 20° and the body tilted by 15° to 20° . With the patient under general anesthesia, the laparoscopic appendectomy was performed using fewer than three trocars with a 0° or 30° angled 5-mm camera. The port placement was according to the surgeon's preference. To prevent visceral organ injury, especially in the pregnant group, the initial incision for the first trocar was always made through the umbilicus and the fascia was opened under direct vision. The mesoappendix was identified and resected with a vessel-sealing device. An Endoloop ligature (Ethicon, Somerville, NJ, USA) was used twice to close the appendiceal stump. The specimen was placed in a bag and retrieved via the 10-mm port. Intraabdominal drains were inserted when necessary according to the presence of abscess and severity of inflammation.

Statistical analysis

We calculated the propensity score using a multivariable logistic model that included the variables age, American Society of Anesthesiologists physical status (ASA PS) classification, and the operative finding of simple or complicated appendicitis. Using the logit of the estimated propensity score and using a caliper of 0.2, one patient in the pregnant group was matched with two in the nonpregnant group. We matched 15 patients in the pregnant group with 30 in the nonpregnant group using the propensity score. Covariate balance and the surgical outcomes in the matched groups were compared after matching. Only one patient was not matched in the pregnant group, and 510 were

Table 1. Patients characteristic before propensity score matching

Variable	Pregnancy group ($n = 16$)	Non-pregnancy group ($n = 540$)	p value
Age (yr)	31.4 ± 3.8	31.0 ± 7.9	0.686
Body mass index (kg/m ²)	23.1 ± 3.7	22.7 ± 3.6	0.748
ASA			0.942
I	14 (87.5)	469 (86.9)	
ll	2 (12.5)	67 (12.4)	
III	0 (0)	4 (0.7)	
Operative finding			0.365
Uncomplicated appendicitis	11 (68.8)	422 (78.1)	
Complicated appendicitis	5 (31.3)	118 (21.9)	
Complication			
Intraoperative	0 (0)	2 (0.4)	1.000
Postoperative	6 (37.5)	44 (8.1)	0.002
Mortality	0 (0)	0 (0)	-

Values are presented as mean \pm standard deviation or number (%).

ASA, American Society of Anesthesiologists physical status classification.

not matched in the nonpregnant group. Statistical analysis was performed using IBM SPSS for Windows (version 24; IBM Corp., Armonk, NY, USA). Continuous variables were compared using Student *t* test or the Mann-Whitney *U* test, and categorical variables were analyzed using the chi-squared or Fisher exact test. A *p* value of < 0.05 was considered to be significant.

RESULTS

All 2,449 patients with acute appendicitis were surgically treated during the study period. Of these, 556 women aged 18 to 45 years (reproductive age) at the time of surgery were identified. A total of 16 pregnant women with acute appendicitis underwent laparoscopic appendectomy during the study period. These pregnant patients were compared with 540 patients in the nonpregnant group.

The patient characteristics and morbidity of the two groups before propensity score matching are shown in Table 1. Without matching, age, body mass index, and ASA PS classification were similar between the two groups. Complicated appendicitis was 1.5 times more frequent in pregnant women than those of the nonpregnant group (31.3% vs. 21.9%); however, the difference did not reach the statistically significant level. Two intraoperative complication cases were found in the nonpregnant group; each was a spillage of appendicolith and bladder injury, respectively. There was no intraoperative complication in the pregnant group. The rate of intraoperative complications did not differ significantly between the two groups. The rate of postoperative complications (not including obstetric adverse outcome) was significantly higher in the pregnant group (37.5%) than in the nonpregnant group (8.1%). All the postoperative complications observed in the pregnant group were Clavien-Dindo grade I or II, such as superficial surgical site infection needed open dressing or minor complications resolved with pharmacologic management. On the contrary, two patients in the nonpregnant group required percutaneous drainage procedure under local anesthesia, and the other two required reoperation under general anesthesia, graded as IIIa and IIIb, respectively.

Because complicated appendicitis is a major risk factor for postappendectomy complications, we performed propensity score matching to reduce the potential confounding effect of the operative finding. The patient characteristics and perioperative outcomes, including intraoperative and postoperative complications, of the two groups after matching are shown in Table 2. Age, body mass index, ASA PS classification, and leukocytosis at the time of diagnosis did not differ significantly between the two groups. The ratio of uncomplicated to complicated appendicitis was adjusted and found to be evenly distributed in the two groups. Parameters related to the diagnostic process, including the duration from symptom onset to the hospital visit, the duration from symptom onset to operation, and the duration from the hospital visit to the operation, were not significantly longer in the pregnant group. Operative outcomes, including operating time, anesthesia time, and estimated blood loss, did not differ significantly between the two groups. Parameters related to the postoperative recovery, including total and postoperative hospital

Variable	Pregnancy group ($n = 15$)	Non-pregnancy group ($n = 30$)	<i>p</i> value	
Age (yr)	31.3 ± 3.9	32.5 ± 8.1	0.508	
Body mass index (kg/m ²)	23.1 ± 3.7	22.6 ± 3.6	0.714	
ASA			0.591	
I	13 (86.7)	28 (93.3)		
I	2 (13.3)	2 (6.7)		
Leukocytosis	14 (93.3)	29 (96.7)	1.000	
Operative finding			1.000	
Uncomplicated appendicitis	11 (73.3)	22 (73.3)		
Complicated appendicitis	4 (26.7)	8 (26.7)		
Symptom onset to hospital visit (hr)	25.3 ± 26.4	20.9 ± 22.6	0.561	
Symptom onset to operation (hr)	35.4 ± 23.7	32.5 ± 23.4	0.698	
Hospital visit to operation (hr)	10.1 ± 5.9	8.1 ± 3.6	0.169	
Operating time (min)	38.7 ± 19.8	43.7 ± 14.5	0.340	
Anesthesia time (min)	69.0 ± 24.6	76.0 ± 17.8	0.282	
Estimated blood loss (mL)	25.3 ± 25.9	16.3 ± 16.1	0.158	
Hospital stay (day)	4.4 ± 2.0	4.4 ± 2.1	1.000	
Postoperative hospital stay (day)	3.6 ± 2.0	3.7 ± 2.0	0.831	
Return of bowel activity (day)	1.8 ± 0.7	2.7 ± 5.5	0.553	
Return to soft diet (day)	1.8 ± 1.2	1.6 ± 0.7	0.446	
Complication				
Intraoperative	0 (0)	1 (3.3)	1.000	
Postoperative	5 (33.3)	5 (16.7)	0.263	
lleus	1	0		
Superficial surgical site infection	2	2		
Deep surgical site infection	1	2		
Others ^{a)}	1	1		
Postoperative complication grade by Clavien-Dindo classification				
Grade I	2	2		
Grade II	3	2		
Grade III	0	1		
Mortality	0	0	-	

Values are presented as mean \pm standard deviation, number (%), or number only.

Propensity score was calculated using a multivariable logistic model that included the variables age, ASA physical status classification, and the operative finding of simple or complicated appendicitis.

ASA, American Society of Anesthesiologists physical status classification.

^{a)}One patient in the pregnant group developed urticaria. One patient in the nonpregnant group suffered from phlebitis, which needed prolonged antibiotics and anti-inflammatory drug usage.

stay, time to the return of bowel activity, and time to start a soft diet, also did not differ significantly between the two groups. The rate of intraoperative complications was still not different between the two groups. The rate of postoperative complications, which differed significantly before matching, remained higher in the pregnant group, but this difference was no longer significant

Variable	First trimester (n = 9)	Second trimester ($n = 5$)) Third trimester (n = 2)	Total (n = 16)			
Gestational age at appendectomy (wk)				12 (4–30)			
Maternal postoperative complication	2 (22.2)	3 (60.0)	1 (50.0)				
lleus	-	1	-				
Superficial surgical site infection	1	1	1				
Deep surgical site infection	-	1	-				
Other ^{a)}	1	-	-				
Maternal postoperative complication grade by Clavien-Dindo classification							
Grade I	1	1	1	2			
Grade II	1	2		3			
Preterm labor	0 (0)	1 (20.0)	0 (0)	1 (6.3)			
Preterm delivery	0 (0)	0 (0)	0 (0)	0 (0)			
Full term delivery	7 (77.8)	5 (100)	2 (100)	14 (87.5)			
Fetal loss	2 (22.2)	0 (0)	0 (0)	2 (12.5)			

Table 3. Maternal complications and obstetric outcomes according to the trimester of pregnancy group

Values are presented as number (%).

^{a)}One patient in the first trimester developed urticaria postoperatively.

after matching.

The detailed maternal complications and obstetric outcomes according to the trimester of the pregnant group (n = 16) are shown in Table 3. Most of the patients were in the first or second trimester at the time of surgery, and only two patients were in their third trimester. Two of nine patients in the first trimester developed postoperative complication. One needed additional outpatient clinic visits for wound dressing because of superficial surgical site infection after discharge. One developed urticaria during hospitalization, which was controlled with conservative management. Three of five patients in the second trimester developed postoperative complications. One developed postoperative paralytic ileus, which needed prolonged abstinence and fluid therapy. Two patients exhibited a surgical site infection, one superficial and one deep. The deep surgical site infection was a small abscess around the operation field that was resolved with oral antibiotics without the need for drainage. One of two thirdtrimester patients developed a superficial surgical site infection in the umbilical wound and needed additional outpatient clinic visits for wound dressing. One in the second-trimester patient developed preterm labor after the operation, but this disappeared without any medication after 1 day of obstetric surveillance. Two patients in the first trimester, whose gestational age was 4 and 5 weeks, respectively, did not know that they were pregnant and found out through a serum human chorionic gonadotropin test in the emergency room. Both received obstetric image surveillance before and after the operation without any abnormal findings; however, they both decided to terminate the pregnancy because of concerns about the unproven adverse effects of an operation under general anesthesia during the fetal organogenesis period. These two cases, which accounted for 12.5% (2 of 16) of all cases in pregnant group, were counted as fetal loss.

DISCUSSION

Acute appendicitis is the most frequent abdominal emergency encountered during pregnancy. With an estimated incidence of up to 0.13% of all pregnant women [1,2], it is a threat that cannot be ignored.

Pregnancy was considered as an absolute or relative contraindication for laparoscopic procedures initially because of the concerns about high intraabdominal pressure caused by pneumoperitoneum during operation, which can result in decreased venous return and cardiac output and eventually decreased fetal blood flow, and the CO₂ gas for pneumoperitoneum that may enter the fetal blood flow resulting in acidosis; eventually resulted in miscarriage or could influence fetal development. According to the animal study conducted in the early 90s, increased intraabdominal pressure inflated with CO₂ by about 20 mmHg in ewes can reduce 40% of maternal placental blood. However, despite the marked decrease in maternal placental blood flow of ewes, the fetal placental perfusion pressure and blood flow, pH, and blood gas tensions were unaffected by the presence of pneumoperitoneum [10]. Despite the stubborn resistance, attempts have been continued to introduce laparoscopy surgery to pregnant women. Several studies and meta-analyses have been

reported the safety and feasibility of laparoscopic appendectomy during pregnancy [5-8]. Most recently, Lee et al. [7] demonstrated in the updated meta-analysis, including 22 comparative cohort studies, that laparoscopic appendectomy during pregnancy was not associated with a greater risk of fetal loss compared with open. They also concluded that the laparoscopic appendectomy group had faster postoperative recovery and a lower wound infection risk than those of the open group, which was duplicating the result of a comparative study between laparoscopic appendectomy vs. open in the general population. Consequently, the recommendation for surgical interventions during pregnancy, including appendectomy, has been slowly changed. For example, the recommendation from Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) for laparoscopic appendectomy during pregnancy has been changed from "Laparoscopic appendectomy may be performed safely in pregnant patients with appendicitis" in 2011 [11], to "Laparoscopic appendectomy is the treatment of choice for pregnant patients with acute appendicitis" in 2017 although its estimated evidence level was weak [12].

In our institution, laparoscopic appendectomy in pregnant women has been performed since 2007. At the time, open and laparoscopy was both a selectable treatment option for pregnant women coming to our institution with acute appendicitis. We reported the clinical efficacy and safety of laparoscopic appendectomy during pregnancy compared with an open procedure in 2012 [5]. We experienced similar postoperative and obstetric outcomes in both groups, with shorter operating time and decreased postoperative analgesics usage in the laparoscopy group. Based on this experience, from the early 2010s, all the patients diagnosed with acute appendicitis during pregnancy were admitted to the department of surgery and treated with laparoscopic appendectomy regardless of the gestational age of the fetus. Perioperative preparations were almost the same as in the general population, except for fetal monitoring under obstetric consultation. In the operating room, laparoscopic procedures for the pregnant patients were according to the guidelines from SAGES. Patients beyond the first trimester were placed in the partial left lateral decubitus position to minimize compression of the vena cava, and intraabdominal CO2 insufflation pressure was maintained about 12 mmHg. SAGES recommended that CO₂ insufflation between 10 and 15 mmHg can be safely used for laparoscopy in the pregnant patient [11,12]. Although some have argued that insufflation less than 12 mmHg may not provide adequate visualization of the intraabdominal cavity, it was always enough to get secure surgical field in our experience. The latest version of SAGES guidelines for the use of laparoscopy during pregnancy stated that initial abdominal access can be safely accomplished with an open Hasson, Veress needle, or optical trocar technique, by surgeons experienced with these techniques, if the location is adjusted according to fundal height [12]. In our institution, the

initial incision for the first trocar was always made through the umbilicus, and the fascia was opened under direct vision. Even in the patients in their third trimester, the first trocar through the umbilicus seemed to be a safe option for achieving pneumoperitoneum. After the abdominal cavity was inflated, second and third trocars were placed according to the duty surgeon's preference, generally going upwards as the gestational age increase. Because all the cases in the pregnancy group were performed by surgical staff who were experienced in laparoscopy, the adjustment of the site of the additional trocars has not been a significant issue.

According to previous studies, the rates of fetal loss after appendectomy during pregnancy range from 3% to 36% [13,14]. Several studies have reported that the risk of fetal loss is increased when the appendix perforates or when there is generalized peritonitis or abscess [14]. However, with the technical development of laparoscopy, this risk seems to be decreasing. In the general population, laparoscopy is thought to be superior to an open technique because of its enhanced visualization and easier access to the infection focus, especially when appendicitis is complicated. In the case of pregnant women, we can expect similar advantages. Laparoscopy may provide better access with the smaller incision to the infection focus, which may be deviated from the original anatomic position and obstructed by the enlarged uterus. The reduced operation time and special considerations when operating on a pregnant woman (e.g., restricted intraabdominal pressure to 10-12 mmHg to maintain the pneumoperitoneum) may help to improve outcomes further. In recent studies, fetal loss has not been reported after laparoscopic appendectomy during pregnancy [15-18]. In this study, no spontaneous abortion or intrauterine fetal death occurred, and the two cases of fetal loss involved termination of the pregnancy based on the patient's decision.

The diagnosis of acute appendicitis is more difficult to make in a pregnant than in a nonpregnant woman. The risk of perforation is increased because of a delayed diagnosis, and complicated appendicitis may increase the rate of maternal morbidity as well as obstetric adverse effects. Symptoms and signs are vague and can be difficult to distinguish from the normal physiological changes in pregnancy, and the diagnostic tools are limited. Given the risk of radiation, abdominopelvic computed tomography, the most commonly used imaging tool for diagnosis of acute appendicitis, is not generally recommended during pregnancy. Not surprisingly, the rate of negative appendectomy is higher in pregnant than in nonpregnant women (24% vs. 9.8%, respectively) [13,19,20]. Magnetic resonance imaging (MRI) is a possible alternative for the diagnosis of acute appendicitis in pregnant women when the clinical examination and ultrasonography are not conclusive [21]. The use of MRI can reduce the unnecessary appendectomy rate during pregnancy by 50% [22]. In this study, all patients in the pregnant group received an ultrasonographic examination and more than half (9 of 16, 56.3%) received MRI. As a result, there were no negative appendectomies in the pregnant group. Regarding the duration from symptom onset to the operation and the duration from a hospital visit to operation shown in Table 2, the diagnosis and treatment did not seem to be delayed significantly in the pregnant group compared with non-pregnant group.

Nevertheless, the rate of complicated appendicitis was higher in the pregnant group before propensity score matching (31.3% vs. 21.9%, respectively) in this study, although this difference was not significant. In the initial analysis, the significantly higher postoperative complication rate observed in the pregnant than in the nonpregnant group (37.5% vs. 8.1%, respectively) may reflect this. Postoperative complications, although most of them were a superficial wound infection, were more frequently observed in the pregnant group, despite all the cases of pregnant group were performed by experienced surgeons. The rate of complications of appendicitis, including perforation, is known to be increased by trimester [23,24]. Previous studies have reported that maternal morbidity in pregnant women after appendectomy is similar to that of nonpregnant women, but is increased by complicated appendicitis [25].

Pregnant women may be more vulnerable to infectious complications due to physiologic immune modulation and limited antibiotic options. In the case of perforated appendicitis, it is easier to lead to wound infection or generalized peritonitis in pregnant than in nonpregnant women because the omentum cannot isolate the infection during pregnancy [24,26]. Infectious complication may be propagated by increased abdominal pressure or by a grown belly due to pregnancy. Although traditional literatures describe that the rate of postoperative complications is not significantly increased in appendectomy during pregnancy comparing with the general population, these are all written in the era of laparotomy. As in the general population, laparoscopic appendectomy during pregnancy is getting popular and becoming into daily practice. Frame shifting from open to laparoscopy, even in the pregnant patient group, has already come. In this laparoscopic era, we tried to illuminate whether the postoperative complication (not focused on the obstetric adverse effect) in the pregnant group increases or not, compared with the general population.

In this study, the rate of postoperative complications in the pregnant group was still twofold higher than that of the nonpregnant group after propensity score matching, adjusting the ratio of complicated appendicitis; however, the difference did not reach the statistical significance level. We could include only a small number of pregnant women with appendicitis in this retrospective analysis, and it is the major limitation of this study. Assuming roughly, it may result in a significant difference if the case number increases.

However, with this result our experience suggests that, given the same severity or complexity of appendicitis, the postoperative complication after laparoscopic appendectomy during pregnancy is comparable for the general population. Nevertheless, because the risk of complicated appendicitis is increased during pregnancy, postoperative complications, especially infectious, after laparoscopic appendectomy may be increased than that of the general population. Therefore, to reduce the risk of infectious complications, surgeons should be more careful when manipulating the wound and removing the infection focus when performing appendectomy in a pregnant woman, even in this totally laparoscopic age.

In conclusion, laparoscopic appendectomy during pregnancy can be performed safely and has a similar risk of postoperative morbidity compared with the nonpregnant population and reasonable obstetric outcomes. However, it is worth mentioning that the surgeon should make every effort, including perioperative fetal surveillance, to avoid maternal and obstetric complications.

NOTES

Ethical statements

This retrospective study was approved by the Institutional Review Board of Kangbuk Samsung Hospital (IRB No. 2020-09-007), and informed consent was waived.

Authors' contributions

Data curation, Formal analysis, Investigation, Visualization: JWS, KUJ Methodology: JTS, SRL Project administration: KUJ, HOK Writing–original draft: JWS, JTS Writing–review & editing: KUJ, SRL, HOK All authors read and approved the final manuscript.

Conflict of interest

All authors have no conflicts of interest to declare.

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