

P R A C E O R Y G I N A L N E
położnictwo

Maternal and fetal outcomes after laparoscopic vs. Open appendectomy in pregnant women: data from two tertiary referral centers

Matczyne i płodowe wyniki operacji usunięcia wyrostka drogą laparoskopową i otwartą u ciężarnych: dane z dwóch ośrodków referencyjnych trzeciego stopnia

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Abstract

Objectives: Appendectomy is the most common cause of non-obstetric surgery in pregnant women. Our aim was to compare the clinical characteristics, peri- and post-operative data of pregnant women undergoing either laparoscopic appendectomy (LA) or open appendectomy (OA).

Material and methods: This was a retrospective study of medical records of all pregnant women diagnosed and treated surgically for acute appendicitis at two referral centers of Yuzuncu Yil University Medical Faculty and Kafkas University Medical Faculty, from January 2010 to January 2015.

Results: The study included 48 patients, divided to two groups (12 - LA and 36 - OA). There were no significant differences in demographic characteristics of the studied population, including age, BMI, gestational age at operation, gravidity, parity, and history of cesarean sections. As far as obstetric and fetal outcomes are concerned, no significant differences were found in terms of preterm delivery, fetal loss, delivery mode, birth weight, APGAR score, and maternal death between the two investigated groups. One perioperative complication of intra-abdominal abscess was noted in the OA group. However, the LA group had shorter hospital stay (3.25 ± 2.45 vs. 4.28 ± 3.31 , $p=0.004$), earlier mobilization time (8.1 ± 2.2 vs. 10.1 ± 1.6 , $p=0.025$), and shorter time to first flatus (2.3 ± 0.3 vs. 4.0 ± 1.6 , $p=0.032$) as compared to the OA group. The OA group had statistically shorter operation time than the LA group (38.61 ± 11.5 vs. 49.42 ± 11.38 , $p=0.007$).

Conclusion: LA is related to shorter hospital stay, faster return to daily activities, and shorter time to first flatus. LA appears to be as safe and effective as OA in pregnant patients without increasing adverse perinatal outcomes.

Key words: **appendectomy / laparoscopy / pregnancy /**

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Streszczenie

Cel pracy: Appendektomia jest najczęstszym niepołożniczym zabiegiem operacyjnym u kobiet ciężarnych. Celem naszego badania było porównanie cech klinicznych oraz danych przed i pooperacyjnych od kobiet ciężarnych poddanych laparoskopowej appendektomii (LA) lub otwartej appendektomii (OA).

Materiał i metoda: Retrospektywnie przeanalizowano historie chorób od wszystkich pacjentek ciężarnych diagnozowanych i operowanych z powodu ostrego zapalenia wyrostka robaczkowego w dwóch ośrodkach referencyjnych: Yuzuncu Yil University Medical Faculty i Kafkas University Medical Faculty, w okresie od stycznia 2010 do stycznia 2015.

Wyniki: Do badania włączono 48 pacjentek, które podzielono na dwie grupy (12 - LA i 36 - OA). Nie znaleziono istotnych różnic w cechach demograficznych badanej populacji, włączając w to wiek pacjentek, BMI, wiek ciążowy w momencie operacji, liczbę ciąż, porodów i przebyte cięcia cesarskie. Pod względem wyników matczyńskich i płodowych nie znaleziono istotnych różnic w ilości porodów przedwczesnych, utraty ciąży, rodzaju porodu, wagi urodzeniowej, punktacji APGAR i zgonów matek pomiędzy dwoma badanymi grupami. Obserwowano jedno powikłanie okołoperacyjne – ropień wewnątrzbrzuszny w grupie OA.

Aczkolwiek w grupie LA obserwowano krótszy pobyt w szpitalu ($3,25 \pm 2,45$ vs. $4,28 \pm 3,31$, $p=0,004$), szybszy czas mobilizacji ($8,1 \pm 2,2$ vs. $10,1 \pm 1,6$, $p=0,025$), i krótszy czas do pierwszych gazów ($2,3 \pm 0,3$ vs. $4,0 \pm 1,6$, $p=0,032$) w porównaniu do grupy OA. Grupa OA miała statystycznie krótszy czas operacji niż grupa LA ($38,61 \pm 11,5$ vs. $49,42 \pm 11,38$, $p=0,007$).

Wnioski: LA wiąże się z krótszym pobytem w szpitalu, szybszym powrotem do aktywności i krótszym czasem do oddania pierwszych gazów. LA wydaje się być równie bezpieczna i skuteczna jak OA w ciężarnych pacjentkach, nie zwiększając ilości niekorzystnych wyników położniczych.

Słowa kluczowe: **appendektomia / laparoscopia / ciąża /**

Introduction

Appendectomy is the most common non-obstetric surgical operation during pregnancy, affecting from 1/800 to 1/1500 pregnancies worldwide [1]. Appendicitis during pregnancy has been reported to increase poor pregnancy outcomes such as fetal loss, preterm labor, as well as perinatal morbidity and mortality [2, 3]. The rate of fetal loss is reported to be 20% in perforated appendicitis as compared to 1.5% for uncomplicated appendicitis [4]. However, the maternal mortality rate may be very low with the help of early diagnosis and intervention, advanced antibiotics, and close monitoring of the mother and the fetus.

The diagnosis of acute appendicitis in pregnancy presents a challenge due to the physiological leukocytosis of pregnancy, anatomic changes of the appendix resulting from the enlarged uterus, and non-specific abdominal discomfort symptoms of pregnancy such as anorexia, nausea, vomiting and lower abdominal pain, which are common features both, in acute appendicitis and normal pregnancy. Therefore, any delay in the diagnosis of acute appendicitis increases the risk of complications in the mother and the fetus. While open appendectomy (OA) is the standard intervention for acute appendicitis in many centers, there are several reports supporting the laparoscopic approach as the first-line therapy, which is now a commonly accepted approach due to its efficacy, safety, and low complication rates [5, 6]. The surgical treatment of appendectomy has changed from OA to the laparoscopic appendectomy (LA) both, in pregnant women and the general population for the last few decades [4]. It is a well-known fact that LA has some advantages in the general population, such as better visualization, fewer wound infections, less post-operative pain, shorter hospital stay, and earlier return to daily activities as compared to OA [7]. A recent systematic review of 28 observational studies reported LA to have a higher

rate of fetal loss but a similar or lower rate of preterm delivery as compared to open appendectomy [8]. However, another recent study reported LA to be a safer procedure for presumed acute appendicitis during pregnancy, with fewer post-operative complications as compared to OA, which was associated with higher post-operative fever and higher incidence of uterine contractions [9]. The choice of the optimal surgical intervention for acute appendicitis during pregnancy, be it OA or LA, remains the topic of much controversy. Therefore, our retrospective observational study was carried out to investigate maternal and fetal outcomes, including peri-operative complications and pregnancy outcomes.

Material and methods

Our study was conducted as a retrospective observational investigation of pregnant women who underwent either open or laparoscopic appendectomy for acute appendicitis in two centers of the Yuzuncu Yil University Teaching Hospital, Department of General Surgery, Van, Turkey and Kafkas University Medical Faculty, Department of General Surgery, Kars in Turkey, during a 5-year period between January 2010 and January 2015. All patients were followed up and gave birth at one of the obstetric clinics of these two centers. The retrospective chart reviews of patients were retrieved from their medical records and analyzed. Local Ethics Committee approved of the study. Pregnant women who underwent a surgery for appendectomy, with the confirmed diagnosis of appendicitis on pathologic examination, were included in the study.

The patients were divided into two groups: LA (group 1) and OA (group 2). Demographic data including age, gravidity, parity, history of cesarean section and weight were retrieved from the database of medical records. Perioperative clinical data,

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including leukocyte count, surgical delay time, total surgical duration, the length of hospitalization, timing of the operation (day or night), and intra- or post-operative complications were obtained from the operation charts. All patients were examined and followed by an obstetrician in the pre- and post-operative period. Primary maternal and fetal outcomes were evaluated using the following variables: maternal mortality, concomitant cesarean section, onset of preterm labor, the need for tocolysis, incidence of preterm birth, fetal loss, gestational age at surgery and delivery, mode of delivery, and fetal outcomes (including fetal loss, birth weight and Apgar score at 1 minute). All these variables were compared between the two groups.

Statistical analysis was performed using a software package SPSS, version 20. Data were reported as mean±SD, and descriptive statistics were used for continuous variables. Mann-Whitney U test or χ^2 test were used as appropriate to compare between the groups. The p-value of <0.05 was considered as statistically significant.

Results

The study included 48 pregnant women (12 – LA and 36 – OA) who underwent appendectomy during the study period. No cases of conversion from LA to OA were observed. Patient age ranged from 17 to 51 years (mean: 27.9±6.9). Mean age was 27.08±5.48 and 28.81±8.35 for the LA and OA groups, respectively and the difference was not statistically significant. Mean gravidity and parity were 2.08±1.16 vs. 2.64±1.61 and 0.92±1 vs. 1.47±1.48 for the LA and OA groups, respectively and the difference was not statistically significant ($p>0.05$). There were no significant differences in the BMI (22.6±2.7 vs. 22.9±2.5 $p=0.82$) and the number of previous cesarean sections (3 in LA and 8 in OA). Mean gestational age at surgery was not statistically different between the two groups. In the LA group, 1 (8.3%) patient was in the first, 7 (58.3%) in the second, and 4 (33.3%) in the third trimester. In the OA group, 2 (5.5%) patients were in the first, 12 (33.3%) in the second, and 22 (61.1%) in the third trimester. Table 1 shows the demographic characteristics of the studied population.

When comparing the pre-operative laboratory data of the two groups, we found that mean leukocyte count in the LA and OA groups was 13.92±5.10 and 13.62±5.40, respectively and the difference was not statistically significant ($p=0.817$). For peri-operative outcomes, mean duration of the surgery was 49.42±11.38 min. vs. 38.61±11.50 min. in the LA and OA groups, respectively. The duration of surgery was statistically longer in the LA group ($p=0.007$). Mean time to first flatus in the LA group was significantly shorter than in the OA group (2.3±0.3 h vs. 4.0±1.6 h, $p=0.032$). Mean length of the hospital stay was 3.25±2.45 and 4.28±3.31 days in the LA and OA groups, respectively. The LA group had a shorter hospital stay than the OA group ($p=0.023$). Seven (58.3%) subjects in the LA group were operated on during the day whereas 17 (47.2%) patients in the OA group were operated at night. There was a slight increase in the number of patients operated on at night in the OA group but the difference was not statistically significant ($p=0.054$). Only 1 patient experienced complications (wound infection and intra-abdominal abscess) in the OA group: a 30-year-old woman at 28 weeks of gestation who was hospitalized due to wound infection and intra-abdominal abscess 1 week after OA. She underwent

reoperation one week after appendectomy and concomitant cesarean section was performed at 29 weeks of gestation due to breech presentation with cervical dilatation. She was successfully treated with appropriate antibiotics and discharged on postoperative day 10. When analyzing surgical delay time from first admission to the operation, we found no statistically significant differences between the groups (18.42±17.15h in the LA group vs. 13.83±13.45h in the OA group, $p=0.34$). Perioperative characteristics of the studied population are presented in Table II.

No cases of maternal death were observed. All deliveries took place at our hospitals. Two fetal losses were noted: 1 missed abortion 2 weeks after the operation in the LA group (at 15 weeks of gestation) and 1 intrauterine fetal death 5 weeks later the operation (surgery at 25 weeks of gestation) in the OA group. There were no significant differences in the incidence of preterm labor (3/25% vs. 9/25%) or delivery mode ($p = 0.43$) between the groups. The LA and OA groups had similar fetal outcomes in terms of gestational age at delivery, birth weight, and APGAR score at 1 minute. Obstetric and fetal outcomes of the two groups are presented in Table III.

Discussion

Appendicitis, the most common cause of non-obstetric surgical operation during pregnancy, is reported to have significant implications on the health of both, the mother and the fetus [29]. The incidence of appendicitis in pregnancy is reported to be similar to the general population, i.e. 0.05-0.13% [10]. However, there are some diagnostic difficulties in pregnancy which may delay timely clinical diagnosis of acute appendicitis due to the anatomical and physiological changes that occur during pregnancy [6]. Therefore, the rate of appendiceal perforation during pregnancy is reported to be as high as 43% as compared to 19% in the general population [1]. Acute appendicitis in pregnant patients can be treated surgically with open or laparoscopic appendectomy, similarly to the general population. In fact, laparoscopic technique is the preferred method for treating appendicitis in the general population due to its numerous advantages over the open technique, i.e. less postoperative pain, shorter length of hospital stay, decreased incidence of thromboembolic events, faster recovery, improved cosmetic outcome, and decreased rates of postoperative ileus [11]. Regardless, the literature offers conflicting reports on the safety and efficacy of LA in pregnancy. In a recent meta-analysis, Wilasrusmee et al., suggested that laparoscopic appendectomy in pregnancy results in an almost two-fold higher risk of fetal loss as compared to open appendectomy [12]. In another systematic review of LA in pregnancy, which included 28 articles, the authors noticed that LA in pregnancy was associated with a significantly higher rate of fetal loss as compared to OA [8]. On the other hand, many studies confirmed the safety and effectiveness of LA during pregnancy. Jun Chul et al., conducted a retrospective study enrolling 61 patients who underwent appendectomy (22 laparoscopic and 39 open), and showed no differences in terms of surgery duration, postoperative complication rate, obstetric and fetal outcomes, including incidence of preterm labor, delivery mode, gestational age at delivery, birth weight and APGAR scores. These authors suggested that LA should be considered as a standard treatment alternative to OA [13]. In another large case

Erbil Karaman et al. *Maternal and fetal outcomes after laparoscopic vs. Open appendectomy in pregnant women: data from two tertiary referral centers.***Table I.** Demographic characteristics of pregnant women undergoing laparoscopic or open appendectomy.

Variables	LA (n=12)	OA (n=36)	P value
Age, year (mean±SD)	27.08±5.48	28.81±8.35	0.509
BMI (mean±SD)	22.6±2,7	22.9±2.5	0.82
Gestational age at operation, wk (mean±SD)	22.42±8.25	25.67±6.57	0.171
First trimester (n, %)	1 (8.3%)	2 (5,5%)	
Second trimester (n, %)	7 (58.3)	12 (33,3%)	
Third trimester (n, %)	4 (33.3%)	22 (61,1%)	
Gravida (mean±SD)	2.08±1.16	2.64±1.61	0.276
Parity (mean±SD)	0.92±1	1.47±1.48	0.234
Previous cesarean section (n, %)	3 (25%)	8 (22.2%)	0.64

BMI: body mass index, SD: standart deviation, n: number, LA: laparoscopic appendectomy, OA: open appendectomy

Table II. Comparison of variables of those women who underwent LA or OA.

Variables	LA (n=12)	OA (n=36)	P value
Operation time, min. (mean±SD)	49.42±11.38	38.61±11.50	0.007*
Operation session			
Daytime (n, %)	7 (58.3%)	17 (47.2%)	0.28
Nighttime (n, %)	5 (41.6%)	19 (52.8%)	0.86
Delay time to operation, h (mean±SD)	18.42±17.15	13.83±13.45	0.34
Length of stay in hospital, min. (mean±SD)	3.25±2.45	4.28±3.31	0.004*
Time to first flatus, h (mean±SD)	2.3±0.3	4.0±1.6	0.032*
Complication (n)	0	1	
Lecocyte (mean±SD)	13.92±5.10	13.62±5.40	0.817
Neutrophil ratio (mean±SD)	80.53±9.19	78.04±10	0.483

SD: standart deviation, n: number, LA: laparoscopic appendectomy, OA: open appendectomy, * indicates statistically significant difference

Table III. Comparison of obstetric and fetal outcomes of those women who underwent LA or OA.

Variables	LA (n=12)	OA (n=36)	P value
Preterm delivery (n, %)	3 (25%)	9 (25%)	-
Birth weight, gr (mean±SD)	3030±744	2944±664	0.711
APGAR score at 1 st min. (mean±SD)	8.42±1.08	8.11±1.62	0.552
Gestational age at delivery, wk (mean±SD)	37.25±3.41	36.72±4.84	0.729
Delivery type			
Vaginal delivery (n, %)	8 (66.7%)	25 (69.4%)	0.439
Cesarean delivery (n, %)	4 (33,3%)	11 (30.5%)	
Fetal loss ¹ (n, %)	1 (8.3%)	1 (2,7%)	0.34
Maternal death (n, %)	0	0	

SD: standart deviation, n: number, LA: laparoscopic appendectomy, OA: open appendectomy, 1: including missed abortion and intrauterine demise, p<0.05 indicates statistically significant difference

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series of 45 pregnant women who underwent LA, the authors reported low rate of preterm delivery and absence of fetal loss after laparoscopic appendectomy (14). In light of the fact that the results of these studies are often conflicting, we aimed to conduct this retrospective study to reflect on our experience. Our study results also confirm the safety of LA because there were no differences in terms of perioperative morbidity and mortality. Also, we demonstrated that LA has some advantages over OA with regard to shorter hospital stay, and faster time to first flatus.

One major concern is the fetal loss during abdominal surgery in pregnant patients. Studies indicate that there is a slight increase in the miscarriage rate during abdominal surgery, but it remains unclear whether the surgical procedure or anesthesia are responsible [15, 16]. Some studies suggested that laparoscopy has a higher miscarriage rate than laparotomy, especially in case of appendicitis [17]. There are specific effects of laparoscopy on the pregnant patients, such as the effect of increased intra-abdominal pressure and fetal acidosis during carbon dioxide pneumoperitoneum. In addition, it has been reported that carbon dioxide is also absorbed across the peritoneum, which leads to fetal acidosis [18]. McGory et al., in their large population-based study, including the largest number of 3133 pregnant women who underwent appendectomy, found that laparoscopy was associated with a higher rate of fetal loss as compared to open appendectomy (6.8% vs. 3.2%) [2]. In our study, we observed two fetal losses (a missed abortion at 15 weeks of gestation and intrauterine fetal demise at 30 weeks of gestation). These two patients had perforated phlegmonous appendicitis: one underwent LA at 13 weeks and the other underwent OA at 25 weeks of gestation, respectively. In our opinion, the subsequent spontaneous missed abortion and fetal demise were associated with maternal disease severity (both had phlegmonous-perforated appendicitis) rather than the surgical techniques.

Laparoscopy is believed to be safest in the second trimester of gestation because of the possible danger of injury to the gravid uterus in the third trimester, which is especially likely to occur during the insertion of the trocar into the abdominal cavity. Also, some authors suggested that laparoscopic procedures performed during the first trimester are usually associated with greater risk of fetal loss because of teratogenicity of medications and decreased uterine blood due to the pneumoperitoneum [1, 19]. In their study of 45 cases of laparoscopic appendectomy in pregnant women, Patrice et al., reported that they faced a serious complication of violation of the uterine cavity in one case that occurred with the open technique. Prompt recognition of the problem and conversion to a midline laparotomy to suture the uterus prevented harm to that patient and her fetus. The puncture of the uterus with a Veress needle is another serious complication. Friedman et al., reported a young pregnant woman at 21 weeks of gestation who underwent LA and suffered a Veress needle injury to the uterus, resulting in postoperative pneumoamnion and subsequent fetal loss [20]. In our study, there were no cases of injury to the uterus in the peri-operative period of LA. In the LA group, 4 out of 12 patients (33.3%) were in the third, 7 (58.3%) in the second and 1 (8.3%) in the first trimester (8 weeks of gestation) of pregnancy. We used the Hasson open method to introduce the first trocar in order to prevent injury to the gravid uterus in all of our LA operations in the third trimester. In our opinion, the open technique should be used, especially in the third trimester,

to avoid injury to the gravid uterus during laparoscopy.

It is argued that pneumoperitoneum during laparoscopy increases intra-abdominal pressure, what may lead to preterm contractions and delivery. In a large population-based study in Sweden, which included 2181 laparoscopies and 1522 laparotomies, Reedy et al., found no differences between the two groups in terms of preterm births [17]. In our study, we found 12 cases of preterm birth (12/48, 25%), which was defined as delivery <37 weeks of gestation and was higher than in the literature: 3 (25%) in the laparoscopy group and 9 (25%) in the laparotomy group, which was not statistically significant. Interestingly, the majority of preterm (10 out of 12) births in our study population were late preterm births, between 34 to 37 weeks of gestations. In their retrospective study including 45 pregnant patients with LA and 17 with OA, Sadot et al., reported no difference in terms of fetal loss, APGAR score, birth weight, and preterm delivery rate, what was consistent with our data [21].

The well-known advantages of laparoscopic surgery in the general population, like shorter length of the hospital stay, lower rates of wound infection, less need for analgesics, shorter time to first flatus, and faster return to daily activities, were also evaluated in our study. We found a statistically significantly shorter hospital stay, faster return to daily activities, and shorter time to first flatus in the LA group ($p < 0.05$). Mean length of the hospital stay was 3.25 ± 2.45 in the LA group and 4.28 ± 3.31 in the OA group, and the difference was statistically significant ($p < 0.05$). In our study, the operation time was significantly longer in the LA group as compared to the OA group. We think the reasons might have been technical difficulty of laparoscopy due to the gravid uterus and the fact that 5 out of 12 operations in the LA group were performed by residents, who were not experienced enough to complete the operation faster.

When analyzing postoperative complications, there were no significant differences between the two groups in terms of post-operative wound infection, intra-abdominal abscess formation, and bowel dysfunctions. There was only one case with intra-abdominal abscess formation and wound infection on postoperative day 7 in a patient who underwent OA at 28 weeks of gestation. She underwent laparotomy and cesarean section concomitantly one week later due to intra-abdominal abscess formation and gave birth to a baby boy (weight: 1750 g). Jun Chul et al., reported that 3 patients out of 61 cases of appendectomy (22 LA and 39 OA) experienced complications, including intra-abdominal abscess formation in one patient who underwent LA (1/22, 4.5%), and intra-abdominal abscess and wound infection (2/39, 5.1%) in two patients from the OA group [13]. However, their findings also lacked statistical significance.

The limitations of our study include its retrospective observational character with small sample size in each group. Also, data were reviewed from medical records which may have been incomplete. Another important limitation is the potential confounding factor relating to the surgeons because some of the operations were performed by residents of the General Surgery Department during the day, what may have had some effect on the postoperative outcomes like operation time or complication rates. On the other hand, the strength of our study was that all patients who underwent appendectomy in the study group were followed up regularly and gave birth in our institutions, which are the only referral centers in this region of Turkey.

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Conclusions

LA can be performed in any trimester of pregnancy by surgeons who have enough experience with the technique. Our results also demonstrated LA to be a safe and effective technique for the treatment of appendicitis during pregnancy, with similar rates of complications to OA. In addition, LA is associated with shorter hospital stay, faster return to daily activities and shorter time to first flatus. Thus, it should be preferred as a valuable alternative to open surgery in pregnant patients. However, to confirm these findings, there is a need for further evaluation including randomized control trial comparing LA with OA, even though it will be difficult to conduct such a randomized trial in pregnant patients.

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Authors' contribution:

1. Erbil Karaman – study design, concept, analysis and interpretation of data, article draft, revised article critically, corresponding author.
2. Abbas Aras – acquisition of data, assumptions, interpretation of data, study design.
3. Numan Çim – acquisition of data, analysis and interpretation of data.
4. Ali Kolusan – acquisition of data, article draft.
5. Remzi Kiziltan – acquisition of data, concept.
6. Sebahattin Çelik – analysis and interpretation of data.
7. Turgut Anuk – acquisition of data, study design.

Authors' statement

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