

Long term outcomes of radical and conservative surgery for late diagnosed tubal pregnancies

Długoterminowe wyniki radykalnej i zachowawczej chirurgii w późno rozpoznanych ciążach jajowodowych

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Abstract

Objective: To investigate long-term postoperative outcomes of conservative and radical surgery in ectopic tubal pregnancies, and evaluate the results of these techniques.

Methods: A total of 145 patients that operated for tubal pregnancy between January 2006 and January 2009 were reviewed. Data on patient age, reproductive and surgical history, history of ectopic pregnancies, serum hCG levels at the time of diagnosis and intraoperative observation were retrospectively obtained from hospital records. Telephone interviews were used to obtain information about exact postoperative time interval in which the patients were trying to get pregnant, and the time when they spontaneously became pregnant.

Results: There was no significant difference in cumulative spontaneous intrauterine pregnancy rate for a 2-year of conception period subsequent to conservative (64.3%) and radical (58.3%) surgery ($p=0.636$). During the same time interval, the rates of development of ectopic pregnancy for the conservative and radical surgery groups were 17.9% and 4.2%, respectively ($p=0.093$). The patients who developed ectopic pregnancy after conservative surgery had significantly higher levels of serum hCG levels (7413 ± 3155 IU/L) compared with those of patients who not-developed ectopic pregnancy (3436 ± 2668 IU/L) ($p=0.007$).

Conclusion: In late-diagnosed cases with higher serum hCG levels, conservative treatment should not be the first choice. Indeed, our results suggested that the cumulative pregnancy rates are not significantly higher, and the risk of ectopic pregnancy recurrence may be increased with conservative surgery in late tubal pregnancies.

Key words: **tubal pregnancy / ectopic / salpingotomy / salpingectomy / fertility rate / HCG-beta /**

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Streszczenie

Cel: Badanie długoterminowych pooperacyjnych wyników leczenia zachowawczego i radykalnego w ektopowych ciążyach jajowodowych i ocena rezultatów tych metod.

Metody: Przeanalizowano grupę 145 pacjentek operowanych z powodu ciąży jajowodowej pomiędzy styczniem 2006 i styczniem 2009. Dane dotyczące wieku pacjentek, przeszłości położniczej, operacji, ciąży ektopowych, poziomu hCG w surowicy w momencie postawienia diagnozy oraz obserwacje z przebiegu operacji zostały retrospektywnie uzyskane z dokumentacji szpitalnej. Informacje na temat dokładnego czasu po operacji, w którym pacjentka starała się zajść w ciążę oraz czas do zajścia w ciążę uzyskano w rozmowie telefonicznej.

Wyniki: Nie znaleziono istotnej różnicy w skumulowanym wskaźniku spontanicznych ciąż wewnątrzmacicznych w ciągu 2 lat obserwacji po zachowawczym (64,3%) i radykalnym (58,3%) leczeniu operacyjnym ($p=0,636$). W tym samym przedziale czasu, odsetek ciąż ektopowych wynosił dla zachowawczej i radykalnej chirurgii odpowiednio, 17,9% i 4,2%, $p=0,093$. Pacjentki, u których doszło do rozwoju ciąży pozamacicznej po zachowawczej operacji miały istotnie wyższe poziomy surowiczego hCG (7413 ± 3155 IU/L) w porównaniu do tych pacjentek, u których nie doszło do ciąży pozamacicznej (3436 ± 2668 IU/L), $p=0,007$.

Wnioski: W późno rozpoznanych przypadkach ciąży ektopowej z wyższym poziomem hCG, zachowawcze postępowanie nie powinno być leczeniem z wyboru. Nasze wyniki wskazują na to, że skumulowany wskaźnik ciąż nie jest istotnie wyższy a ryzyko ponownej ciąży pozamacicznej może być zwiększone w przypadkach późnego rozpoznania ciąży jajowodowej leczonej zachowawczą chirurgią.

Słowa kluczowe: **cięża jajowodowa / ektopowa / nacięcie jajowodu / wycięcie jajowodu / beta hCG / wskaźnik płodności /**

Introduction

Ectopic pregnancy is defined as implantation of fertilized ovum outside uterine cavity. Estimated global prevalence of ectopic pregnancy is 1-2 percent [1, 2]. Ninety-five percent of ectopic pregnancies are tubal pregnancies [3]. Management of ectopic tubal pregnancies is easier with a better early-term prognosis when compared with non-tubal ectopic ones. However, in tubal pregnancies long-term prognosis is worse due to potential tubal damage. [4]. For the surgical management of tubal pregnancies, conservative or radical treatment approaches are available. Although conservative surgery has been assumed to increase expectancy of conception by preserving tubal integrity, it carries a risk of persistent trophoblastic activity and recurrence of ectopic tubal pregnancy in the operated uterine tubes.

In this study our aim was to investigate long-term postoperative outcomes of conservative, and radical surgery in ectopic tubal pregnancies, and evaluate the effectiveness of these techniques.

Material and methods

The study protocol was approved by the Ethics Committee of Dicle University, School of Medicine. A total of 145 patients that operated for tubal pregnancy between January 2006 and January 2009 at the Clinics of Department of Obstetrics and Gynecology, Dicle University, School of Medicine were included.

According to the surgical procedure, the patients were allocated in conservative (salpingo(s)tomy), and radical (salpingectomy) groups. Information related to patient's age, reproductive (gravidity, parity, infertility) and surgical history, history of previous ectopic pregnancies, serum human chorionic gonadotropin (hCG) levels at the time of diagnosis, intraoperative observation and phone numbers were retrospectively retrieved from hospital records.

Five patients who developed tubal pregnancy after in vitro fertilization (IVF) therapy and 6 patients either with a history of tubal surgery or had a contralateral tubal pathology (serious

peritubal adhesion, congenital tubal anomaly, and salpingectomy) that observed during the operation were excluded from the study. Twelve patients who desired contraception preoperatively and thus underwent bilateral tubal ligation, and two patients diagnosed as heterotopic pregnancy were also excluded. All telephone interviews were conducted by the same doctor to obtain information about the exact postoperative time interval in which the patients were trying to get pregnant, and the time when they spontaneously became pregnant. Twenty five patients who did not respond to our phone calls, 17 patients who used some means of birth control with no intention of getting pregnant and 2 patients who became pregnant with postoperative IVF therapy were not included in the evaluation. After obtaining verbal consent of 76 patients who were trying to conceive their relevant data were analyzed. Algorithms and exclusion criteria that used in this study were shown in Figure 1.

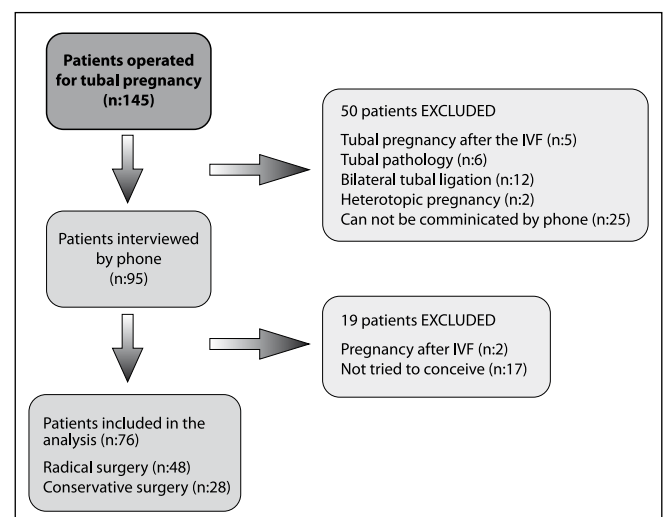


Figure 1. The flowchart for selection of patients for analysis.

Statistical Analyses:

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software (version 15.0 for Windows). All differences associated with a chance probability of 0.05 or less were considered statistically significant. Means, standard deviations and percentages were used to describe continuous and categorical variables, respectively. Chi square test with Yates correction was used, when applicable. For the continuous variables, unpaired Student's t test was applied. The estimated cumulative pregnancy rate was evaluated by plotting Kaplan-Meier survival curves and the log rank test.

Result

Laparoscopy (n=32) or laparotomy (n=44) were performed in a total of 76 patients whose data were analyzed. Basic characteristics of 28 patients who had conservative surgery, and 48 patients who underwent radical surgery were presented in Table 1.

Mean ages of the patients who had conservative or radical surgery were found to be 27.7±4.45 and 30.0±5.29 years, respectively. Mean serum hCG levels of the patients who had conservative or radical surgery were detected to be 4187.2±3026.6 and 3928.9±3040.8 IU/L, respectively. A statistically significant difference was not detected between two groups regarding the mean age and the mean serum hCG levels of the patients ($p>0,05$). Kaplan-Meier curves for cumulative spontaneous IUP for 2-year of conception period after the surgery were presented in Figure 2.

The 2-year cumulative spontaneous intrauterine pregnancy (IUP) rate for conservative and radical surgery were found as 64.3% and 58.3% and the estimated mean and standard error for conception period in both treatments were calculated as 6.89±1.19 and 6.95±0.97, respectively. According to the results of Log Rank (Mantel-Cox) test, the difference between two treatment modalities was not statistically significant ($p=0.773$). Postoperative time interval required for the conception was found to be 18 months in 96.4% of the patients in the conservative, and 95.8% of the patients in the radical surgery group. Outcomes of intrauterine pregnancy and mean time to conception are presented in Table 2.

During the same time interval, the rates of development of ectopic pregnancy for the conservative, and radical surgery groups were found to be 17.9% and 4.2%, respectively. A statistically significant difference was not detected in recurrence rates of ectopic pregnancy between two groups ($p=0.093$). Recurrence rates for ectopic pregnancy were shown in Table 2. The mean and SD values of serum hCG levels in patients who developed and not developed ectopic pregnancy after conservative surgery were 7413±3155 IU/L and 3436±2668 IU/L, respectively. Significant difference was found in hCG values between two groups ($t=2.93$; $p=0.007$). The confidence interval (95%CI) of hCG variable in patients who developed ectopic pregnancy after conservative surgery was 3496-11330 IU/L.

Discussion

In hemodynamically stable patients with established diagnosis of tubal ectopic pregnancy, laparoscopic approach should be preferred over open surgery [5]. When compared with the open surgery, laparoscopic approach is markedly associated

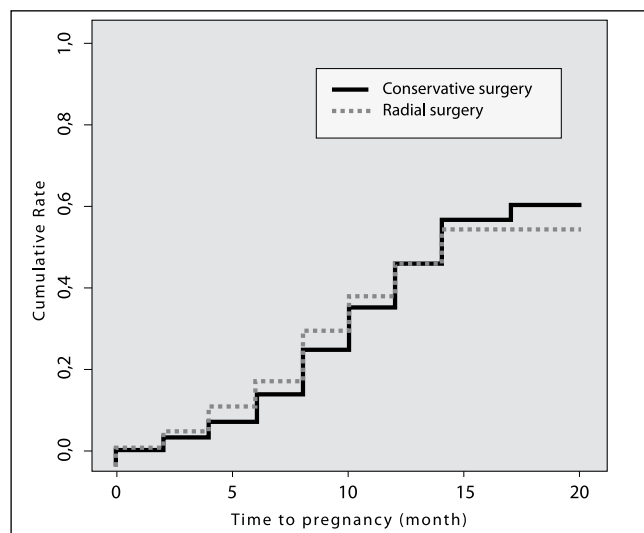


Figure 2. Kaplan-Meier curves: Cumulative spontaneous intrauterine pregnancy rates for both groups after surgery.

with shorter operative time, hospital stay, recovery period, and less bleeding [6]. However, a recently published meta-analysis reported that there is no significant difference in postoperative fertility between laparoscopic, and open surgery [7]. Therefore, we did not divide our patients into laparoscopy and open surgery subgroups while analyzing our data, under the light of mentioned meta-analysis.

In our study, the number of patients who underwent radical surgery was more than the number of patients who underwent conservative surgery. However, in some studies patients who had conservative surgery were more numerous [8-10]. We attribute this phenomenon to referral of late-diagnosed, hemodynamically instable patients or cases with tubal rupture to our hospital, which is a tertiary reference center in southeast of Turkey. When compared with the studies, which reported the incidence (1-2%) of tubal rupture among clinical characteristics of the patients enrolled, the rate of tubal rupture in our study is relatively higher (44%) [9, 10]. This difference can be seen as a reflection of higher frequency of radical surgery in the present study.

In some of previous studies related to cumulative pregnancy rates after conservative and radical surgery, relatively higher cumulative pregnancy rates were detected in the conservative surgery group [9, 11, 12], while other studies could not find a statistically significant difference between conservative and radical surgery groups [10, 13]. In three studies, which reported higher pregnancy rates in the conservative surgery group, no information has been given about the serum hCG levels at the time of diagnosis. In our study, no significant difference was found between both groups regarding mean serum hCG levels, and mean ages of the patients, which we thought to have an impact on pregnancy rates. To determine the effects of each of both surgical approaches on cumulative pregnancy rates more precisely from a statistical perspective, cases with a history of tubal surgery and those with tubal pathologies observed during surgery were excluded at the time of enrollment. If we had included these patients in the study, spontaneous pregnancy rates in the radical surgery group would be markedly lower as reported

Table I. Baseline characteristics of patients in conservative and radical surgery group (values are given as number of patients with percentage in the parentheses).

Patients included in the analysis (n=76)	Conservative surgery group (n=28)	Radical surgery group (n=48)
Mean age (years ± SD)	27.7 ± 4.45 *	30.0 ± 5.29 *
Mean serum hCG levels (IU/L ± SD)	4187 ± 3027 **	3929 ± 3041 **
Nulliparity	9 (32.1)	18 (18.8)
History of a abdominopelvic surgery	13 (28,6)	21 (27,1)
Rupture	7 (25.0)	27 (56.3)
Laparoscopy	15 (53.5)	17 (35.4)
Laparotomy	13 (46.5)	31 (64.6)

$p < 0.05$ is considered to indicate statistical significance (* $p = 0.277$; ** $p = 0.930$)

Table II. Intrauterine and repeat ectopic pregnancy outcomes.

Patients included in the analysis (n=76)	Conservative group (n=28)	Salpingectomy group (n=48)	p value
Intrauterine pregnancy rate (%)	18 (64.3)	28 (58.3)	0.636
Mean time to pregnancy (months ± SD)	6.89 ± 1.19	6.95 ± 0.97	0.773
Ectopic pregnancy rate (%)	5 (17.9)	2 (4.2)	0.093

$p < 0.05$ is considered to indicate statistical significance.

in the literature [11]. In these patients, preservation of tubal passage with conservative surgery will be more appropriate.

According to the results of our study, at the completion of an 18-month postoperative period during which women try to conceive, almost all of the potential pregnancies will be accomplished. Healthy individuals may be pregnant within 12 months period of conceive, however following tubal surgery the patients will have to wait approximately for 18 months for being pregnant.

In studies investigating postoperative recurrence rates of ectopic pregnancy after conservative, and radical surgery, statistically insignificantly higher rates in the conservative surgery group have been detected [9, 11, 14, 15]. We found higher (17.9%) postoperative recurrence rates after conservative surgery when compared with the radical surgery (4.2%) without any significant intergroup difference in compliance with the literature. In the conservative surgery group, we found statistically significantly higher preoperative serum hCG levels in patients with recurrence of ectopic pregnancy when compared with cases who did not develop ectopic pregnancy. Therefore, increased serum hCG level can be a warning sign for the recurrence in the conservative surgery group.

Conclusion

In conclusion, in late-diagnosed tubal pregnancy cases with higher serum hCG levels, conservative treatment should not be the first choice. Cumulative pregnancy rates were not significantly higher and recurrence risk of ectopic pregnancy can be increased following conservative surgery.

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