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Analysis of outcomes of fertility restoration surgery in women with infertility secondary to tubal pregnancy: a series of 77 cases

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Summary

Purpose: To assess pregnancy outcomes after minimally-invasive fertility restoration surgery in women with infertility secondary to tubal pregnancy treated with salpingectomy. *Materials and Methods:* The study included 77 women diagnosed with infertility after salpingectomy for tubal pregnancy between December 2008 and October 2010 for intraoperative assessment and treatment of tubal and pelvic adhesions. The mean age of the patients was 31.12 ±3.58 years and their duration of infertility was 3.91 ±2.80 years. Chi-square test, Student's *t*-test, rank-sum test, and Kaplan-Meier test was used. A p-value < 0.05 was considered significant. *Results:* Tubal function was restored in 68.8% of women, 33.77% experienced intrauterine conception, 32.47% had a live birth, 5.19% had an ectopic pregnancy, and 1.30% had a spontaneous abortion within the three-year follow up period. *Conclusions:* Minimally-invasive fertility restoration surgery after tubal pregnancy treated with salpingectomy restored tubal function in the contralateral fallopian tube in the majority of women.

Key words: Infertility; Tubal pregnancy, Salpingectomy; Laparoscopy; Laparotomy; Hysteroscopic tubal catheterization.

Introduction

Ectopic pregnancy represents 1.5-2% of all pregnancies, and tubal pregnancy accounts for more than 95% of these cases [1, 2]. When tubal ruptures occur, tubal pregnancy may impact physical health. Importantly, infertility results in about 30% of women [3], and these women have a three-fold increased risk of recurrent ectopic pregnancies [1, 4]. The probability of intrauterine pregnancy within one year of trying to conceive is approximately 70% [5]. Methods for the treatment of tubal pregnancies include medication, salpingotomy (surgical incision into a fallopian tube), and salpingectomy (resection of the affected fallopian tube). However, all three of these methods may decrease the chance of subsequent spontaneous conception [6], and the impact on long-term outcomes such as secondary ectopic pregnancy and infertility cannot be ignored.

Salpingectomy is still one of the main methods used to treat tubal pregnancy and a laparoscopic approach has recently gained popularity [7]. However, the more traditional laparotomic approach is still used in some cases, particularly in women with severe damage to the salpinx, internal bleeding, or hemorrhagic shock caused by tube rupture [8]. In addition, a lack of experience in laparoscopy for many clinicians limits its use as an alternative to laparotomy [9, 10].

Maintaining or restoring fertility after salpingectomy treatment or tubal pregnancy is of vital importance to the women who undergo these procedures [11]. The objective of the present study was to assess pregnancy outcomes after minimally-invasive fertility restoration surgery in women with infertility secondary to tubal pregnancy, treated with salpingectomy in a Chinese population. Results of the present study could help practitioners select the best approach to preserving fertility in women with tubal pregnancy as well as improving their pregnancy outcomes.

Materials and Methods

Patients

This study is a case series of 77 women who were hospitalized and treated at the Affiliated Hospital of Logistics College of the Chinese People's Armed Police Forces between December 2008 and October 2010. Inclusion criteria were: 1) a history of tubal pregnancy treated with laparotomic or laparoscopic salpingectomy; 2) a history of regular menstrual cycles and normal sexual intercourse; 3) > one year of infertility; 4) successful treatment of a tubal pregnancy, which was the most recent pregnancy; and 5) no history of any other abdominal surgery. Exclusion criteria were: 1) a history of two or more tubal pregnancies; 2) being in a relationship with a male suffering from dysspermy; 3) any abdominal surgery; 4) tubal pregnancy after in vitro fertilization; 5)

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any treatment other than surgery for tubal pregnancy; 6) inability to undergo surgery for severe pelvic adhesion; or 7) incomplete follow-up data.

In total, 77 women were included in the present study. This study was approved by the Ethics Committee of the Affiliated Hospital of Logistics College of Chinese People's Armed Police Forces.

Information on general characteristics (age and occupation), menstrual cycle (regularity, length of menstrual periods and menstrual duration, and dysmenorrhea), reproductive history (induced abortion, medical abortion, ectopic pregnancy, and spontaneous abortion), past medical history (pelvic inflammatory disease, appendicitis, etc.), and previous history of abdominopelvic cavity operation were collected. Additional data on previous tubal pregnancies including which side and treatment method (laparotomic or laparoscopic salpingectomy, and whether the fallopian tube was resected or preserved) were collected.

Fertility exploration procedure

Hysteroscopic-laparoscopic exploration was performed 3-7 days after menstruation by an experienced gynecologic endoscopist. Uterine size and shape were examined with a combined hysteroscope and laparoscope. The fallopian tube bearing the ectopic pregnancy had been resected, only the shape of the contralateral fallopian tube and tubal fimbria, as well as the size and shape of the ovary, were recorded. Pelvic adhesions were also recorded. An infusion of methylene blue was performed by laparoscopy-assisted hysteroscopic tubal liquid instillation, and the patency of the fallopian tube was evaluated by observing the effusion of methylene blue from the tubal fimbria. The function of the fallopian tube and reasons for infertility were evaluated according to the results of the laparoscopic exploration and the patency of the fallopian tube.

Laparoscopic minimally-invasive surgery-assisted techniques (including laparoscope-assisted lysis of pelvic adhesions, salpingostomy of the fimbriated extremity with hydrosalpinx or atresia tubalis, ovarian cystectomy, and electrocautery of endometriosis) were performed according to the results of the laparoscopic exploration. For patients with an obstructed fallopian tube, a guidewire (0.035 inch in diameter by 150 cm in length-was passed through the catheter that had been inserted into the fallopian tube with the assistance of the laparoscope to clear the obstruction, and methylene blue was infused again to evaluate the patency of the fallopian tube. In addition, hysteroscopic incision of the uterine septum and hysteroscopic resection of uterine polyps were performed in the presence of polyps. Chitosan or an absorbable adhesion barrier was used to cover incisions in the pelvic cavity to prevent adhesion after the surgery.

Classification of pelvic adhesions

The modified Adhesion Scoring Group [12] scoring system was used for pelvic and abdominal adhesions, which were classified as: Grade 0 (no pelvic adhesion), Grade I (filmy and/or avascular pelvic adhesion), Grade II (vascular and/or dense pelvic adhesion), Grade III (vascular and/or dense pelvic adhesion that may or may not respond to treatment), and Grade IV (cohesive adhesion that could not undergo treatment). In the present study, all patients with Grade IV adhesions were excluded since surgical treatment was not possible.

Follow-up

Follow-up was performed for all patients by telephone interview at 3, 6, 12, 18, and 36 months after surgery to collect information about pregnancy and pregnancy outcomes. For patients with several pregnancies during the three-year follow-up period, only data from the first pregnancy was included in the analysis.

Table 1. — *Characteristics of infertile women.*

Characteristic	Patient values (n=77)
Age (years) mean ± SD	31.12 ± 3.58
Gravida (n) mean ± SD	2.30 ± 1.42
Duration of infertility (years) mean ± SD	3.91 ± 2.80
Permanently employed	
Yes n (%)	50 (64.9)
No n (%)	27 (35.1)
Education level higher than college	
Yes n (%)	13 (16.9)
No n (%)	64 (83.1)
History of pelvic inflammation	
Yes n (%)	23 (29.9)
No n (%)	54 (70.1)
History of intrauterine conception	
Yes n (%)	53 (68.8)
No n (%)	24 (31.2)
Position of tubal pregnancy	
Left n (%)	24 (31.2)
Right n (%)	53 (68.8)
Salpingectomy surgical method	
Laparotomy n (%)	54 (70.1)
Laparoscopy n (%)	23 (29.9)

Statistical analysis

SPSS 17.0 was used for the statistical analyses. The Chi-square test was used for categorical variables, Student's *t*-test was used for continuous variables, the rank-sum test was used for the analysis of adhesion degree, and the Kaplan-Meier test was used for the analysis of pregnancy outcomes. *P*-values < 0.05 were considered significant.

Results

Patient characteristics are presented in Table 1. Seventy-seven patients with infertility secondary to salpingectomy for tubal pregnancy were included in the present study. Fifty-four (70%) patients were treated with laparotomy salpingectomy, and 23 (30%) patients were treated with laparoscopic salpingectomy.

Tubal obstructions were reported in nearly all patients (92.2%). The majority of patients also had an abnormally shaped contralateral fallopian tube (71.4%). Tubal fimbria abnormalities occurred in 57.1% of patients (Table 2).

There was a high prevalence of pelvic adhesions. Grade 0, I, II, and III pelvic adhesions occurred in 14.3%, 26.0%, 24.7% and 35.1% of the patients, respectively. The prevalence of other pelvic risk factors was low, with all of them present at less than 10%. Endometriosis was found in seven patients (9.1%), ovarian cysts in seven patients (9.1%), endometrial polyps in seven patients (9.1%), and uterine mediastinal defects in five patients (6.5%).

After hysteroscopic-laparoscopic exploration and fertility restoration treatment, restoration of tubal patency and normal fallopian tube and tubal fimbria were used to judge whether fertility had been restored. Most of the patients had

Table 2. — *Characteristics of the contralateral fallopian tube.*

Characteristic		n (%)
Shape of the fallopian tube	Normal	22 (28.6)
	Abnormal	55 (71.4)
Tubal fimbria	Normal	33 (42.9)
	Atresia or hydrops	44 (57.1)
Tubal patency	Unobstructed	6 (7.8)
	Obstructed	71 (92.2)

Table 3. — *Restoration of tubal fertility after minimally-invasive surgery-assisted fertility restoration.*

Characteristic		n (%)
Tubal shape	Normal	58 (75.3)
	Abnormal	19 (24.7)
Tubal fimbria	Normal	71 (92.2)
	Abnormal	6 (7.8)
Tubal patency	Unobstructed	64 (83.1)
	Obstructed	13 (16.9)
Tubal function restoration		53 (68.8)

a normal tubal shape (75.3%) and tubal fimbria (92.2%). Most patients additionally did not have an obstruction (83.1%). Tubal function was restored in the majority of patients (68.8%). Figure 1 shows the surgical processes (normal *vs*. abnormal), and the results are shown in Table 3.

Patients were followed for three years after treatment. Table 4 shows the pregnancy outcomes. Six women (7.79%) were lost to follow-up. After treatment, 33.77% of the patients experienced intrauterine conception, 32.47% had a live birth, 5.2% experienced an ectopic pregnancy, and 1.3% had a spontaneous abortion. Among the women who experienced spontaneous intrauterine conception, only two (8.00%) were ≥ 35-years-old. The cumulative conception rate after fertility restoration surgery using a Kaplan-Meier curve is displayed in Figure 2.

Discussion

Tubal pregnancies and their treatment may reduce a woman's fertility. With the development of early diagnostic techniques, the major concern for tubal pregnancy has changed from the treatment of an immediate life-threatening condition to the preservation of fertility. In this study, the authors observed that 96.1% of women with infertility secondary to radical treatment of tubal pregnancy had impaired contralateral tubal function. The

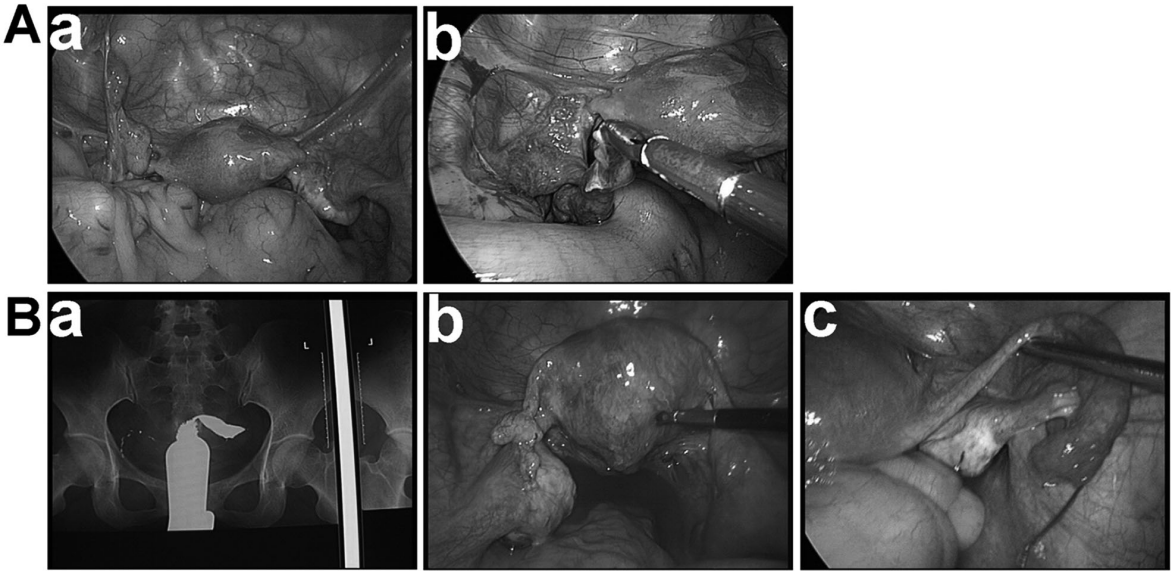

Figure 1. — A: Salpingectomy of the right fallopian tube was performed for the treatment of tubal pregnancy and secondary infertility was observed. (a) Laparoscopic exploration was performed and shows that the tubal fimbria adheres to the left lower abdominal wall and could not effectively capture ovum. (b) Adhesiolysis was performed using a laparoscope, and the left fallopian tube was restored to a normal position. Hysteroscopic tubal liquid instillations shows that the tube is unobstructed. The woman became pregnant two months after the operation and had a live birth. B: Laparotomy salpingectomy was performed for resection of the left ampulla and tubal fimbria for the treatment of tubal patency. (a) Uterine iodine oil radiography and (b) laparoscopy-assisted hysteroscopic tubal liquid instillation indicate an obstruction between the right tubal isthmus and ampulla. (c) Tubal patency is restored by laparoscopy-assisted hysteroscopic tubal catheterization in which the guidewire is inserted through the tubal fimbria into the abdominal cavity. This woman became pregnant eight months after the operation and achieved a live birth.

Table 4. — *Pregnancy outcomes after minimally-invasive surgery-assisted fertility restoration.*

Outcome	n (%)
Intrauterine conception	26 (33.77)
Live birth	25 (32.47)
Ectopic pregnancy	4 (5.19)
Spontaneous abortion	1 (1.30)

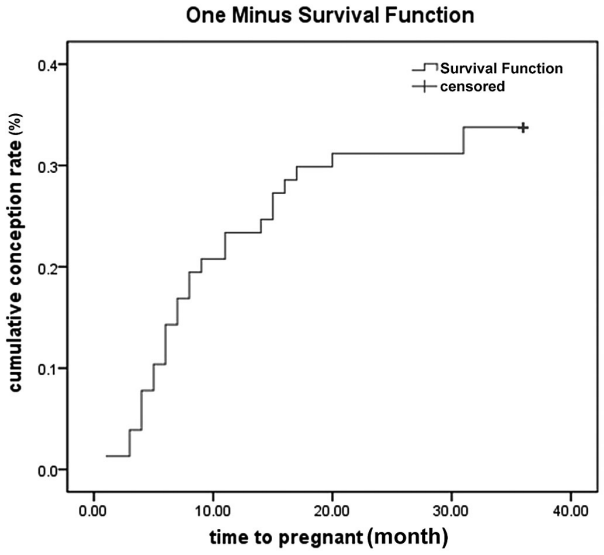

Figure 2. — Statistical test to compare the two curves. Cumulative rate of spontaneous intrauterine conception after treatment of assisted reproduction.

most commonly found condition was contralateral tube obstruction, followed by abnormal tube shape. Additionally, more than half of the women included in this study had abnormal tubal fimbria. These fertility-compromising conditions may be a consequence of tubal pregnancy or treatment efforts. Factors other than tubal conditions (such as uterine conditions and ovulation) could also affect fertility. In the current study, the prevalence of endometriosis, ovarian cysts, and uterine polyps was significantly lower than tubal conditions.

Few studies have investigated infertility secondary to tubal pregnancy. Mueller *et al*. [13] reported that about one-fifth of women who had tubal pregnancies developed secondary infertility, with 92% of these cases explained by tubal conditions. While laparoscopic exploration has been regarded as the gold standard for evaluating tubal function and identifying the causes of infertility, in the present study, both laparoscopic exploration and hysteroscopic tubal liquid instillations were used to ensure objective results.

Age is an independent factor that could influence fertility in women [14]. Studies have demonstrated that fertility decreases significantly in women older than 35 years. In the present study, the mean age of women with infertility secondary to tubal pregnancy was 30 years or older, and the duration of infertility was about three to four years. In a few cases, the duration of infertility was as long as 12 years. Only two women were older than 35 years and recovered their tubal fertility after minimally-invasive surgery. These findings suggest that the delay in treatment for women with infertility secondary to tubal pregnancy could be due to the fact that the causes of infertility were not clearly identified.

Previous studies have reported that the possibility of spontaneous intrauterine conception is about 56% within the first year after tubal pregnancy, and about 67% within the first two years after tubal pregnancy [15-17]. Most spontaneous conceptions occur within the first year after the treatment of tubal pregnancy. The most frequent causes of infertility secondary to the radical treatment of tubal pregnancy are tubal conditions which cannot be effectively treated by medications or expectation. In these cases, minimally-invasive surgery-assisted or in vitro-assisted reproduction may help patients restore fertility.

In contrast to many recent studies in which laparoscopy is the preferred technique, a large proportion of the patients in this study underwent laparotomy instead. One possible explanation for this is that the patient population treated in the present clinic was treated in centers less experienced in laparoscopy. In a two-year follow-up study by van Beek *et al*. [18] in women with ectopic pregnancy, there was no difference in the rate of intrauterine conception between women originally treated with laparotomic or laparoscopic salpingectomy, suggesting that these two treatment methods would not differentially affect fertility. In the present study, 29.9% of women had a history of pelvic inflammation, suggesting that infertility secondary to radical treatment of tubal pregnancy was not caused by the surgical methods, but may have been due to pre-existing fertility-influencing factors, including pre-existing contralateral tubal conditions. However, tubal pregnancy might aggravate the effects of these conditions. Additionally, these conditions may contribute to recurrent tubal pregnancies.

In the present study, hysteroscopic-laparoscopic surgeries were performed in women with infertility secondary to radical treatment for tubal pregnancy. The three-year cumulative conception rate was 33.77%. Most spontaneous intrauterine conceptions occurred within the first 20 months after surgery (mean of 18 months). Spontaneous intrauterine conception occurred in two women more than 31 months after the operation. These findings suggest that there may be beneficial effect of surgical fertility restoration, but a case-control study is necessary to confirm this issue.

Laparoscopic exploration has been regarded as the standard method for identifying the tubal and other pelvic factors of infertility [19]. Laparoscopic exploration may be helpful for several processes, including pelvic adhesiolysis, peritubal adheiolysis, and restoration of tubal fimbria

during minimally-invasive surgery-assisted fertility restoration [20]. Laparoscopy-assisted hysteroscopic tubal catheterization can be used to evaluate tubal patency by liquid instillations as well as help restore tubal patency by clearing mucous plugs, debris, and fibrotic tubal lumen, especially at the proximal tubal region [21].

One limitation of this study is the relatively small sample size. The present authors excluded patients who had prior abdominal surgery in order to simplify the study, but in doing so, they may have excluded a large number of patients, potentially introducing some bias into the study. It is also important to note that while they excluded couples with male infertility and women with irregular menses, there are a number of other etiologies for infertility that would have been difficult to exclude. Additionally, they cannot assume that all of the patients enrolled had infertility that was secondary to the prior salpingectomy. Further studies with larger sample sizes are warranted to validate our findings.

Conclusion

In summary, tubal conditions are the critical factors for infertility in women who have undergone radical treatments for tubal pregnancy. Minimally-invasive surgery-assisted fertility restoration could help restore tubal fertility in some women and provide further clinical evidence for choosing treatment methods for infertility.

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