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A 12-years retrospective cohort study

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Fertility outcome after laparoscopic salpingostomy or salpingectomy for tubal ectopic pregnancy. A 12-years retrospective cohort study.

AIM: *To compare the subsequent reproductive outcome after laparoscopic salpingostomy or salpingectomy for tubal ectopic pregnancy (EP).*
MATERIAL OF STUDY: *A retrospective cohort study was conducted between January 2002 and May 2014 on 132 women admitted to Unit of Gynecology and Obstetrics of the Department of Human Pathology in Adulthood and Childhood "G. Barresi", "Gaetano Martino" Hospital, University of Messina (Italy), with EP and who received surgical treatment, including laparoscopic salpingectomy (n=57) or salpingostomy (n=75). Main outcomes included intrauterine pregnancy (IUP), recurrent EP and persistent trophoblastic disease rates.*
RESULTS: *The IUP rates up to 24 months after surgery were 56.1% for salpingectomy and 60% for salpingostomy. The 2-year recurrent EP rates were 5.3% for salpingectomy and 18.7% for salpingostomy. The persistent trophoblastic disease rate were 1.8% for salpingectomy and 12% for salpingostomy.*
DISCUSSION: *Our results show that the reproductive outcomes after laparoscopic salpingectomy are similar to those observed after conservative treatment.*
CONCLUSIONS: *In the surgical treatment of EP, the clinician should choose the best treatment in accordance with the patient, considering the severity of the disease, the clinical characteristics of the patient and her desire to preserve fertility.*

KEY WORDS: Ectopic pregnancy, Salpingectomy,Salpingostomy

Introduction

A proper management of ectopic pregnancy (EP) is crucial to the preservation of woman's fertility. Thus, a prompt diagnosis, the improving of surgical techniques and the choice of medical treatments in unruptured pregnancy, improve patients' fertility and limit the risk of recurrence. Salpingectomy is considered the gold standard treatment, especially in case of ruptured ectopic pregnancy. However, as early as 1914 [1], salpingostomy was demonstrated to be a feasible choice and from 1957 onwards [2], this approach of anatomical preservation was promoted in favor of radical surgery. Thus, conservative surgical treatment of EP has been the preferred operative method in unruptured cases until several series reported a higher risk of subsequent EP and persistent trophoblastic disease [3,4]. Nevertheless, the decision

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whether surgical treatment should be conservative or radical in women wishing to preserve their fertility was debated during the past years. The purpose of this study was to compare the subsequent reproductive outcome in women with a tubal EP, according to the two different laparoscopic treatments. Primary aim was to calculate the intrauterine pregnancy (IUP) rate within 24 months. Secondary aim was to calculate the rate of recurrence of an EP and the persistent trophoblastic disease.

Materials and Methods

We retrospectively reviewed women with a tubal EP who were admitted to hospital for surgical treatment in the Unit of Gynecology and Obstetrics of the Department of Human Pathology in Adulthood and Childhood "G. Barresi", "Gaetano Martino" Hospital, University of Messina (Italy) between January 2002 and May 2014. The study design is in accordance with the Helsinki Declaration, conforms the committee on publication ethics (COPE) guidelines and was approved by the institutional review board (IRB) of the hospital in which it was performed. Each patient who participated in this study was well informed regarding the procedures that they would undergo and signed a consent form for data collection for research purposes. All the design, analysis, interpretation of data, drafting and revisions followed the strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies, available through the enhancing the quality and transparency of health research (EQUATOR) network.

Two choices of laparoscopic surgical approach were available: salpingectomy and salpingostomy. The decision to choose between salpingectomy and salpingostomy was based on the score proposed by Pouly et al. [5]. Diagnosis of tubal pregnancy was obtained combining transvaginal ultrasound and serum beta-human chorionic gonadotropin (β-hCG) evaluation. Before surgery, women underwent routine preoperative preparation. Clinical reports provided information about maternal characteristics and prognostic factors of infertility, such as age, parity, localization of ectopic pregnancy, kind of surgery, previous EP, previous tubal surgery, previous pelvic inflammatory disease. During surgery, we checked the status of the contralateral tube. Serum β-hCG was measured postoperatively until undetectable concentrations were reached. A phone call follow-up was obtained in order to evaluate the surgical outcome, the desire for future pregnancy, the presence of a subsequent IUP or EP. According to ectopic presentation and surgical treatment, women were divided into two groups: Group A, including EP with unruptured tube, who undergone salpingostomy; group B, including women with a ruptured tube or angular pregnancy, who undergone salpingectomy.

The primary outcome was considered an IUP within two years of treatment. This choice was based on previous observational studies in which spontaneous pregnancies following an EP occur most often from 18 to 24 months after treatment [6]. Secondary outcomes were persistent trophoblastic disease and recurrence of EP. The persistent trophoblastic disease was defined as the increase or the persistence of a high concentration of serum β-hCG concentrations after surgery [7]. Recurrent EP was defined as a new ectopic pregnancy that requires a medical and/or a surgical reintervention.

Statistical analysis was performed with IBM SPSS version 20.0.0 (SPSS Inc., Chicago, USA). For the statistical analysis of data a $\chi 2$-test with CI of 95% and one degree of freedom were applied. P-values below 0.05 were regarded as statistically significant. For both groups we obtained cumulative rates of IUP using the survival analysis, over a period of 24 months. The starting date was set at the day of surgery, the final point was the date of the last menstrual period in case of pregnancy. Similarly, we calculated cumulative rates of persistent trophoblastic disease and recurrence of EP, distinguishing between ipsilateral (in case of salpingostomy) or contralateral recurrence.

Results

The study group included 132 women, whose characteristics are reported in table I. Maternal mean age was 32.3 ± 2.1 years (range 19-42 years). Ectopic pregnancy was located in ampulla (n=105; 79.5%), isthmus (n=16; 12.1%) or fimbriae (n=11; 8.3%). Ectopic pregnancy dimension was <1 cm in 4 cases (3%), between 1 and 5 cm in 106 cases (80.3%) and > 5 cm in 22 cases (16.7%). The largest EP was 7 cm. Most patients

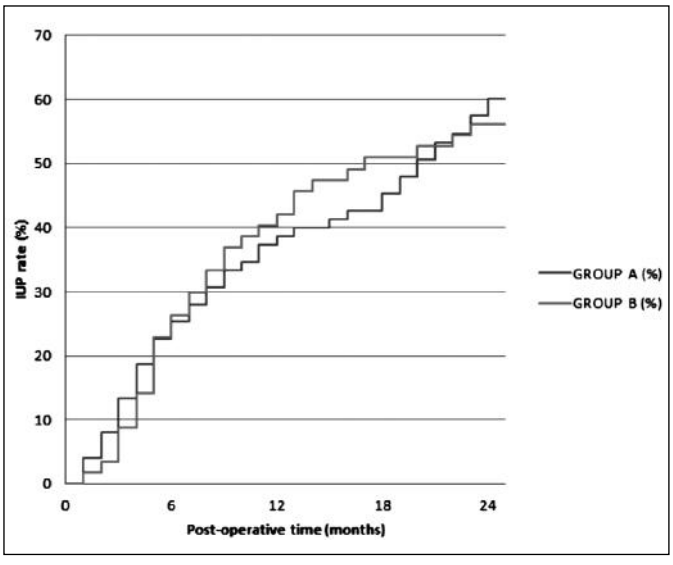

Fig. 1: Intrauterine pregnancy (IUP) rate.

TABLE I - *Baseline characteristics. EP: ectopic pregnancy; IUD: intra-uterine device; hCG: human chorionic gonadotropin.*

	Group A **75 (56.8%)**	**Group B** **57 (43.2%)**
Mean age (years)	32.3±2.1	32.3±2.1
Risk factors for tubal pathology		
Known tubal pathology	2 (2.7%)	1 (1.8%)
Vaginal infection (Chlamydia)	9 (12%)	6 (10.5%)
Anamnesis of pelvic inflammatory disease	1 (1.3%)	3 (5.3%)
Anamnesis of EP	3 (4%)	1 (1.8%)
Previous termination of pregnancy	14 (18.7%)	13 (22.8%)
Use of IUD	1 (1.3%)	1 (1.8%)
Symptoms		
Asymptomatic	4 (5.3%)	2 (3.5%)
Pelvic pain	13 (17.3%)	9 (15.8%)
Vaginal bleeding	8 (10.7%)	6 (10.5%)
Pelvic pain and vaginal bleeding	50 (66.7%)	40 (70.2%)
Ultrasonographic features		
Ectopic mass	49 (65.3%)	38 (66.7%)
Mean dimension of ectopic mass (mm)	2.3 (1.3)	2.4(1.4)
Visualization of fetal heart rate	6 (8%)	6 (10.5%)
Mean value of preoperative beta-hCG (IU\L)	2181 (range 860-4298)	2409 (range 920-6036)
Tubal localization of EP		
Ampulla	60 (80%)	45 (78.9%)
Fimbriae	5 (6.7%)	6 (10.5%)
Isthmus	10 (13.3%)	6 (10.5%)

TABLE II - *Secondary outcomes.*

	Group A **75 (56.8%)**	**Group B** **57 (43.2%)**	**p-value**
Trophoblast persistence	9 (12%)	1 (1.8%)	0.0276
Recurrence of EP	14 (18.7%)	3 (5.3%)	0.0228
ipsilateral tube	10 (13.3%)	0	0.0041
contralateral tube	4 (5.3%)	3 (5.3%)	0.9858

(68.2%) presented pelvic pain and vaginal bleeding, 10.6% (n=14) only vaginal bleeding and 16.7% (n=22) only pelvic pain. Six patients (4.5%) were totally asymptomatic. Among the 132 patients, 75 (56.8%) underwent salpingostomy and 57 (43.2%) salpingectomy. The 24-months cumulative rate of pregnancy obtained by natural conception was similar for both groups: 60% (n=45/75) after salpingostomy and 56.1% (n=32/57) after salpingectomy, with a mean time of 15 months (p=0.6559) (Fig. 1). The persistent trophoblastic disease occurred more frequently (p=0.0276) in group A (n=9; 12%) than in group B (n=1; 1.8%). The recurrence of EP was significantly higher (p=0.0228) in group A (n=14; 18.7%) than in group B (n=3; 5.3%). In particular, in case of salpingostomy, the recurrence occurred most frequently in the previously operated tube than the contralateral tube (13% vs. 5%). As showed in Table II, no statistically significant differences were found comparing recurrence rates in the contralateral tube in the two groups (p = 0.9858).

Discussion and Comments

For most tubal EP, surgery is the gold standard treatment and fertility preservation is a crucial issue. In this view, the adoption of standard protocol that avoid fertility damage is mandatory, ensuring the lowest risk of complication(s). In the recent past, the use of salpingostomy or salpingectomy was debated, taking into account the fertility outcomes after the two procedures. The purpose of this study was to clarify the role of laparoscopic salpingectomy and salpingostomy as surgical alternatives. It is now widely accepted that surgical

treatment of ectopic pregnancy should be laparoscopic, except for a few cases, such as contraindications to laparoscopy, hemodynamic shock, and insufficient experience of the operator. Since the first studies demonstrated the potential effectiveness of salpingostomy [7,8], this treatment has been compared with salpingectomy in numerous non-randomized studies [9]. Salpingostomy is often preferred to salpingectomy because it is believed that the conservation of both tubes ensures more favorable prospects for future fertility. In this setting, the Royal College of Obstetricians and Gynecologists guideline advises salpingectomy as the preferred standard surgical approach for tubal EP [10]. However, there is little evidence to support this thesis, due to the poor methodological approach of the original studies that failed to report essential details, including time to become pregnant, desire for future pregnancy and whether subsequent pregnancies occurred either spontaneously or after fertility treatment. Furthermore, during EP management is mandatory to take into account the condition of the contralateral (not-affected) fallopian tube. In women with a history of bilateral tubal pathology, salpingostomy offered better IUP rates than salpingectomy, while in absence of history of tubal pathology this benefit was less clear [11-14], albeit with a higher risk of recurrence of ectopic pregnancy in case of both the techniques [3] and persistent trophoblastic disease in case of salpingostomy, necessitating further treatment [4,7]. Thus, a rational approach would be salpingostomy for women with a tubal EP in the presence of contralateral tubal pathology with desire for future pregnancy. However, in women without contralateral tubal pathology, the best surgical treatment is still unclear. Despite this lack of evidence, in a clinical setting salpingectomy is preferred in the presence of a healthy contralateral tube, because it is easier, quicker and safer than salpingostomy and has a lower risk of persistent trophoblastic disease and repeated EP in the conserved tube [15]. This approach is supported by a recent meta-analysis [16] of two randomized controlled trials, in which salpingostomy did not improve cumulative rates of ongoing pregnancy by natural conception in women with a tubal pregnancy and a healthy contralateral tube, but was associated with an increased risk of persistent trophoblastic disease. These data are corroborated also by the strong patients' preference towards salpingectomy respect to salpingostomy [17].

Basing on our experience, in the surgical treatment of EP the clinician should choose the best treatment in accordance with the patient, considering the severity of the disease, the clinical characteristics of the patient and her desire to preserve fertility.

Our results show that the reproductive outcomes after laparoscopic salpingectomy are similar to those observed after conservative treatment. In our cohort of 132 women, 60% of patients assigned to salpingostomy and 56.1% of those treated with salpingectomy conceived spontaneously within 24 months and obtained an IUP. This difference was not statistically significant (p=0.6559). Therefore, salpingostomy did not increase the cumulative rates of IUP obtained after natural conception in women with a previous tubal pregnancy, but rather was associated with increased rates of recurrence and persistence of trophoblastic disease of EP. Indeed, recurrence rates of EP and persistent trophoblastic disease after conservative treatment were 18.7% and 12%, much higher than those reported after salpingectomy (respectively 5.3% and 1.8%).

Conclusions

Our results suggest that salpingectomy should generally be preferred to salpingostomy in women with a healthy contralateral tube and eager to preserve their fertility. However, women who express the desire to maximize their fertility may still opt for conservative treatment, especially if they have risk factors for infertility or an unhealthy contralateral tube, taking into account the possibility of a further medical or surgical reintervention to treat complications following surgery (persistent trophoblastic disease or recurrent EP).

Riassunto

Scopo: Confrontare i risultati nella riproduzione dopo salpingotomia o salpingectomia laparoscopica in caso di gravidanza ectopica tubarica (GT).

Materiale dello Studio: Abbiamo effettuato uno studio di coorte retrospettivo nel periodo di riferimento da Gennaio 2002 a Maggio 2014 presso l'Unità di Ginecologia ed Ostetricia del Dipartimento di Patologia Umana dell'Adulto e dell'Età Evolutiva "G. Barresi, Ospedale "Gaetano Martino", Università di Messina (Italia) su 132 pazienti affette da GT e sottoposte a trattamento chirurgico mediante salpingectomia (n=57) o salpingotomia (n=75) laparoscopica. I parametri principali analizzati sono stati una successiva gravidanza intrauterina, una successiva GT o la persistenza di trofoblasto ectopico.

Risultati: La percentuale di successiva gravidanza intrauterine a 24 mesi dopo chirurgia è stata del 56.1% nel gruppo della salpingectomia e del 60% nel gruppo della salpingotomia. La percentuale di successiva GT a 2 anni è stata del 5.3% nel gruppo della salpingectomia e del 18.7% nel gruppo della salpingotomia. La percentuale di persistenza di trofoblasto ectopico è stata dell'1.8% nel gruppo della salpingectomia e del 12% nel gruppo della salpingotomia.

Discussione: I nostri risultati mostrano che l'efficacia sulla riproduzione dopo salpingectomia laparoscopica sono simili a quello osservati nel trattamento conservativo.

Conclusioni: Nel trattamento chirurgico della GT, il chirurgo dovrebbe scegliere il migliore trattamento in

accordo alla paziente, considerando la severità del quadro, le caratteristiche cliniche della paziente ed il suo desiderio di preservare la fertilità.

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