

## Original Article

# Core-pulling salpingectomy: a novel surgery for hydrosalpinx prior to in vitro fertilization and embryo transfer

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Received October 28, 2015; Accepted August 29, 2016; Epub October 15, 2016; Published October 30, 2016

**Abstract:** Objective: This study aims to investigate the effects of a new surgical procedure to treat hydrosalpinx prior to in vitro fertilization and embryo transfer (IVF-ET). Methods: Infertile females receiving treatment for hydrosalpinx (n=633) were divided into one treated group and two comparison groups. The treated group comprised patients received pretreatment with core-pulling salpingectomy (n=105). One comparison group comprised patients who had conventional salpingectomy prior to IVF-ET (n=104), and the other comparison group comprised those received IVF-ET without a prior history of hydrosalpinx (n=424). Outcome in the treated group, ovarian reserve, ovarian responsiveness, and conception rates were compared to the two untreated groups. Results: After core-pulling salpingectomy, antral follicle number, endocrine profile, total dosage of ovulation-inducing agents required for ovarian stimulation, estradiol level on the day of human chorionic gonadotropin administration, and the number of oocytes retrieved following core-pulling salpingectomy were significantly higher compared to conventional salpingectomy, but not different from women without hydrosalpinx. Patients who underwent core-pulling salpingectomy received IVF-ET and achieved an increased clinical conception rate compared to conventional salpingectomy, but the difference was not statistically significant. Conclusions: Laparoscopic core-pulling salpingectomy should be recommended for patients with hydrosalpinx before receiving IVF-ET. This procedure did not interfere with ovarian reserve or responsiveness, and improved the conception rate.

**Keywords:** Infertility, hydrosalpinx, salpingectomy, IVF-ET

## Introduction

In vitro fertilization and embryo transfer (IVF-ET) is the primary treatment option for infertile patients with hydrosalpinx. However, if the hydrosalpinx is not treated first, outcomes of IVF-ET are compromised [1]. The fluids secreted by epithelial cells in dilated Fallopian lumens are toxic to embryos. They interfere with embryo development, embryonic implantation, and conception, and increase the rate of abortion [2-4].

Many different methods have been used to treat hydrosalpinx before IVF-ET [5-7], including salpingectomy, salpingostomy, proximal tubal ligation, proximal tubal occlusion, and ultrasound-guided aspiration of hydrosalpinx fluid. All these methods are associated with an improved conception rate and implantation

rate for IVF-ET. However, conventional salpingectomy can damage the blood vessels and nerves in the tubal mesentery, compromise the ovarian blood supply and follicular development, and result in fewer oocytes retrieved [8, 9]. Hydrosalpinx is subject to relapse following salpingostomy [10], leading to treatment failure or the need for additional surgery. Proximal tubal occlusion requires Essure Micro-insert instruments, but Micro-insert abdominal migration may occur in some cases [11]. This technique can also lead to torsion of a large fallopian cyst secondary to retention of fluids in the Fallopian lumen [12]. It can also compress the ipsilateral tubal mesenteric vessels and compromise the ovarian blood supply, resulting in fewer oocytes retrieved. Ultrasound-guided aspiration of hydrosalpinx fluid is less invasive, convenient, and readily accepted, but is associated with recurrent hydrosalpinx [13].

## Surgery for hydrosalpinx before IVF-ET

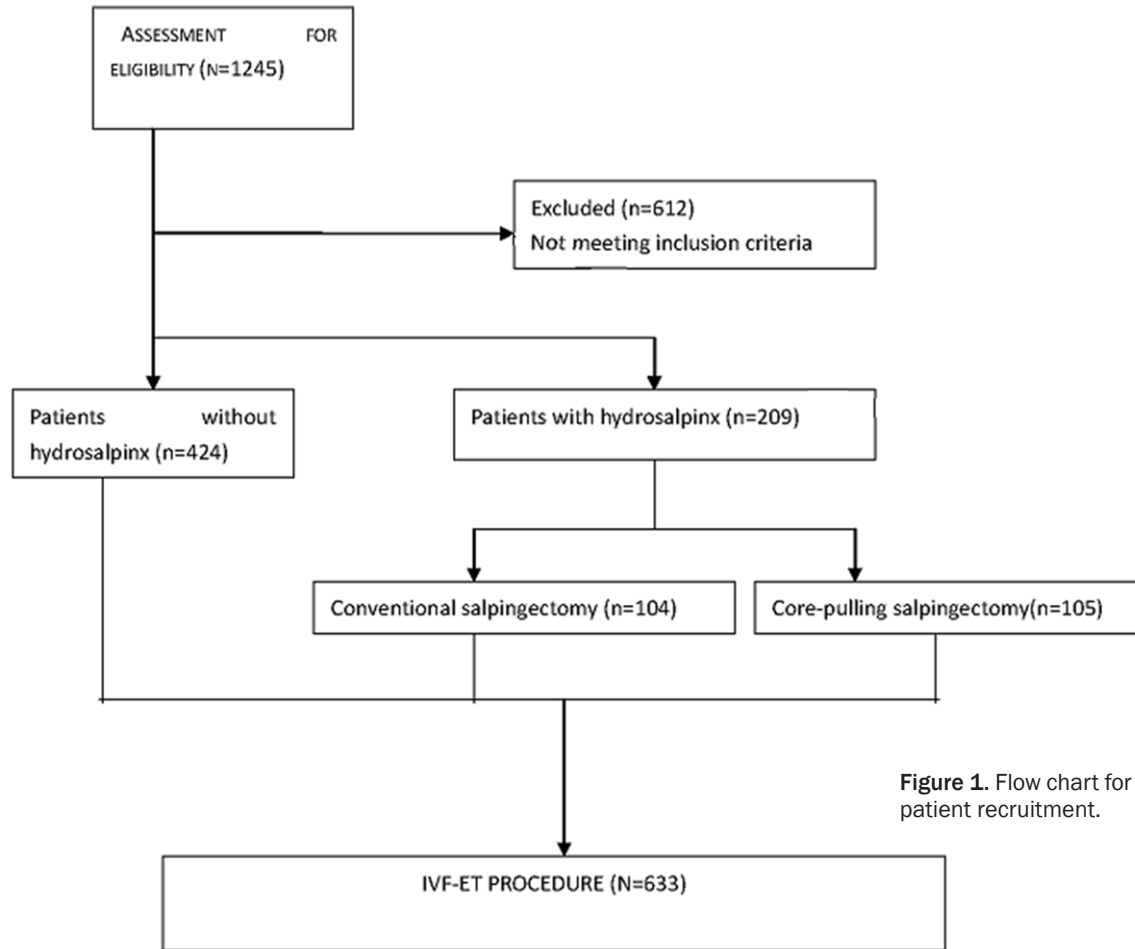


Figure 1. Flow chart for patient recruitment.

The ovarian branch of the uterine artery accounts for 50% of the ovarian blood supply. In 10% of individuals, the ovarian blood supply comes exclusively from the uterine artery. We performed a novel procedure, laparoscopic core-pulling salpingectomy. This surgical procedure treats hydrosalpinx while preserving ovarian blood supply. We compared the results of reproductive efforts with this technique to those in patients receiving conventional salpingectomy, to test the hypothesis that a novel technique that treats hydrosalpinx while preserving ovarian blood supply is superior to conventional salpingectomy, which may disrupt ovarian blood supply.

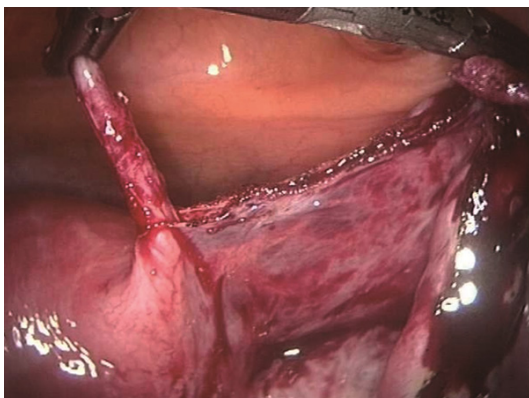
### Materials and methods

#### Study design

This was a prospective cohort study in which women undergoing core-pulling salpingectomy

were compared to two other groups. The study was approved by the ethics committee of Yantai Yuhuangding Hospital. All patients understood the research process and the possible benefits and risks, and signed the informed consent document. Infertile patients seeking treatment for Fallopian tube disorders from July 2010 to December 2012 were enrolled (Figure 1). All received IVF-ET. The participants were women 23 to 44 years old. They were included if they met the following criteria: 1) both ovaries present; 2) follicle-stimulating hormone (FSH) <12 mIU/mL, estradiol <80 pg/mL, and prolactin in the normal range before ovarian stimulation; 3) normal uterine cavity; 4) normal thyroid-stimulating hormone concentration or euthyroid as determined by the investigator; and 5) no current or past diseases affecting the administration of gonadotropins. Couples with male factor infertility or tubal tuberculosis were excluded. Standard diagnostic criteria were used for hydrosalpinx as previously reported [14].

## Surgery for hydrosalpinx before IVF-ET



**Figure 2.** The fallopian tube is seen after core-pulling.

Hydrosalpinx patients were divided into two groups using random numbers. A total 105 patients underwent core-pulling salpingectomy and 104 underwent conventional salpingectomy for hydrosalpinx and subsequent IVF-ET. A second comparison group consisted of 424 women without hydrosalpinx who underwent IVF-ET.

### *Laparoscopic core-pulling salpingectomy*

This procedure was previously described. In brief, normal saline is injected beneath the tubal serosa and the serosa is completely mobilized from the tubal tissue. The visceral peritoneum (serosa) encapsulating the Fallopian tube is dissected from the tubal isthmus proximally to the tubal ampulla distally, exposing the tubal tissue. The tubal tissue is bluntly mobilized and transected at the isthmus (**Figure 2**). The proximal end is cauterized and the distal end dissected. Bleeding on the tubal mesentery is cauterized using a bipolar electrode, or sutured.

### *Laparoscopic conventional salpingectomy*

The mesosalpinx and hydropic tube are dissected free using an ultrasonic knife. The tubal tissue is removed from the isthmus.

### *Postoperative evaluation of ovarian function*

On the morning of the 3rd day of the 3rd postoperative menstrual cycle, fasting blood was obtained for radioimmunoassay (RIA) determination of FSH and estradiol ( $E_2$ ), and vaginal ultrasonography was used to determine the

ovarian volume and the number of antral follicles. The ovarian volume was calculated using the equation: ovarian volume (ml) =  $1/6 \times \pi \times \text{length} \times \text{width} \times \text{thickness}$  ( $\text{cm}^3$ ).

### *IVF-ET*

Patients were administered one tablet of Marvelon daily contraception from the 3rd day (D3) of their menstrual cycle or during withdrawal bleeding until D28. On D21, if ultrasonography detected the absence of large follicles or cysts, patients were administered subcutaneous Decapeptyl every other day starting on 2 days later to achieve serum levels of  $E_2 < 30$  mIU/ml and luteinizing hormone (LH)  $< 3$  mIU/ml. 225 IU. 300 IU Gonadotropin was then administered to induce ovulation. Follicular growth was examined every 2 to 3 days and additional HMG administered when the follicle was 1.4 cm in diameter. When the maximum diameter of the follicle reached 10 to 15 mm, follicular growth was examined once daily. When the diameter of multiple follicles was  $\geq 16$  mm or at least one follicular diameter was  $\geq 18$  mm, 10,000 IU human chorionic gonadotropin (HCG) was injected intramuscularly at 9:00 pm on the evening of the same day, and the  $E_2$  level was determined the next morning in order to calculate the dosage of ovulation-inducing agents. Oocytes were retrieved 36 h after HCG administration and cultured for 4 h, followed by routine in vitro fertilization. On the 3rd day of embryonic culture, embryos were transferred under ultrasonographic guidance. After the transfer, progesterone, HCG, and Progynova were supplemented to support luteal function. Serum HCG levels were determined on the 14th day of embryonic transfer. A serum HCG  $\geq 5.3$  mIU/ml indicated pregnancy. A gestational sac detected by vaginal ultrasonography on the 34th day of embryonic transfer confirmed the pregnancy.

### *Statistical analysis*

Outcome measures of ovarian reserve, ovarian responsiveness, and conception rates were compared to the two untreated groups. Women who underwent core-pulling salpingectomy were compared to those who underwent conventional salpingectomy, and to those without hydrosalpinx or salpingectomy. Continuous variables were expressed as mean  $\pm$  standard

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**Table 1.** Ovarian reserve of each group at baseline

Group	n	Age (yr)	Ovarian volume (ml)	Follicle count	FSH (U/L)	E <sub>2</sub> (pmol/L)
Exposed group	105	32.3 ± 4.1	4.8 ± 0.6	8.8 ± 2.7	6.9 ± 3.5	170.1 ± 28.3
First comparison group	104	31.5 ± 5.3	4.7 ± 0.4	7.9 ± 2.3*	6.6 ± 1.9	171.5 ± 34.2
Second comparison group	424	32.1 ± 5.6	4.8 ± 0.3	8.71 ± 2.5Δ	6.8 ± 2.3	172.4 ± 25.2
F value		0.685	2.976	4.813	0.409	0.308
P value		0.505	0.052	0.008	0.664	0.735

\*Statistically significant compared to exposed group  $P < 0.05$ . Δ, Statistically significant compared to first comparison group  $P < 0.05$ .

deviation, and were compared using analysis of variance (ANOVA) and the Student-Newman-Keuls (SNK) q-test for post hoc comparisons. Categorical data were compared using the  $\chi^2$  test. All patients meeting inclusion criteria during the study period were included; no a priori sample size estimation was performed. All analyses were performed with SPSS13.0 (SPSS, Chicago, IL, USA).

### Results

#### *General patient characteristics*

Of the 633 patients who had IVF-ET, 105 with hydrosalpinx underwent core-pulling salpingectomy, 104 with hydrosalpinx had conventional salpingectomy, and 424 did not have hydrosalpinx. The average patient age was 30.1 years. The duration of infertility ranged from 2 to 12 years. There were no significant differences in age, ovarian volume, basal FSH, or E<sub>2</sub> among the three groups (Table 1).

#### *Ovarian reserve*

The follicle count on D3 in women who underwent core-pulling salpingectomy was significantly higher than in women who had conventional salpingectomy, but not different from women who did not have hydrosalpinx (Table 1).

#### *Ovarian responsiveness and IVF-ET outcome (Table 2)*

*Endocrine profile during the IVF-ET cycle:* All 105 patients who had core-pulling salpingectomy received IVF-ET. The D2 serum FSH and E<sub>2</sub> levels were not significantly different from patients who had conventional salpingectomy, or those who did not have hydrosalpinx. The E<sub>2</sub>

level on the day HCG was administered was higher in women who had core-pulling salpingectomy compared to those who had conventional salpingectomy, but also no different from women without hydrosalpinx.

*Number of oocytes retrieved and dosage of ovulation-inducing agents:* The number of oocytes retrieved was higher with core-pulling compared to conventional salpingectomy, but not different from women without hydrosalpinx. Patients who had core-pulling salpingectomy required lower doses of ovulation-inducing agents than those who had conventional salpingectomy, but the dose was not different from those without hydrosalpinx.

#### *Clinical conception rate*

Patients with core-pulling salpingectomy achieved a conception rate of 61.9% following IVF-ET, which was not significantly different from that of patients undergoing conventional treatment (58.6%) or control treatment (56.1%).

### Discussion

#### *Effects of hydrosalpinx on pregnancy*

Hydrosalpinx results from acute and chronic pelvic inflammation. The presence of hydrosalpinx prevents ova from fusing with sperm, resulting in infertility. Inflammatory agents present in the hydrosalpinx fluid are also toxic to embryos. Chronic hydrosalpinx is likely to compress the ovarian blood supply and compromise the ovarian functional reserve. However, most patients with hydrosalpinx can become pregnant with the assistance of IVF-ET. It is generally accepted that hydrosalpinx adversely affects IVF-ET outcomes unless the hydrosalpinx is surgically treated.

## Surgery for hydrosalpinx before IVF-ET

**Table 2.** Profiles of patients on IVF-ET

Group	n	D <sub>2</sub> FSH (U/L)	FSH (U/L)	D <sub>2</sub> E <sub>2</sub> (pmol/L)	E <sub>2</sub> on HCG day (pmol/L)	N of oocytes retrieved	Dosage of Gn (IU)	Pregnancy outcome			
								Pregnancy (%)	Ongoing Pregnancy (%)	Intrauterine Pregnancy (%)	Multiple Pregnancy (%)
Exposed group	105	7.3 ± 2.8	89.5 ± 19.1	12 235 ± 2 085	14.1 ± 6.0	2350.1 ± 450.5	61.9	53.3	61	9.5	
First comparison group	104	8.3 ± 2.5*	95.3 ± 25.2	10 201 ± 1332*	10.2 ± 5.3*	2850.4 ± 600.3*	58.6	50.9	57.7	9.6	
Second comparison group	424	7.2 ± 2.9Δ	94.6 ± 20.3	12 264 ± 1789Δ	13.7 ± 6.5Δ	2290.6 ± 375.4	56.1	49.3	55.0	10.1	
<i>F/χ<sup>2</sup> value</i>		6.420	2.845	83.655	14.485	70.568	0.886	0.835	0.778	0.756	
<i>P value</i>		0.002	0.059	<0.001	<0.001	<0.001	0.642	0.554	0.545	0.656	

\*Statistically significant compared to exposed group,  $P < 0.05$ . Δ, Statistically significant compared to first comparison group,  $P < 0.05$ .

## Surgery for hydrosalpinx before IVF-ET

Hydrosalpinx influences the success rate of IVF-ET through several mechanisms [2-4]. First, reflux of hydrosalpinx fluids into the uterine cavity can erode embryo attachment and result in hydrohystera. This interferes with the contact of an embryo with the endometrial membrane. Second, hydrosalpinx fluid may contain microbes, tissue debris, lymphocytes, and toxic agents that can induce the release of cytokines, prostaglandin, leukocytic chemokines, and other inflammatory factors. These compounds can enter the endometrial cavity and have a direct or indirect impact on the capillary and lymphatic vessels of the endometrial membrane and on embryonic implantation [15, 16]. Zhong *et al.* [17] reported that patients with hydrosalpinx presented with less  $\alpha_v\beta_3$  on their endometrial membranes than control patients, which would compromise endometrial capacity. Sachdev *et al.* [18] reported that mouse embryos cultured in hydrosalpinx fluids had retardation of blastocyst formation in a dose-dependent manner. Hydrosalpinx fluids have a chemical composition similar to serum, except for a lower concentration of calcium, potassium, glucose, and lactic acid. These different concentrations do not favor the development of mouse embryos into a blastocyst [18]. The lack of active oxidants in hydrosalpinx fluids also compromises blastocyst formation [19].

### *Pretreatment of hydrosalpinx prior to IVF-ET*

Because hydrosalpinx adversely affects the success of IVF-ET, treatment is recommended for patients with hydrosalpinx prior to IVF-ET in order to improve outcomes. We designed the core-pulling salpingectomy in order to treat the hydrosalpinx and maximize preservation of ovarian blood supply and ovarian function [15].

Borell *et al.* [20] reported that ovarian blood supply had a substantial variation in its distribution. Regardless of the ovarian blood supply, the surgical procedure selected should minimize any damage to the ovarian mesenteric blood vessels. In contrast to conventional salpingectomy, laparoscopic core-pulling salpingectomy better preserved the ovarian mesenteric blood vessels, the blood supply to the ovary, and the Fallopian branch of the uterine artery. Preservation of the blood supply is needed for optimal ovarian function and ovulation induction with IVF.

### *Effect of core-pulling salpingectomy on ovarian reserve, ovarian function, and IVF-ET outcomes*

The effects of salpingectomy on ovarian function remain unclear and are controversial. It has been reported that ipsilateral ovaries after salpingectomy are less functional, although some reports of ovarian responsiveness to stimuli did not show significant variation before and after salpingectomy. Rabbits receiving microsurgical tubal fimbriectomy and ovarian-fimbrial vascular anastomosis show fewer ovulation cycles after surgery.

The mechanism through which salpingectomy adversely affects ovarian responsiveness is unclear. No previous study has compared the effects of various surgical procedures on ovarian function. The antral follicle number, endocrine profile, total dosage of ovulation-inducing agents required for ovarian stimulation,  $E_2$  level on the day of HCG administration, and the number of oocytes retrieved following core-pulling salpingectomy were significantly higher compared to conventional salpingectomy, but not different from women without hydrosalpinx. These findings demonstrate the significant difference in outcome after core-pulling, indicating that this procedure has less impact on ovarian reserve and responsiveness. These findings are likely attributable to better preservation of ovarian blood supply.

Patients who underwent core-pulling salpingectomy received IVF-ET, and achieved increased clinical conception rates compared to conventional salpingectomy, but the difference was not statistically significant.

### **Conclusions**

These data suggest that treatment of hydrosalpinx with laparoscopic core-pulling salpingectomy before IVF-ET improves ovarian reserve and responsiveness, and may improve clinical conception rates compared to conventional salpingectomy. A well-powered, randomized controlled trial is needed to confirm these findings.

### **Acknowledgements**

My sincere thanks to all those working staff who have lent me hands in the course of my work. Without their help, it would have been much harder to finish this study. We thank



LetPub (www.letpub.com) for its assistance with the manuscript preparation.

### Disclosure of conflict of interest

None.

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