Conception rates after fluoroscopy-guided fallopian tubal cannulation: an alternative to *in vitro* fertilization for patients with tubal occlusion

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Abstract

Objective: Previous studies show good technical success rates for fallopian tube recanalization. Scarce literature exists regarding advance techniques currently used by interventional radiologists during fallopian tube recanalization procedures. This study investigates the level of intervention and tubal patency and its association with technical success and associated pregnancy outcomes.

Methods: We retrospectively evaluated fallopian tube recanalization procedures performed at a single center in a 24-year period. A total of 160 couples undergoing a basic infertility evaluation were included. Hysterosalpingography with high pressure contrast injection followed by selective contrast, guidewire catheterization at the tubal ostium, and/or microcatheter/microwire recanalization were performed. Comparisons of the tubal fertilization rate by relevant characteristics were tested for statistical significance with *t* tests for continuous data or with Pearson chi-square tests for categorical data.

Results: Technical success rate was 94% (319 of 341 tubes). High pressure contrast injection alone (184 of 341, 54%), selective catheterization (40%), and microcatheter/microwire (6%) interventions yielded technical success rates of 98%, 90%, and 73%, respectively. The overall rate of conception was 35% (17 of 48).

Conclusion: Current techniques of fallopian tube recanalization offer a desirable and safe option with high technical success for patients seeking treatment for infertility due to proximal fallopian tube obstruction.

Keywords: fallopian, infertility, recanalization

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Introduction

Female infertility is a common problem typically addressed by gynecologists. The Centers for Disease Control estimates that 12% of reproductive-age women in the United States have impaired fecundity of which 25% of cases encompass factors related to the fallopian tubes.[1] Previous studies have demonstrated that the frequency of proximal obstruction at the uterotubal junction range from 2% to 25%. A wide range of proposed etiologies causing proximal tubal occlusions includes tubal spasms, occlusions by intraluminal debris, endometriosis, adhesions, and fibrosis.[2] A common treatment for tubal infertility is *in vitro* fertilization (IVF). However, IVF is a costly and sometimes undesirable treatment option for women because of either moral or other personal objections.

The role of radiologists in the evaluation and intervention of proximal tubal occlusion(s) in female patients with infertility has been explored for the

past several decades. Several studies have demonstrated the feasibility and safety of fallopian tube recanalization (FTR).[3–6] The dynamic and evolving field of interventional radiology (IR) correlates well with the advancement in techniques of FTR. The use of selective tubal catherization first proposed by Rosch and Thurmond has now progressed to the usage of a coaxial microcatheter and microwire system for recanalization in many patients. This study aims to describe recent updates in technique while exploring how different levels of fallopian tube intervention may be associated with technical and clinical outcomes among a large data set of female patients with infertility.

Materials and methods

Study design
A total of 160 women undergoing a basic infertility evaluation (BIE) at a reproductive endocrinology and infertility (REI) private practice were referred to a university medical center IR department for suspected tubal occlusion. All patients who underwent the FTR procedure at Rush University Medical Center between June 1993 and January 2018 were selected for this study. Clinical follow-up data were available for retrospective review from the REI practice for 73 couples whose FTR procedure took place between January 2013 and January 2018. Deidentified clinical data were gathered from paper charts stored inside the REI clinic site. Research protocol was approved by the institutional review board prior to the start of the study, and formal consent was not required for this type of study.

Inclusion/exclusion criteria
Patient selection for technical and clinical analysis is demonstrated as follows. For technical outcome analysis, any patients with a documented proximal tube occlusion of one or both fallopian tubes and at least one patent tube after the procedure were included. For clinical outcome analysis, the following inclusion criteria were applied: (1) patients with no contraindications to pregnancy and who are actively pursuing pregnancy and (2) patients who were referred to IR for suspected tubal occlusion. Patients were excluded from clinical outcome analysis if (1) male sperm infertility factor precluded using conception methods that use tubal conception such as timed

intercourse (IC) and/or intrauterine insemination (IUI), (2) they were lost to follow-up after the procedure such that BIE was not completed, (3) patients received IVF after procedure without attempting a tubal conception method (IC or IUI) for any reason, or (4) patients with repeat procedure within 12 months of initial FTR.

The women in the clinical analysis used a variety of supervised artificial reproductive technology after FTR. Many, but not all, cycles using IC or IUI as the method of conception included the use of ovulatory or luteal support. The specific method of conception attempted was not controlled for in this retrospective study. Patients were followed up for clinical outcomes until 6 months past the procedure study period ended. In the case of conception and viable pregnancy, they were followed up until 20 weeks gestation at which time their care was transferred to an obstetrician, as is customary in this REI practice.

Fluoroscopy-guided tubal cannulation
Procedural steps for FTR are described as follow (Figure 1). The patient was positioned on the table in the dorsal lithotomy position. All patients were outpatients, and most had conscious sedation for the procedure, with a few undergoing no sedation. A sterile speculum was advanced into the vaginal canal. Once the cervical os was visualized, Betadine silk gauze was used to sterilize the cervical os. One of the several balloon-tip catheters (i.e. 7 French) was advanced through the cervical os into the uterine canal with subsequent balloon inflation to create a backflow seal. Hysterosalpingography (HSG) with high pressure contrast injection was then performed to evaluate the appearance of the intrauterine cavity and the patency of fallopian tubes. If tubal obstruction persisted despite contrast injection (indicated by a lack of free contrast spillage into the peritoneum), a 4- or 5-French Berenstein catheter and 0.035-in hydrophilic guidewire were used to attempt recanalization of the obstructed tubes. If selective contrast and guidewire catheterization at the tubal ostium failed, the hydrophilic guidewire was then removed and advanced techniques with microcatheter and microguidewires were used with recanalization to the distal end of the tubes. Microcatheter systems included 2.8-French microcatheters and
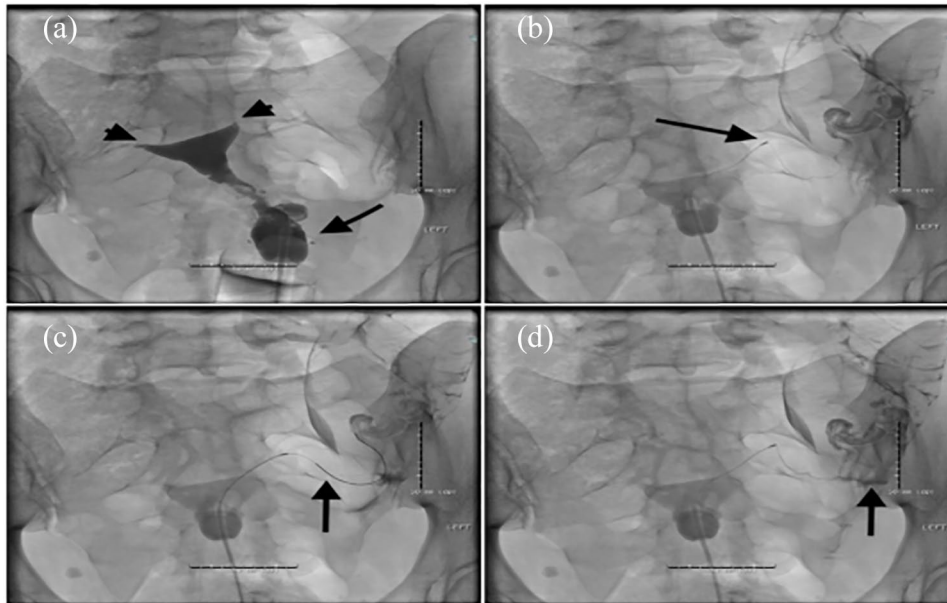
Figure 1. 45-year old woman with bilateral proximal tubal obstructions. (a) The arrow indicates a 9-French balloon retention catheter which was advanced into the cervical os. Retention balloon was insufflated in the endocervical canal. Following high pressure hysterosalpingogram, a lack of free contrast flow indicates obstruction of both fallopian tubes (shown by arrowheads). (b) An angled catheter with a 0.035-in hydrophilic guidewire was used to select for the left fallopian tube. (c) Advanced technique with a 3-French microcatheter and 0.018-in microwire (indicated by an arrow) was used to recanalize the left fallopian tube up to the interstitial portion. (d) Selective contrast injection demonstrates patency of the left fallopian tube with spillage of contrast into the peritoneal cavity.
Right tube cannulated in a similar fashion.

the microwires used usually included 0.018- or 0.014-in wires. Successful recanalization was achieved once free spillage into peritoneum was demonstrated upon contrast injection. All patients were discharged home within 30–60 min postprocedure.

Statistical analysis

Statistical calculations were performed with use of SPSS version 25.0 software.

Comparisons of the tubal fertilization rate by relevant characteristics were tested for statistical significance with Student's t tests of independent samples for continuous data [body mass index (BMI), age] or with Pearson chi-square tests for the categorical data. For continuous data, Levene's test for equality of variance was performed and found to be normally distributed. Multivariable analysis and odds ratios with relevant patient characteristics were also calculated. A value of $p \leqslant 0.05$ was considered significant.

Results

Demographics

Nineteen patients were excluded from the clinical outcome analysis because of a lack of complete BIE or follow-up after FTR. Eight patients were excluded from clinical outcome analysis because they did not attempt a tubal form of conception. Forty-six patients were included in the clinical outcome analysis (Figure 2). The patients in the clinical assessment were found to have a complete range of infertility causes in addition to tubal factors including other structural abnormalities, ovulatory or low reserve, male factors, and lack of partners (Table 1). These demographics are compared between women who achieved tubal fertilization ($n = 17$) and those who did not ($n = 31$) after intervention. There was no significant difference for the following variables relative to fertilization: age, BMI, history of abortion, and primary infertility. There were 35 cases of primary infertility and 13 cases of secondary infertility in the clinical cohort. Of the cases with primary infertility, 11 (31%) achieved fertilization compared with 6
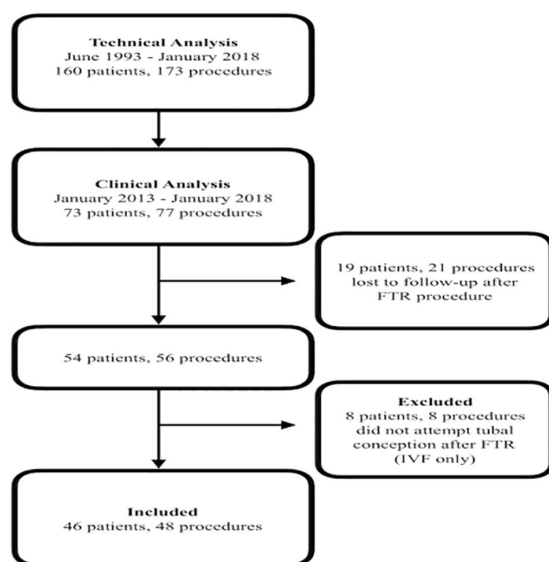
Figure 2. Flowchart illustrating the process of patient exclusion for clinical data analysis. Among 160 patients, 46 patients were included for clinical outcome analysis.

(46%) with secondary infertility, which was not significant. Many patients had more than one identified factor potentially contributing to their infertility. Significantly more women who achieved tubal fertilization had at least one other structural infertility factor present (6 of 17 *versus* 3 of 31, $p = 0.030$). A measure of significance was unable to be calculated for those demographics which were found infrequently as denoted in Table 1 as nonapplicable.

Laterality
Twenty-two of the cases presented with unilateral obstruction and were found to have a postintervention conception rate of 41% (9 of 22). Sixteen cases presented with bilateral obstruction and were found to have a postintervention conception rate of 19% (3 of 16). Two cases presented with no obstruction, and six cases did not have records of a preprocedural HSG. Owing to data limitations, significance between laterality on fertilization was not calculated.

Method of conception
Fifteen women used a timed IC and natural cycle method, which resulted in five successful tubal fertilizations. One of the three women who were supervised for a combination of timed IC and IUI cycles after FTR resulted in a viable pregnancy.

Both these methods had a 33% conception rate. About 10 of the 17 clinically successful cases were conceived by IUI only and 1 by a combination of timed IC and IUI cycles. One of these clinically successful cases resulted in tubal fertilization and viable pregnancy by the IUI method after unsuccessful cycles of IVF. Four women used donor sperm in addition to IUI because of either lacking a male partner or insufficient partner sperm, none of whom achieved tubal fertilization after technically successful FTR.

Patency and conception
A total of 173 procedures were performed on 160 patients [mean age, 37 years (range: 24–48, SD: 5.7)]; bilateral obstruction 55.6% (89 of 160), unilateral obstruction 41.9% (67 of 160), and no obstruction 2.5% (4 of 160) were identified via preprocedural HSG. Bilateral patency was achieved in 86% (137 of 160) of patients and unilateral patency in 13% (20 of 160; Table 2). Technical success rate was 94% (319 of 341 tubes). High pressure contrast injection alone (184 of 341, 54%), selective catheterization (135 of 341, 40%), and microcatheter/microwire (22 of 341, 6%) interventions yielded technical success rates of 98% (181 of 184), 90% (122 of 135), and 73% (16 of 22), respectively. One distal end perforation was noted. Twelve patients had more than one FTR procedure performed during the study period (11 of 12 had 2 procedures and 1 of 12 had 3 procedures). From a technical standpoint, most of the patients who underwent two procedures (9 of 11 patients) achieved successful bilateral tubal recanalization after each procedure. For the other two patients who underwent two procedures, one patient achieved partial success (i.e. unilateral recanalization) after the first case with subsequent bilateral success in the second with vice versa results for the other patient. The one patient with three FTR procedures had unilateral success in the first case followed by bilateral success in the subsequent two cases. From a clinical standpoint, only three patients with repeat procedures were included in the clinical analysis, all of which achieved tubal conception after the second procedure. One of these conceptions was an ectopic pregnancy.

Both successful and unsuccessful clinical cases used all three levels of the intervention. Conception rates of cases undergoing each level of interventions are as follows: HSG 21% (5 of 24 cases),

Table 1. Patient demographics at time of procedure, *n* (%) unless otherwise specified.

	Tubal fertilization	Without tubal fertilization	Total cases	*p* value
N (%)	17 (35.4)	31 (64.6)	48	–
Mean age (SD)	37 (3.7)	39 (5.4)	38	0.244
Mean BMI (SD)	28 (7.5)	28 (7.0)	28	0.869
Primary infertility	11 (64.7)	24 (77.4)	35 (72.9)	0.343
Prior abortion	10 (58.8)	22 (71.0)	32 (66.7)	0.393
Infertility factors present (nonexclusionary)				***p* value**
Tubal only	5 (29.4)	7 (22.6)	12 (25.0)	0.601
Other structural	6 (35.3)	3 (9.7)	9 (18.8)	0.030
Ovulatory/low reserve	8 (47.1)	17 (54.8)	25 (52.1)	0.606
Male factors	5 (29.4)	9 (29.0)	14 (29.2)	0.978
Lacking partner	1 (5.9)	3 (9.7)	4 (8.3)	n/a
Obstruction noted at time of preprocedural HSG[a]				***p* value**
Unilateral	9	13	22	n/a
Bilateral	3	13	16	
None	1	1	2	

BMI, body mass index; HSG, hysterosalpingography; SD, standard deviation.
[a]Eight cases did not have history of preprocedural HSG.

Table 2. Technical outcomes, *n* (%).

	No tubes patent		One tube patent		Two tubes patent[a]	
Preprocedure	89 (55.6)		67 (41.9)		4 (2.5)	
Postprocedure	Bilateral patency	72 (80.9)	Bilateral patency	61 (91.0)	Bilateral patency	4 (100)
	Unilateral patency	14 (15.7)	Unilateral patency	6 (9.0)	Unilateral patency	0 (0.0)
	No patency	3 (3.4)	No patency	0 (0.0)	No patency	0 (0.0)

FTC, fallopian tube cannulation; HSG, hysterosalpingography.
[a]Despite these four patients having a recorded preprocedural HSG with bilateral patency, FTC was pursued in the setting of continued infertility and/or additional imaging (i.e. ultrasound) that demonstrated possible fallopian tube obstruction.

selective catheterization 39% (7 of 18 cases), and microcatheter/microwire 67% (4 of 6 cases).

Overall rate of tubal conception was 35% (17 of 48). Median time from the FTR procedure date to the first positive serum beta-HCG was 125 days (approximately 4 months) with a range of 13–843 days (interquartile range 126.5 days). Fifty-three percent (9 of 17) of tubal fertilizations developed into viable pregnancies with a noted positive fetal heart tracing and intrauterine location. Of those, six pregnancies (67% of viable pregnancies, 12.5% of total clinical cases) successfully reached the second trimester and had their obstetric care

transferred out of the REI practice to an obstetrician, as is standard in this practice.

Safety

Two cases resulted in pregnancies of abnormal location after FTR requiring medical management. One of these ectopic pregnancies was conceived by IUI (tubal fertilization), the other by IVF. No serious adverse events were noted in this case series.

Discussion

Current techniques of fluoroscopic-guided FTR, including the use of a microcatheter and microwire system, demonstrate high efficacy in achieving tubal patency. This high technical throughput along with the lower associated cost, morbidity, and risks supports its viability as a first-line intervention for those with identifiable proximal tubal occlusion.[4,7,8] Attention to alternatives to fluoroscopic-guided FTR, including the development of endoscopic intervention such as falloscopy/hysteroscopy/laparoscopy, is important to consider when devising an optimal treatment plan. Proponents of transuterine falloscopy and hysteroscopy argue for the ability to obtain direct visualization and characterization of endotubal disease while delivering therapeutic interventions. These techniques demonstrate potential diagnostic and therapeutic power, but technical shortcomings including physician expertise, imaging clarity affected by the proximity of the bright light near endoluminal tissue, and the impediment of successful falloposcopy insertion barred its routine use in clinical practice at this time.[6] The use of laparoscope intervention in conjunction with hysteroscopy has also been described. The ability to ablate peritubal adhesions laparoscopically while evaluating for patency of tubes via free dye spillage from the hysteroscope provides the added benefit of extraluminal intervention.[9] However, careful patient selection is necessary to properly identify those who have clinically significant adhesions that would warrant a more invasive laparoscopic procedure. Evaluation for patency of the tube can also be achieved fluoroscopically without succumbing patients to the general risks associated with surgery.

Although the number of patent tubes in our study following FTR does appear to have a positive correlation with pregnancy outcomes, many other cofactors were investigated to determine their impact on clinical outcomes. Some of these factors include the age of the patient, prior gynecology intervention, primary *versus* secondary infertility, and etiologies of infertility other than tubal factors.[10] In this study, secondary infertility cases appear to demonstrate higher spontaneous conception rates compared with those with primary infertility. This finding is explained by the notion that women who have had pregnancies in the past tend to have a higher incidence of fallopian tube occlusion and tend to have a higher chance of pregnancy once the underlying cause of infertility is addressed compared with their primary infertility counterparts.[11] Further investigation is warranted with a larger sample size as this difference was not significant in our study. The only demographic factor found to be significantly more common in patients who achieved tubal fertilization was having another structural infertility factor identified, such as intracavitary lesions. This finding is hard to explain as information on how or whether the other structural abnormality was treated was not collected through this study. Although the clinical data for our patients with repeated FTR procedures were small, multiple FTR procedures for one patient did not impact her ability to achieve successful conception. Significance, however, was not able to be evaluated. Investigation into other variables that may significantly impact the clinical success following FTR will provide insight into which patients would be the best candidates for this procedure.

Our overall conception rate was 35%, which falls among pregnancy rates reported in the literature following fluoroscopic-guided FTR varying from 12.8% to 51%.[7,12–15] These rates are also comparable to the data from endoscopic studies. In Tanaka and colleagues, pregnancy rates were reported at 34.2%. Technically speaking, more than half of the fallopian tubes required only high pressure hysterosalpingogram for tubal recanalization. This is unsurprising as chromopertubation of the tubes as a means of rejuvenating tubal function has long been demonstrated to show high technical success. In our study, there were more clinically successful cases in those that required higher levels of intervention including selective catherization and microcatheter/microwire intervention. However, in multivariate analysis where other suspected causes of infertility were controlled for, an increasing level of intervention was negatively, but not significantly, associated with conception. Further investigation

should be pursued to determine if patency achieved via HSG alone (chromopertubation effect) is a permanent or transient solution as well as how that effect is different from the more invasive intervention levels used in many FTR procedures. One study found that two consecutive HSGs following each other by 2 weeks compared with FTR have similar outcomes when the second HSG shows presence of tubal patency.[14] Nevertheless, we were able to show that even patients who required more invasive techniques of FTR achieved successful outcomes, often making this minimally invasive outpatient procedure a desirable option for many patients.

Limitations of this study include the relatively smaller sample size available for clinical evaluation. This was in part due to what was available through paper charting and in the volume of this particular practice. The clinical data set is comparable to sample sizes in previous studies.[3–8,10–12] Furthermore, reporting of clinical outcomes of FTR across studies appears to be variable in that there are a staggering array of numerators and denominators used in the calculation of pregnancy rates. This may create variability in approaches to data analysis. Future meta-analysis that stratifies and compares studies that have similar study design and determinants of outcome variables may be warranted. The authors do not believe that the length of clinical follow-up (at maximum to the second trimester) is a significant limitation of this article as the outcomes beyond this point are unlikely to be affected by the health of the fallopian tubes. Future studies including head-on comparisons between the different methods of FTR are warranted.

Conclusion

The growing arsenal of minimally invasive FTR procedures including fluoroscopic and endoscopic guided interventions are promising for patients battling infertility due to fallopian tube obstruction. Careful patient selection is necessary to determine which combination of procedures is necessary to achieve optimal clinical success for any given patient. With comparable clinical and technical success rates to other minimally invasive techniques, fluoroscopic-guided FTR continues to be a low-risk and cost-effective option for these patients.

Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. All authors have met the criteria for authorship and have participated sufficiently in the work to take responsibility for it.

The authors whose names are listed certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this article. The authors have no relevant disclosures. All individuals have given their permission for inclusion in this article and for publication.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was conducted with institutional review board approval and complied with the Health Insurance Portability and Accountability Act.

Informed consent

For this type of study, formal consent is not required.

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