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The outcomes of pregnancies after laparoscopic surgeries for pathologic changes on distal oviduct: A systematic review and meta-analysis[1]

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ABSTRACT

Objective: This systematic review and meta-analysis were aimed to summarize the body of evidence on the prognosis after laparoscopic surgeries for pathological conditions on distal oviducts, then, furthermore, to evaluate prognostic factors for pregnancy outcomes.

Methods: We conducted a systematic review and meta-analysis to summarize the body of evidence on this topic, with the review question formulated as "what is the prognosis after the laparoscopic fimbrioplasty, salpingostomy, or salpingoneostomy for patients with pathologic conditions on the distal oviducts." We searched Medline and EMBASE on June 1st, 2020. Two investigators (HH and ZY) independently screened the references of all retrieved records for potentially eligible studies by firstly, through titles and abstract, and then full-text. A study would be included if it was a primary study reporting pregnancy outcomes of patients after laparascopic surgery. A meta-analysis of the rates of pregnancy, ectopic pregnancy, live birth, and miscarriage was performed using a random effect model.

Results: We identified 3861 records and included 21 reports with 2473 participants. The pooled estimate for the pregnancy rate was 35.1% (95% CI: 30.7%–39.7%, $I^2 = 78\%$, low certainty). The pooled estimates for the live birth rate, ectopic pregnancy rate, and miscarriage were 24.4% (95% CI: 20.2%–28.8%, $I^2 = 58\%$; 1154 participants; low certainty), 6.2% (95% CI: 4.4%–8.2%, $I^2 = 61\%$; 2363 participants; low certainty), and 4.6% (95% CI: 2.8%–6.9%, $I^2 = 10\%$; 544 participants; low certainty). Our analyses suggested that the more damaged tubal was associated with a decreased pregnancy rate, and patients with moderate or severe adhesion had lower pregnancy rates compared with patients with mild pelvic adhesion.

Conclusion: We estimated the pregnancy rate, ectopic pregnancy rate, and miscarriage rate of patients with distal tubal pathology after the laparoscopic fimbrioplasty or salpingostomy. Low certainty evidence suggested that laparoscopic surgery can restore the tubal function and cure infertility and should be considered as an alternative to *in vitro* fertilization. Tubal damage stage and adhesion are associated with worse pregnancy outcomes.

1. Introduction

The pathologic conditions on distal fallopian tube include hydrosalpinxes and fimbrial phimosis. Hydrosalpinx refers to a condition that the tube is completely occluded, which is characterized by a distally blocked fallopian tube filled with fluid while fimbrial phimosis refers to a narrow phimotic tubal opening resulted from fimbrial agglutinative adhesions. Tubal diseases account for 25%–35% of female infertilities, of

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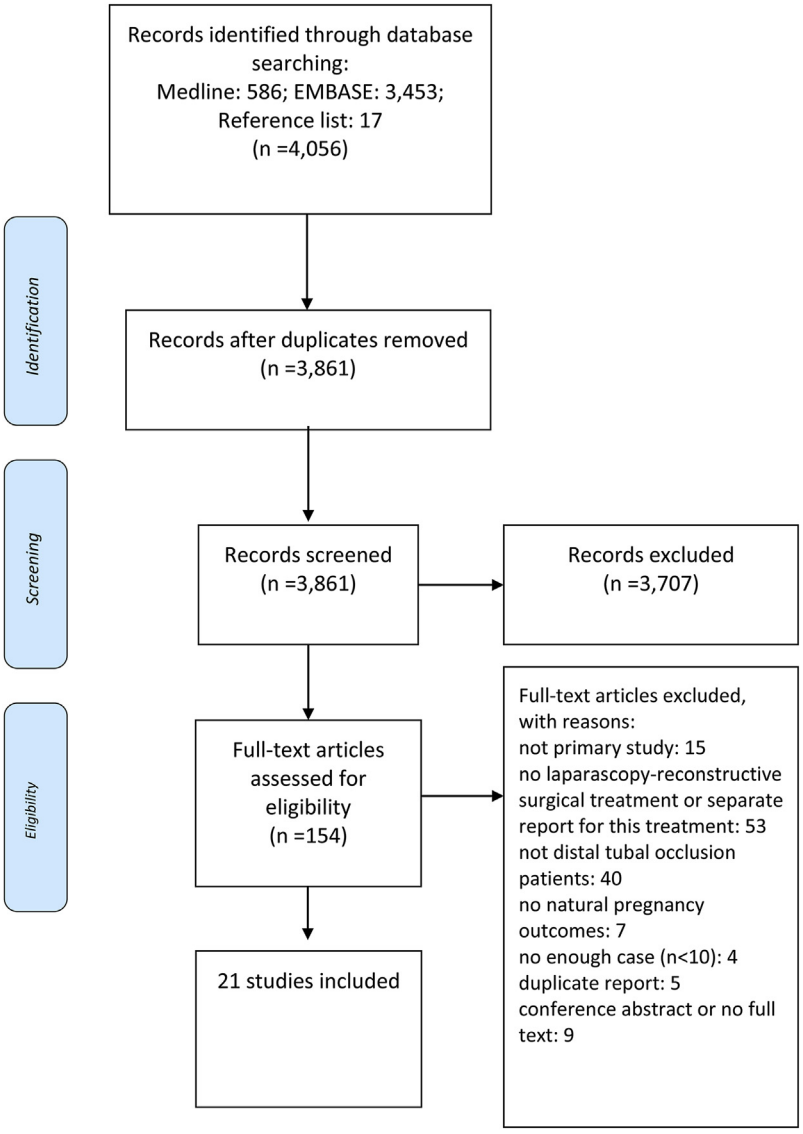

Fig. 1. Flow Diagram for systematic review.

which the pathologic conditions on distal fallopian tube is a major part. Empirical studies suggested that pathologic conditions on distal fallopian tube decrease the rate of fertilized-egg implantation and pregnancy rate. Patients with distal-tubal-problem related infertility can choose assisted reproductive technology. However, surgical correction can also restore the tubal structure or function and cure infertility. Therefore, it is an alternative to assisted reproductive technology. Laparoscopic fimbrioplasty is an operation to treat phimosis on the incompletely obstructed distal part of the tube, whereas salpingostomy and salpingoneostomy are the surgical techniques to restore the tubal function via opening the distally occluded end.

Surgical correction may be a cost-effective alternative to assisted reproductive technology, such as *in vitro* fertilization (IVF) [1]. Healthcare providers should understand the prognosis after surgeries, the time to pregnancy after treatment, and prognostic factors, cost of treatment, and patient preferences to make an informed decision [2]. There have been multiple reports on the effects of the surgical correction on pregnancy outcomes [3–6]. However, previous reports were mostly on the results from a single institution, and the pregnancy outcomes also depend on the surgeons' expertise and experience or the technical standards of local institutions. Moreover, treatment in previous reports may not represent the state of arts. Along with the evolvement of technology, assisted reproductive technology gains popularity. It is relevant to consider the latest evidence on laparoscopic surgeries in the current setting [7]. Furthermore, it is crucial to review and analyze all pregnancy-related outcomes including intrauterine pregnancy, ectopic pregnancy, miscarriage, and live birth. Since the systematic review method is effective in summarizing the body of evidence on prognosis, this systematic review and meta-analysis aimed to summarize the body of evidence on the prognosis after laparoscopic surgery treatment of the pathologic conditions in the distal fallopian tube, and to evaluate prognosis factors for pregnancy outcomes.

2. Methods

We conducted this systematic review and meta-analysis to answer the research question "what is the prognosis after the laparoscopic fimbrioplasty or salpingostomy for patients with pathologic conditions on the distal oviducts." The systematic review with meta-analysis was registered on PROSPERO (CRD42018084496). Ethical approval was not applicable because all the work was developed using published data.

2.1. Study selection and outcome measures

A team worked out the inclusion and exclusion criteria to identify eligible studies for the research question. Based on the criteria, we

Table 1
Key characteristics of included studies.

Study ID/ Country	Study design, Study time and sampling strategy	Patient population	Disease severity (number, %)	Other disease history (number, %)	Surgery and related interventions	Follow up
Audebert 2014 France	Prospective, case series From June 1988 to December 2000 Consecutive sampling	Patient population: 434 patients with tubal infertility Tubes affected: patients for whom both tubes were blocked or who had only one tube blocked were included; patients with a unilateral hydrosalpinx and a contralateral normal tube were not included), no patent tube before surgery Age: mean of 30.5; ranging from 22 to 37 Primary or secondary infertility: 244 primary, and 190 secondary Duration of infertility: 284 < 4 years, and 150 > 4 years	Tubal stage Stage 1: 100, 23.0% Stage 2: 146, 33.6% Stage 3: 123, 28.3% Stage 4: 65, 15.0%	Abdominal adhesions: 407; 93.8% Childbirth history: 65, 15.0% Intrauterine pregnancy: 113, 26.0% Ectopic pregnancy:38, 8.8% Tubal surgery: 40, 9.2% Endometriosis: 28, 6.5% Smoking history: 228, 52.5% Chlamydial serology positive: 321, 74.0% Proximal occlusion, natural miscarriage, medical abortion and procedural abortion, abdominal and pelvic surgery: not reported	Fimbrioplasty and salpingoneostomy Adhesiolysis was performed first, when necessary No IVF	5 years of follow up No patient was lost for follow-up during the first 6 months. Just over one-quarter (27.9%) were lost after 1 year, 32.0% after 3 years, and 35.0% after 5 years
Bontis 1996 Greece	Retrospective, case series From January 1980 and December 1993 Consecutive sampling	Patient population: 99 patients with various types of tubal infertility Tubes affected: not reported Age: not reported Primary or secondary infertility: not reported Duration of infertility: mean of 42 (Standard deviation of 27 months) for all the 763 patients	Partial distal tubal occlusion: 28 with mild disease 32 with severe disease Complete distal tubal occlusion (tubal stage) Stage 1: 23, 59.0% Stage 2: 14, 35.9% Stage 3: 2, 5.1% Stage 4: 0, 0%	not reported	Fimbrioplasty and salpingostomy Adhesiolysis was performed first, when necessary No IVF	All participants were followed up until July 1994
Canis 1991 France	Retrospective, case series From October 1985 and June 1989 Consecutive sampling	Patient population: 87 patients with distal tubal occlusion Tubes affected: no patent tube (tuboplasty was carried out bilaterally except when one tube was either absent or severely damaged) Age: mean of 29.1; standard deviation of 4.5; ranging from 21 to 42 Primary or secondary infertility: 42 primary, and 45 secondary. Duration of infertility: mean of 33 months (standard deviation of 25.9 months, ranging from 12 to 120 months)	Tubal stage (n, %) Stage 1: 32, 36.8% Stage 2: 37, 42.5% Stage 3: 12, 13.8% Stage 4: 6, 6.9%	Ectopic pregnancy history: 6, 6.9% Prior laparoscopic adhesiolysis: 29, 33.3% Previous microsurgical salpingostomy history: 3, 3.4% Previous salpingectomy or adnexectomy history: 13, 14.9%	Salpingostomy Adhesiolysis was performed first, when necessary No IVF	Patients were followed up until December 1989
Daniell 1984 USA	Retrospective, case series From January 1st, 1982 to December 31, 1982 Consecutive sampling	Patient population: 21 patients with hydrosalpinges Tubes affected: no patent tube (6 with only one tube available for repair, 16 with bilateral hydrosalpinx) Age: not reported Primary or secondary infertility: not reported Duration of infertility: not reported	Not reported	Proximal occlusion: 0, 0% Previous major laparotomy with some form of tuboplasty for infertility: 21, 100%	Salpingostomy Co-interventions not reported Patients receiving IVF were excluded	21 of 22 women followed up for a duration of 6–18 months
Dlugi 1994 USA	Prospective cohort study From March 1989 to July 1992 Consecutive sampling	Patient population: 113 patients with distal tubal occlusive disease Tubes affected: 51 patients with bilateral tubal surgeries, and 62 with unilateral tubal surgeries;	Not reported	Abdominal adhesion: mentioned adhesion but no numbers reported Endometriosis: 39, 34.5%	Salpingostomy and salpingoneostomy Adhesiolysis was performed as needed No IVF	All patients were followed up from a minimum of 6 months and up to 39 months from the time of their surgical procedure

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Table 1 (*continued*)

Study ID/ Country	Study design, Study time and sampling strategy	Patient population	Disease severity (number, %)	Other disease history (number, %)	Surgery and related interventions	Follow up
		it is unclear for people receiving unilateral surgeries, the other tube was patent or not Age: mean of 31.5; standard deviation of 4.3; ranging from 21.3 to 45.4 Primary or secondary infertility: not reported Duration of infertility: mean of 3.7 years (standard deviation of 3.0 years)				
Dubuisson 1990 France	Retrospective, case series From May 1986 to May 1988 Consecutive sampling	Patient population: 31 patients with distal tubal obstruction Tubes affected: not reported Age: mean of 30.6; ranging from 22 to 39 Primary or secondary infertility: primary in 34 cases and secondary in 31 cases Duration of infertility: mean of 3.5 years (range: 1–8 years)	Not reported for 31 patients receiving fimbrioplasty	Abdominal adhesion: mentioned adhesion but no numbers reported	Fimbrioplasty Adhesiolysis was performed as needed No IVF	Follow up duration: 18 months
Dubuisson 1995 France	Retrospective, case series from May 1986 to June 1993 Consecutive sampling	Patient population: 112 single or bilateral hydrosalpinx Tubes affected: 66 patients with bilateral tubal surgeries, and 46 with unilateral tubal surgeries; it is unclear for people receiving unilateral surgeries, the other tube was patent or not Age: mean of 28.5; standard deviation of 4.9; ranging from 19 to 39 Primary or secondary infertility: 73 (60%) primary and 50 (40%) secondary Duration of infertility: mean of 3.4 years (standard deviation of 0.5; range: 1–8 years)	Tubal stage Stage 1: 18, 16.1% Stage 2: 36, 32.1% Stage 3: 27, 24.1% Stage 4: 31, 27.7%	Abdominal adhesion: mentioned adhesion but no numbers reported	Salpingostomy Adhesiolysis was performed as needed No IVF	112 (91.1%) patients were followed up, with a mean duration of 36 months (standard deviation of 8 months)
Dunphy 1997 Canada	Retrospective, case series From January 1991 to January 1995 Consecutive sampling	Patient population: 46 patients with distal tubal occlusive disease Tubes affected: no patent tube (26 women had bilateral distal occlusion; 20 women had previously undergone a salpingectomy (17 due to ectopic and three due to pain), and had distal occlusion in the remaining Fallopian tube) Age: mean of 31.2; standard deviation of 5.19 Primary or secondary infertility: 19 primary and 27 secondary infertility Duration of infertility: mean of 51.4 months (standard deviation of 34.0 months)	Not reported	Previous salpingectomy: 20, 43.5% Peritubal and/or peri-ovarian adhesions: 39, 84.8%	Salpingostomy Adhesiolysis was performed as needed Six received IVF	A mean follow up duration of 23.4 months (standard deviation of 13.9 months). Two subjects were lost to follow-up at 14 and 15 months following the procedure. One couple was divorced. Six women underwent treatment by in-vitro fertilization (IVF).
Eyraud 1993 France	Case series Between January 1987 and May	Patient population: 44 patients with distal tubal pathology	Tubal stage Stage 1: 16, 36.4% Stage 2: 13, 29.5%	Abdominal adhesion: 42, 95.5%	Fimbrioplasty and salpingoneostomy Adhesiolysis was	37 patients were followed up, and 5

(*continued on next page*)

Table 1 (*continued*)

Study ID/ Country	Study design, Study time and sampling strategy	Patient population	Disease severity (number, %)	Other disease history (number, %)	Surgery and related interventions	Follow up
	1990 Consecutive sampling	Tubes affected: no patent tube (20 received bilateral surgeries and 24 received unilateral surgeries, but the contralateral tube was either missing or not operable) Age: mean of 33; ranging from 23 to 42 Primary or secondary infertility: 12 primary and 32 secondary infertility Duration of infertility: not reported	Stage 3: 15, 34.1% Stage 4: 0, 0%		performed as needed No IVF	patients only had 3 months of follow up
Filippini 1996 France	Case series Between January 1988 and June 1993 Sampling strategy not reported	Patient population: 104 patients with distal tubal occlusion Tubes affected: no patent tube (bilateral procedure conducted except missing or not operable) Age: mean of 32 Primary or secondary infertility: 44 primary (42.3%) and 60 secondary (57.7%) Duration of infertility: mean of 3.2 years	Tubal stage Stage 1: 21, 20.2% Stage 2: 49, 47.1% Stage 3: 22, 21.2% Stage 4: 12, 11.5%	not reported	Fimbrioplasty Co-interventions not reported No IVF	All patients were followed up for at least 1 year
Kasia 1997 Cameroon	Case series Between May 1992 and May 1994 Consecutive sampling	Patient population: 194 patients with laparoscopic distal tuboplasty Tubes affected: not reported Age: mean of 31.1; standard deviation of 4.3; ranging from 20 to 40 Primary or secondary infertility: 65 primary and 129 secondary Duration of infertility (mean ± SD, years): 6.6 ± 3.6	Tubal stage Stage 1: 78, 40.2% Stage 2: 46, 23.7% Stage 3: 47, 24.2% Stage 4: 23, 11.9%	Laparotomy history: 27, 13.9% Voluntary abortion history: 37, 19.1% Peritoneal endometriosis: 10, 5.2% Fitz-Hugh-Curtis syndrome: 47, 24.2% *Chlamydia trachomatis* serology positive: 111, 57.2%	Fimbrioplasty and salpingoneostomy Adhesiolysis was performed first, when necessary No IVF	16 patients were lost to follow up.
Lavergne 1996 France	Retrospective, case series Sampling strategy unclear	Patient population: 46 patients with distal tubal disease Other information: unclear	Unclear	Unclear	Unclear	Unclear
Li 2013 China	Randomized controlled trial Between 2005 and 2008 Sampling strategy not reported	Patient population: 180 patients with distal tubal occlusion Tubes affected: bilateral distal tubal occlusion Age: mean of 28.28; standard deviation of 3.23; ranging from 22 to 36 in intra-operative hydrotubation group; mean of 28.11; standard deviation of 3.04; ranging from 22 to 36 in post-operative hydrotubation group; mean of 27.86; standard deviation of 3.66; ranging from 21 to 37 Primary or secondary infertility: Fallopian tubal occlusion Duration of infertility (mean ± SD (range), months): Intra-operative hydrotubation group (n = 60): 38.04 ± 12.96 (25–61) Postoperative	Pelvic condition staging: the pelvic score was the sum of the adhesion score (a maximum score of 40) and tubal occlusion score (a maximum score of 20). The stage of pelvic condition was assigned as 0, I, II, III, and IV with scores of 0, 1–15, 16–30, 31–45, and 46–60, respectively. Intra-operative hydrotubation group (n = 60): Stage 1: 2, 3.33% Stage 2: 15, 25.00% Stage 3: 34, 56.67%) Stage 4: 9 (15.00%) Postoperative hydrotubation group (n = 61): Stage 1: 4 (6.56%) Stage 2: 21 (34.43%) Stage 3: 32 (52.46%) Stage 4: 4 (6.56%) Control group (n = 59): Stage 1: 1 (1.69%) Stage 2: 15 (25.42%)	Abdominal adhesion was mentioned but no numbers reported Childbirth history: Parity times mean of 0.12 in intra-operative hydrotubation group; mean of 0.08 (in post-operative hydrotubation group; mean of 0.10 in control group. Gravidity times mean of 1.93 in intra-operative hydrotubation group; mean of 1.69 in post-operative hydrotubation group; mean of 1.80 in control group. Medical abortion and procedural abortion: mean of 1.84 in intra-operative hydrotubation group; mean of 1.61 in post-operative hydrotubation group; mean of 1.69 in control group. No tubal surgery, abdominal and pelvic surgery, endometriosis,	Salpingostomy Adhesiolysis was performed for all patients No IVF	180 patients (92.3%) were followed up for 2 years

(*continued on next page*)

Table 1 (*continued*)

Study ID/ Country	Study design, Study time and sampling strategy	Patient population	Disease severity (number, %)	Other disease history (number, %)	Surgery and related interventions	Follow up
		hydrotubation group (n = 61): 39.12 ± 12.60 (26–59) Control group (n = 59): 37 ± 14.11 (27–72)	Stage 3: 36 (61.02%) Stage 4: 7 (11.86%)	proximal occlusion, or smoking history		
McComb 2001 Canada	Retrospective cohort study From 1988 to 1997 Consecutive sampling	Patient population: 23 patients with unilateral hydrosalpinx and a patent contralateral fallopian tube Tubes affected: unilateral hydrosalpinx Age: mean of 31.9; ranging from 25 to 39 Primary or secondary infertility: not reported Duration of infertility: mean: 53.6 months (range, 19–146 months)	Not reported	Adhesions: 5, 21.7% Pregnancy history: 12, 52.2% Ectopic pregnancy history: 2, 8.7% Pelvic inflammatory disease: 4, 17.4% Intrauterine device use: 5, 21.7% Gonorrhea: 2, 8.7%	Salpingostomy Co-interventions not reported	All patients were followed up Follow up duration not reported, likely longer than 6 years
Mettler 1979 Germany	Retrospective case series 1971 to 1976 Consecutive sampling	Patient population: 89 patients with tubal obstruction Tubes affected: not reported Age not reported Primary or secondary infertility: not reported Duration of infertility (mean ± SD): not reported	not reported	not reported	Fimbrioplasty and salpingostomy Adhesiolysis was performed first, when necessary No IVF	Patients were followed up until October 1977
Milingos 2002 Greece	Randomized controlled trial Jan 1990 to June 1999 Consecutive sampling	Patient population: 61 patients with bilateral hydrosalpinges Tubes affected: bilateral Age: mean of 31; standard deviation of 3.49; ranging from 19 to 38 Primary or secondary infertility: 46 (75%) primary infertility; 15 (25%) secondary infertility Duration of infertility (mean ± SD): 3.5 ± 2.3 years	Revised American Fertility Society (AFS) scoring system: For those without periadnexal or with negligible adhesions (n = 44) Mild: 13, 29.5% Moderate: 16, 36.4% Severe: 15, 34.1%	Abdominal adhesions: 17, 27.9%	Salpingoneostomy Adhesiolysis was performed as needed No IVF	All patients were followed up for 2 years
Mossa 2005 Italy	Randomized controlled trial From 1987 to 2001 Consecutive sampling	Patient population: 113 patients with infertility due to distal tubal occlusion Other information: unclear	Unclear	Unclear	Unclear	2 years follow up period
Oh 1996 Korea	Case series Study time not reported Sampling strategy not reported	Patient population: 82 patients with terminal tubal obstructions Tubes affected: bilateral Age: mean of 30.4; standard deviation of 4.5 in type 1 surgery group; mean of 33.1; standard deviation of 6.2 in type 2 surgery group; mean of 32.8 standard deviation of 3.8 in type 3 surgery group Primary or secondary infertility: not reported Duration of infertility: not reported	Prognostic factor score based on tubal mucosa, hydrosalpinx wall, diameter of hydrosalpinx, and adhesions, with 10–12 as a favorable prognostic factor score, 7 to 9 as an intermediate score, and 4 to 6 as a poor score. Patients receiving type 1 salpingoneostomy Poor prognostic factor: 5, 19.2% Intermediate prognostic factor: 11, 42.3% Favorable prognostic factor: 10, 38.5% Patients receiving type 2 salpingoneostomy Poor prognostic factor: 6, 22.2% Intermediate prognostic factor: 10, 37.0% Favorable prognostic factor: 11, 40.7%	Abdominal adhesion: 82, 100%	Salpingoneostomy Adhesiolysis was performed for all patients No IVF	All patients were followed up for 3 years

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Table 1 (*continued*)

Study ID/ Country	Study design, Study time and sampling strategy	Patient population	Disease severity (number, %)	Other disease history (number, %)	Surgery and related interventions	Follow up
			Patients receiving type 3 salpingoneostomy Poor prognostic factor: 7, 24.1% Intermediate prognostic factor: 8, 27.6% Favorable prognostic factor: 14, 48.3%			
Prapas 1995 Greece	Retrospective case series Study time unclear Consecutive sampling	Patient population: 32 patients with distal tubal obstruction Other information: unclear	Unclear	Unclear	Unclear	Unclear
Taylor 2001 Canada	Prospective cohort study From April 24, 1984 to May 6, 1998 Consecutive sampling	Patient population: 139 hydrosalpinx Tubes affected: no patent tube (either unilateral hydrosalpinx with an absent or inoperable contralateral oviduct or bilateral hydrosalpinx) Age: mean of 30.9; standard deviation of 4.1; ranging from 21.4 to 41.1 Primary or secondary infertility: primary in 65 cases and secondary in 74 cases Duration of infertility: mean: 58 months (range, 2–212 months)	Not reported	Adhesions: 42, 30.2% (15 with moderately dense/ vascular adhesions and 27 with severely dense adhesion)	Salpingostomy Co-interventions not reported	166 patients (96.5%) were followed up until June 1998
Yuan 2019 China	Retrospective, case series December 2011 and December 2013 Consecutive sampling	Patient population: 423 patients of our hospital with tubal factor infertility as principal diagnosis Tubes affected: not reported (people with either uni- or bilateral tubal factor infertility were eligible) Age: mean of 29.05; standard deviation of 4.46; ranging from 19 to 43 Primary or secondary infertility: not reported Duration of infertility: not reported	The modified classification of fallopian tube status considered tubal wall consistency, diameter of hydrosalpinx, adnexal adhesions, and tubal potency, with a score of <8 as mild, 8–15 as moderate, and >15 as severe. Mild (<8): 158, 37.4% Moderate [8–15]: 246, 58.2% Severe (>15): 19, 4.5% AFS distal tubal occlusion score Normal (0): 8, 1.9% Mild [1–3]: 9, 2.1% Moderate [3–10]: 95, 22.5% Severe (>10): 311, 73.5%	not reported	Unclear Co-interventions not reported 121 patients (21.3%) received IVF	423 patients were followed up for 2 years

included studies if they were 1) primary studies, 2) on laparoscopic surgeries as either fimbrioplasty or salpingostomy (with or without adhesiolysis) purposed to preserve or restore the tubal function, 3) for patients with laparoscopically confirmed conditions in their distal fallopian tube(s), 4) with at least 10 patients, and 5) with reports on pregnancy outcomes including the rates of pregnancy, live birth, ectopic pregnancy, and miscarriage. We excluded studies if they were 1) comments or commentary, editorials, letters, communications, 2) about laparotomy, 3) about salpingectomy or hysterectomy, or 4) without reporting on any pregnancy-related outcome.

2.2. Literature search and screening

Literatures were searched from those published on Medline and EMBASE available till to June 1st, 2020. The keywords for searching were “fallopian tube disease” for the diseases and “laparoscopy”, “fimbrioplasty”, and “salpingostomy” for the treatment. Boolean logic “AND” was used to combine the two sets of terms. No limits in language or publication date was set.

Two authors (HH and ZY) independently screened all titles and abstracts and retrieved the full text of any article considered definitely or possibly eligible. Both authors then reviewed the full text articles against the eligibility criteria. Any disagreement between the two authors was resolved by discussion. The reference list of the eligible studies was also screened.

2.3. Data extraction

Data were collaboratively extracted from eligible studies by two investigators (HH and ZY) through a data collection form, which was prior designed to include the first author, the year of publication, the characteristics of the participants including the age, disease histories, disease severities, and the surgeries performed, pregnancy outcomes, and follow-up. We assessed the methodological quality of the included studies using the QUIPS (Quality in Prognostic Studies) tool, which evaluate the methodology in six domains as the study population, the study attrition,

Table 2
Risk of bias in included studies.

Study	Study population	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis
Audebert 2014	Low	Low	Low	Low	Low	Low
Bontis 1996	Moderate	Low	Low	Low	Moderate	Moderate
Canis 1991	Low	Low	Low	Low	Moderate	Moderate
Daniell 1984	Moderate	Low	Low	Low	Moderate	Moderate
Dlugi 1994	Low	Low	Low	Low	Moderate	Moderate
Dubuisson 1990	Moderate	Low	Low	Low	Moderate	Moderate
Dubuisson 1995	Low	Low	Low	Low	Moderate	Moderate
Dunphy 1997	Low	Low	Low	Low	Low	Moderate
Eyraud 1993	Low	Moderate	Low	Low	Moderate	Moderate
Filippini 1996	Moderate	Low	Low	Low	Moderate	Moderate
Kasia 1997	Low	Moderate	Low	Low	Moderate	Moderate
Lavergne 1996	Moderate	Low	Low	Low	Moderate	Moderate
Li 2013	Moderate	Low	Low	Low	Low	Low
McComb 2001	Low	Low	Low	Low	Moderate	Moderate
Mettler 1979	Moderate	Low	Low	Low	Moderate	Moderate
Milingos 2002	Low	Low	Low	Low	Moderate	Moderate
Mossa 2005	Moderate	Low	Low	Low	Moderate	Moderate
Oh 1996	Moderate	Low	Low	Low	Moderate	Moderate
Prapas 1995	Moderate	Moderate	Low	Low	Moderate	Moderate
Taylor 2001	Low	Low	Low	Low	Low	Low
Yuan 2019	Low	Low	Low	Low	Low	Moderate

the prognostic factor measurement, the outcome measurement, the study confounding, and the statistical analysis. Any disagreements between the two investigators conducting data extraction was firstly resolved through discussion, or by consulting the principal investigator of the study if no consensus could be achieved.

2.4. Statistical analysis

We performed meta-analyses to estimate the pregnancy rate, ectopic pregnancy rate, and miscarriage rate, using the inverse variance method and random effect model. All meta-analyses were conducted through R package *metafor* [8]. We reported the pooled estimates and their 95% confidence intervals (CI). We conducted subgroup analyses by the surgery types, tubal damage stages, and adhesion. We did not set statistical

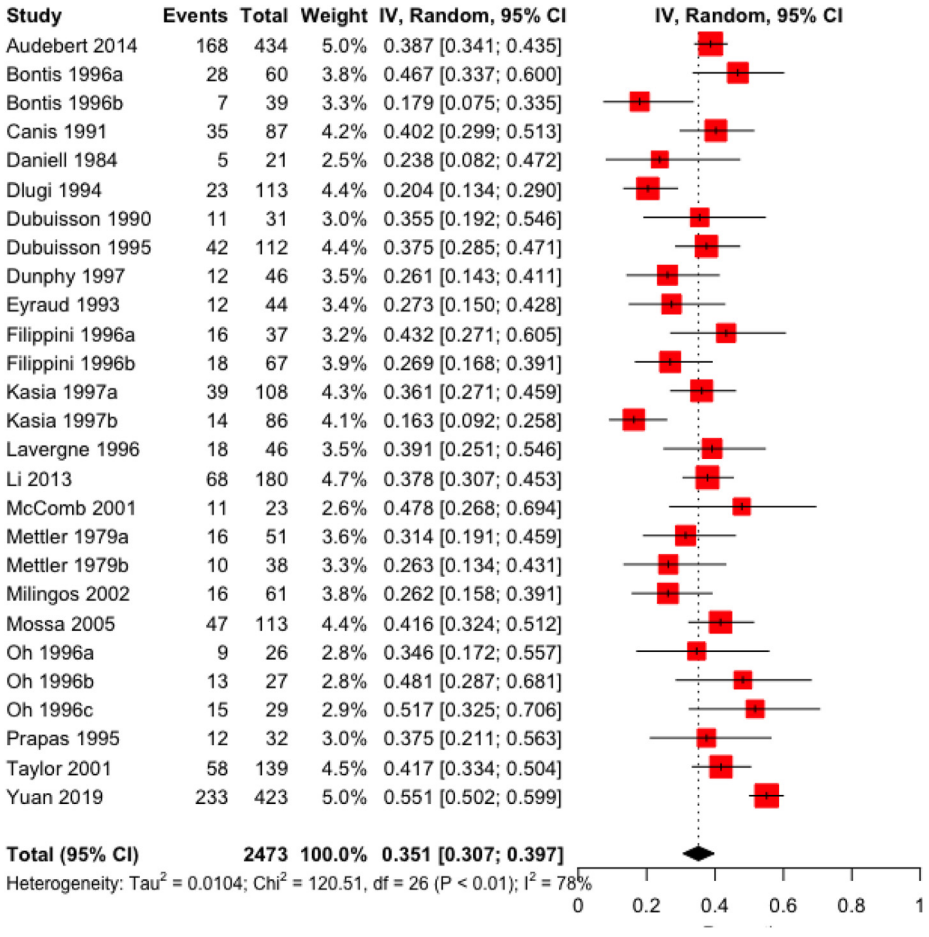

Fig. 2. Meta-analysis of pregnancy rates after laparoscopic surgeries for distal tubal occlusion.

Table 3
Summary of findings for prognosis of patients receiving laparoscopic surgery for distal tubal occlusion.

Outcomes*	N° of participants (studies) Follow up	Certainty of the evidence (Grade)	Estimate (%) (95% CI)
Pregnancy rate	2473 (21 observational studies)	⊕⊕○○ LOW[a,b,c]	**35.1** (30.7–39.7)
Ectopic pregnancy rate	2363 (20 observational studies)	⊕⊕○○ LOW[a,b,d]	**6.2** (4.4–8.2)
Delivery rate	1154 (5 observational studies)	⊕⊕○○ LOW[a,b,e]	**24.4** (20.2–28.8)
Miscarriage rate	544 (6 observational studies)	⊕⊕○○ LOW[a,f]	**4.6** (2.8–6.9)

* follow up: range 6 months to 5 years.
GRADE Working Group grades of evidence ⊕⊕⊕⊕ High certainty: We are very confident that the true effect lies close to that of the estimate of the effect ⊕⊕⊕○ Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different ⊕⊕○○ Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect ⊕○○○ Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a] The estimate was mainly based on studies with moderate risk of bias regarding study confounding and statistical analysis.
[b] There was unexplained heterogeneity.
[c] $I^2 = 78\%$.
[d] $I^2 = 61\%$.
[e] $I^2 = 58\%$.
[f] The number of events was small, 28 in total.

significance level because no between-group comparison was made.

2.5. Certainty of evidence assessment

We used the GRADE approach (The Grades of Recommendation, Assessment, Development, and Evaluation) to assess the certainty of evidence. The certainty of evidence starts from high and we downgraded the certainty for concerns on risk of bias, inconsistency, indirectness, imprecision, and publication bias.

3. Results

We identified 4039 title and abstract records for screening through systematic search, and 17 records from reference lists. After de-duplicating, 3861 records were finally listed for title and abstract screening. We then retrieved the full texts of 157 studies for further screening and 21 studies concerning 2473 participants were finally included (see Fig. 1. Flow chart). We quantitatively synthesized the results of the 21 included studies. Table 1 summarizes the key characteristics of the eligible studies. Of the 21 studies, 12 studies were from Europe (7 from France, 3 Greece, and 1 each from Germany and Italy), 3 from Asia (2 from China, and 1 from South Korea), 5 from North America (3 from Canada, and 2 from the United States), and 1 from Cameroon. Eleven of the 21 were retrospective analyses, 6 were prospective studies, and 4 did not provide sufficient information. Regarding the types of surgery conducted, patients from 11 studies received salpingostomy. In contrast, 8 studies were on fimbrioplasty and 6 on salpingoneostomy. The median of mean age across the studies was 31, ranging from 28 to 33 years. Of the 21 studies, only 1 study was on women with unilateral tubal pathology, while the study population in 10 studies were women without patent tubes at baseline because either they had bilateral tubal pathology or they had unilateral tubal pathology but the other tube was missing or not operable. Ten other studies did not provide sufficient information on tube patency at baseline. However, only 7 studies were published after year 2000, among them, 3 were published in the last decade.

As for the risk of bias, the confounding and statistical analysis of the studies were considered as the two major concerns (Table 2). Most of the included studies only reported the pregnancy outcomes by subgroups, rather than adjusting for confounders using multivariate analyses.

3.1. Pooled estimates

The pooled estimate for the cumulative pregnancy rate of the 2473 participants was 35.1% (95% CI: 30.7%–39.7%, $I^2 = 78\%$). The certainty of evidence is low due to serious risk of bias and inconsistency (Fig. 2 and Table 3). We explored the source of heterogeneity across studies by subgroup analysis according to the types of surgery (Fig. 3) and meta-analyses of the pregnancy rates at 1 year and 2 years after surgery (Fig. 4). The pregnancy rates of the patients receiving laparoscopic fimbrioplasty, salpingostomy, salpingoneostomy were 38.0% (95% CI: 32.5%–43.7%, $I^2 = 0\%$; 301 patients), 33.6% (95% CI: 28.9%–38.4%, $I^2 = 43\%$; 793 patients), and 27.9% (95% CI: 16.7%–40.6%, $I^2 = 81\%$; 310 patients), respectively. Heterogeneity exists in subgroups of patients receiving salpingostomy and salpingoneostomy.

The rates of the cumulative pregnancy in 1 and 2 year post-surgery were estimated to be 24.8% (95% CI: 13.8%–37.6%, $I^2 = 95\%$; 1058 patients) and 33.7% (95% CI: 20.1%–48.7%, $I^2 = 94\%$; 823 patients), respectively.

The pooled estimates for the rates of ectopic pregnancies, live births, and miscarriage were 6.2% (95% CI: 4.4%–8.2%, $I^2 = 61\%$; 2363 patients; low certainty of evidence due to serious risk of bias and inconsistency), 24.4% (95% CI: 20.2%–28.8%, $I^2 = 58\%$; 1154 patients; low certainty due to risk of bias and inconsistency, and 4.6% (95% CI: 2.8%–6.9%, $I^2 = 10\%$; 544 patients; low certainty of evidence due to risk of bias and imprecision) (Fig. 5 and Table 3).

3.2. Influential factors

We also explored the influential factors of pregnancy prognosis. Of all influential factors, tubal damage stages and adhesion were the mostly reported two factors. Tubal damage stage accounts for the tubal blockage, the quality of the mucosa, and the tubal wall. We adopted scores of 2–5, 6–10, 11–15, >15 to indicate the Stages I, II, III, and IV, respectively. Our analyses indicated that decreasing of the pregnancy rate was associated with the severity of the tubal damages. The pregnancy rates for Stages I, II, III, and IV, were 43.0% (95% CI: 34.7%–51.6%, $I^2 = 43\%$; 288 patients), 35.2% (95% CI: 28.5%–42.1%, $I^2 = 30\%$; 341 patients), and 14.5% (95% CI: 9.7%–19.9%, $I^2 = 0\%$; 248 patients), and 1.3% (95% CI: 0.0%–9.3%, $I^2 = 64\%$; 137 patients), respectively (see Fig. 6). Some studies reported the outcomes by tubal damage stages via figures, with no exact numbers of events available. Those studies were not included in our meta-analysis. However, those studies also showed a similar trend with our meta-analysis results. The only study that reported the odds ratios to indicate the association between damaged tubal and pregnancy outcomes were conducted by Audebert et al., who reported that, compared with tubal damage Stage I patients, the odds ratio of delivery for Stage II, Stage III, and Stage IV patients were 0.695 (95% CI: 0.372–1.299), 0.240 (95% CI: 0.112–0.515), and 0.282 (95% CI: 0.108–0.735), respectively. Those odds ratios were based on multivariate analysis, adjusting for age, previous tubal plasty, adhesion, operation technique, and positive Chlamydia testing results. Fig. 7 shows that patients with moderate or severe adhesion had lower pregnancy rates than the patients with mild pelvic adhesion. Audebert et al. also reported a trend showing that severity of tubal adhesion was associated with a lower delivery rate (odds ratio for patients with severe adhesion than patients without adhesion: 0.215, 95% CI: 0.062–0.741) [3].

Since only one study was on unilateral hydrosalpinx and the majority of the study participants were without patent tubes, we did not conduct subgroup analysis to compare the prognosis of those patients with unilateral versus those with bilateral tubal pathology. Nevertheless, the single study on participants with unilateral hydrosalpinx reported higher probabilities of pregnancy (11 of 23 participants, 47.8%) and

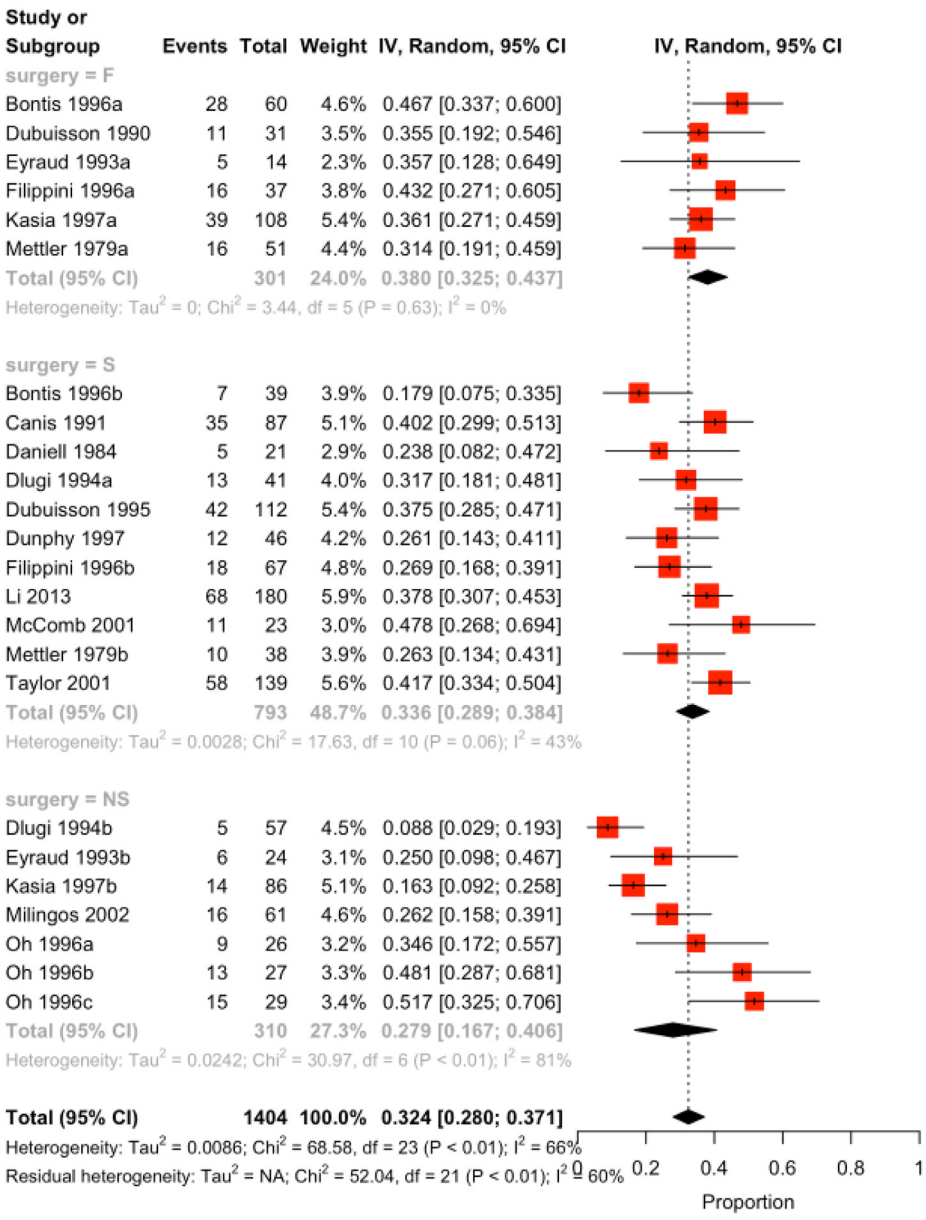

Fig. 3. Subgroup analysis of pregnancy rates by types of surgery. F, fimbrioplasty; S, salpingostomy; NS, salpingoneostomy.

intrauterine pregnancy (10 of 23 participants, 43.5%). Table 4 summarizes the results for other influential factors including age, previous hydrosalpinx, other disease or surgery history, i.e., endometriosis. There were only few studies and conflicting results on those factors.

3.3. Postoperative reocclusion

We further summarized the evidence on the postoperative reocclusion. There were only three studies that reported patency followed-up after surgery. Because of the variations in following-up time and outcome reporting, we were unable to perform meta-analysis. Oh et al. (1996) reported tubal patency checked via hysterosalpingogram (HSG) in 2 months after operation. Thirteen of 26, 23 of 27, and 28 of 29 patients who respectively received type 1, type 2, and type 3 salpingoneostomy had 1 or both patent tubes patent [9]. In another study, HSG performed on patients in 2 years after surgeries for nonpregnant showed that all the patients with mild disease but no adhesion had both tubes patent, and 80% of the patients with mild disease and adhesions had patent tubes (10). Taylor and colleagues reported that, with a total of 192 tubes undergoing operations, 109 tubes were reassessed postoperatively for nonpregnant patients, 89 of which were patent [5].

4. Discussion

4.1. Summary of findings

With a systematic review and meta-analysis approach, we evaluated the prognosis of the patients underwent laparoscopic surgery treatments for pathology conditions on distal tubal and explored the prognostic factors for pregnancy outcomes for these patients. The cumulative pregnancy rate after laparoscopic surgeries were estimated to be 35.1%. Our estimation represents the prognosis of the patients with pathology conditions on both of the tubes and that of the patients with pathology conditions on the unilateral tube with the other tube missed or inoperable. The results from our estimation are similar to those from another systematic review, which estimated a pregnancy rate of 27% for patients with hydrosalpinx after salpingostomy [11]. The rates for living birth, ectopic pregnancies, and miscarriage were estimated to be 24.4%, 6.2%,

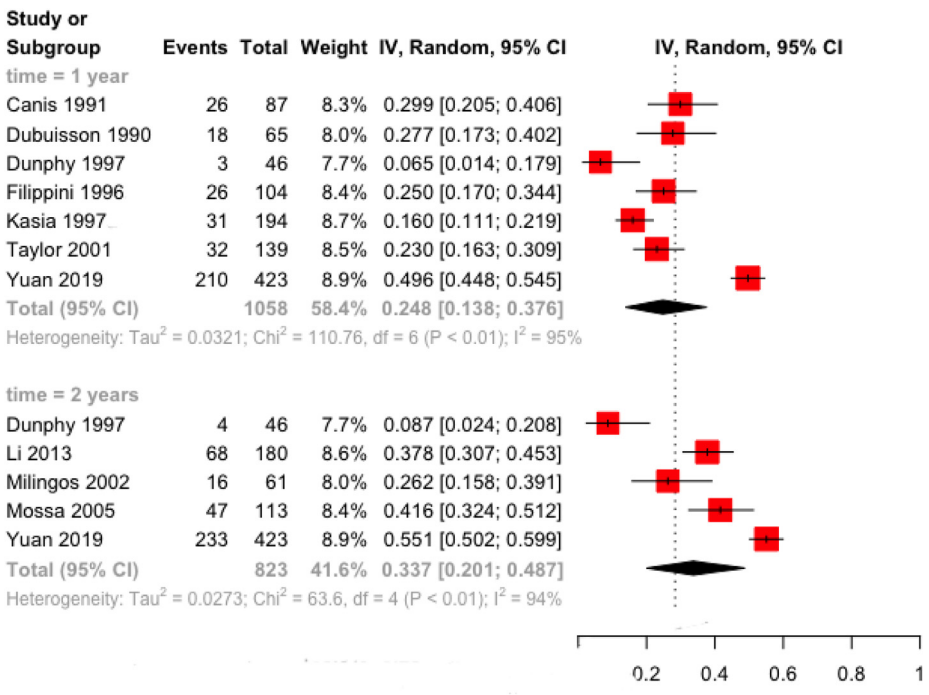

Fig. 4. Meta-analyses of pregnancy rates at different time points after laparoscopic surgeries.

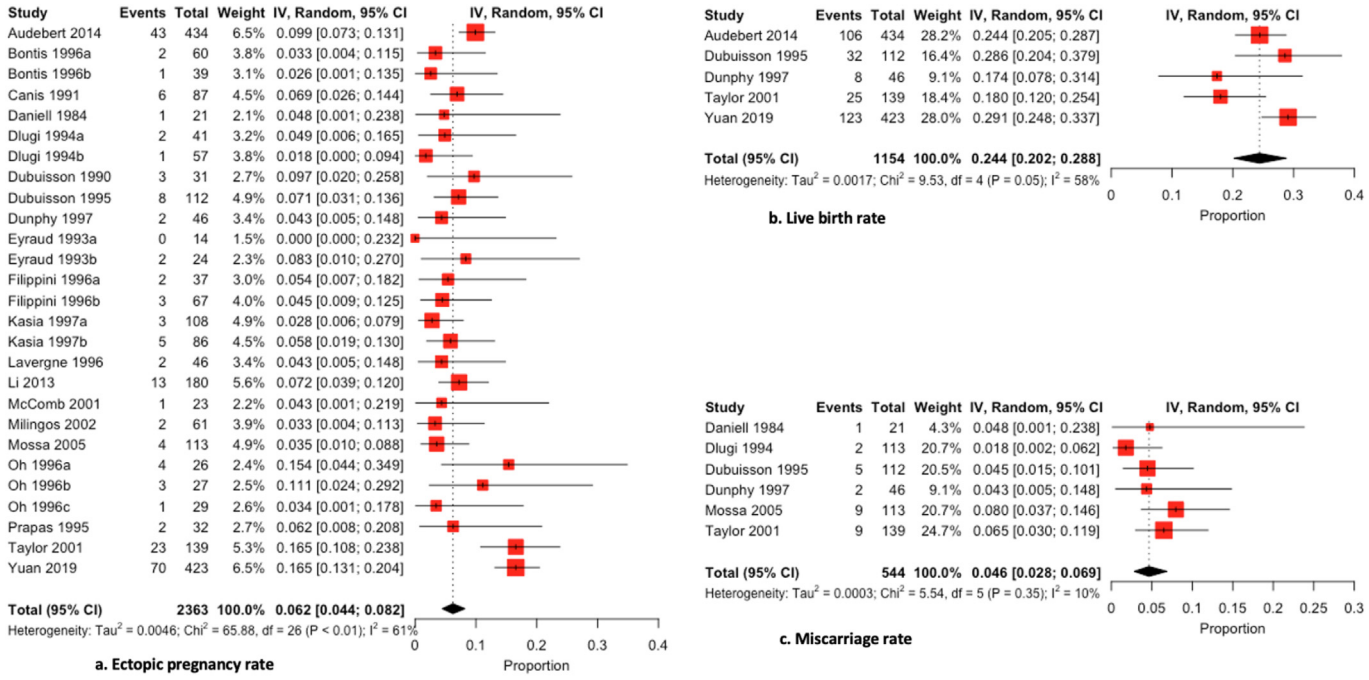

Fig. 5. Ectopic pregnancy, live birth, and miscarriage after laparoscopic surgeries for distal tubal occlusion.

and 4.6%, respectively. We further investigated the potential prognostic factors, and found that stage of tubal damages and tubal adhesion were the two that were commonly studied and were associated with worse pregnancy outcomes. However, evidences regarding other prognostic factors are still inconclusive.

Using the GRADE approach [12], we assessed the certainty of evidences in the estimation to the rates of pregnancies, ectopic pregnancies, deliveries, and miscarriages, and concluded that such estimation was based on the studies that were risk of biases concerning confounding and statistical analysis. Confounders accounting for essential bias because the unadjusted reports of pregnancy outcomes make results less comparable across studies. Nevertheless, only two studies undertook multivariate analysis to adjust for confounders. Unexplained heterogeneity, or inconsistency, is another concern. We assessed the certainty of evidence as low for the rates of pregnancies, deliveries, and ectopic pregnancies due to the potential bias and inconsistency. In regarding to the miscarriage rate, the number of events was small, and the estimate was susceptible to random error. Thus, the certainty of evidence for miscarriage rate was also judged to be low due to serious risk of bias and imprecision.

Our subgroup analyses by the surgery types and tubal disease

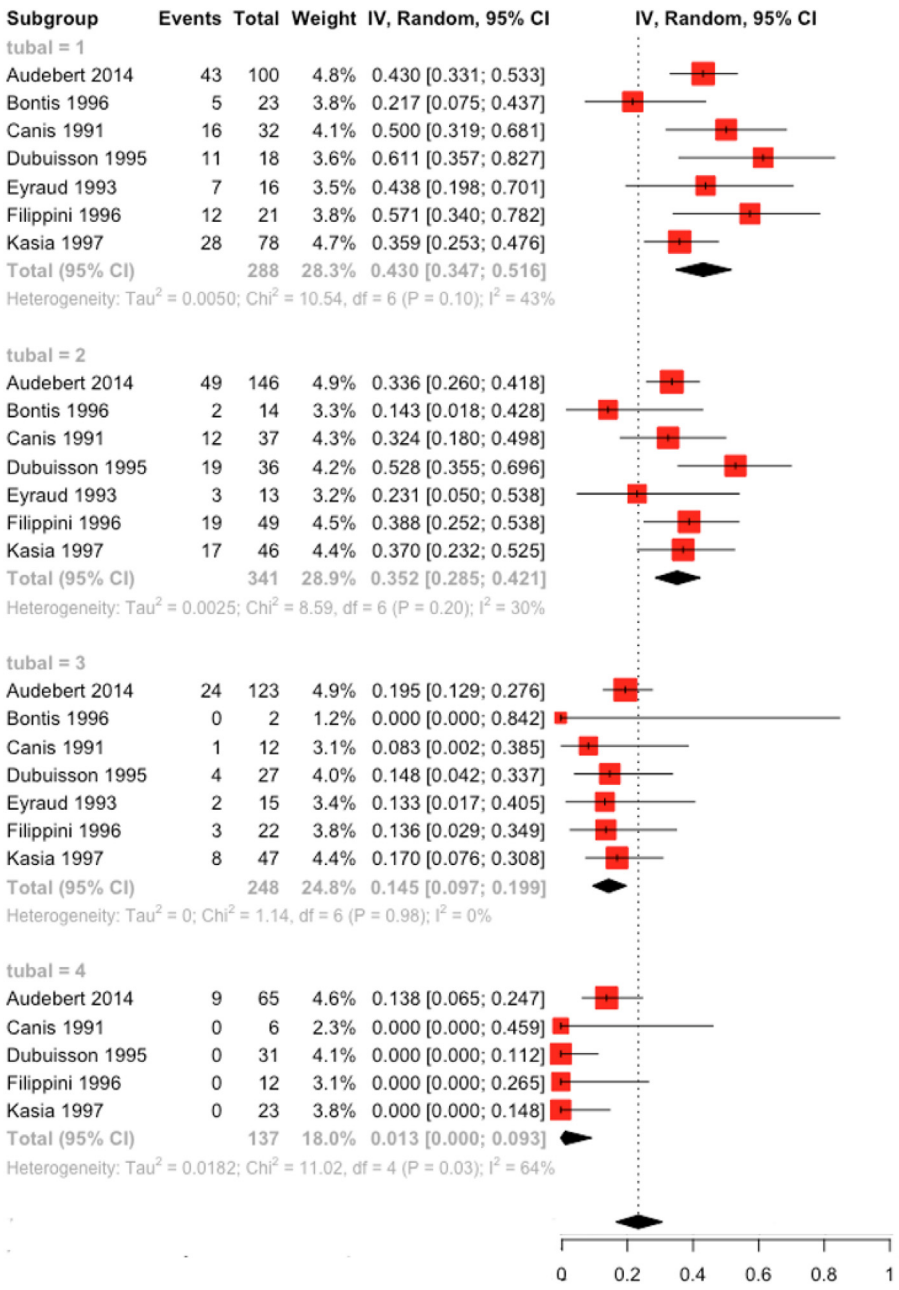

Fig. 6. Pregnancy rates for patients with different tubal damage severities.

severities also showed a higher pregnancy rates in patients receiving fimbrioplasty than in those receiving salpingostomy and salpingoneostomy [5,13,14]. This may be because the surgery received by a patient represents the indication, or more precisely, the baseline characteristics of the patient [15,16]. This systematic review includes patients with partial and total distal tubal occlusion. Salpingoneostomy is tended to surgically form a new tubal ostium, whereas fimbrioplasty is projected to reconstruct an existent fimbria via desagglutination and dilatation, with serosal incision on a completely occluded tube or a combination of multiple techniques. Our subgroup analysis by baseline tubal disease severity further demonstrated that the degree of pre-surgery tubal damage was associated with the post-surgery decrease of pregnancy rate. It is likely that patients with less severe disease required less complicated surgery, and had better pregnancy outcomes (5). In other words, the observed differences in pregnancy rates after different types of surgery is probably a reflection of baseline disease severity. However, heterogeneity still exists within subgroups of patients receiving salpingostomy and salpingoneostomy, which means that surgery types solely could not explain all the heterogeneity. Notably, inoperable hydrosalpinges, typically characterized by extensive thick-walled, encased, and thick adhesions similar to a frozen pelvis and a worse prognosis, were not considered within the scope of this systematic review.

4.2. *Implications for practice*

The findings of our systematic review suggest that laparoscopic salpingostomy or fimbrioplasty are alternative strategies for patients with distal tubal pathology, especially for those who are reluctant to receive assisted reproductive treatment. However, multiple factors may have impacts on pregnancy outcomes. We identified several factors including

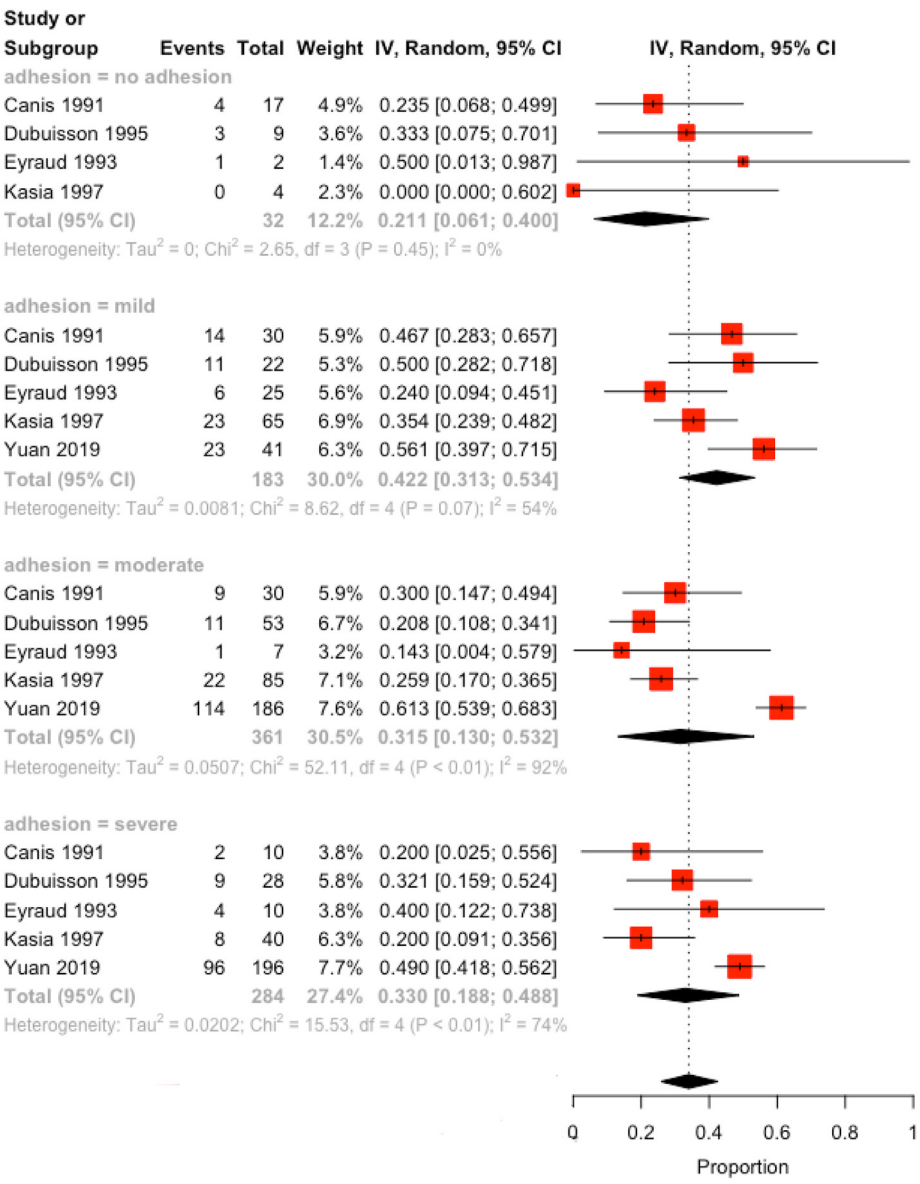

Fig. 7. Pregnancy rates for patients with pelvic adhesion severities.

stage of tubal damage and adhesion [3,10,17,18]. Physicians need to discuss with patients about their disease history, uncertainties of evidence, and their expectations. The decision-making process should include consideration to patient preferences, especially for those who have strong preference to preserve fallopian tubes or wish to avoid IVF.

The pregnancy rates at 1 year and 2 years after the surgeries were estimated to be 24.8% and 33.7%, respectively. The estimated rate at 2 years is close to the rate (35.1%) from overall pooled estimate. The studies reporting 2-year post-surgery outcomes suggested that pregnancy would be mostly possible within 2 years after the laparoscopic intervention. Our findings are similar to another review on salpingostomy for hydrosalpinx [11]. With these findings, we suggest that patients who receive surgeries and attempt spontaneous conception should not wait more than 2 years after the surgeries before switching to IVF.

Another concern about surgical correction of the pathological conditions on distal tube is postoperative reocclusion. Our systematic review provided limited evidence on the incidence of postoperative reocclusion. Patients should be informed all alternative strategies preoperatively, because a salpingectomy or proximal tubal occlusion may need to be performed additionally for potential postoperative reocclusion [19].

4.3. Implication for future studies

Prospectively, studies with large size of samples are needed to identify the patients how would mostly benefit from laparoscopic surgeries and the appropriate surgery types for them. Future studies on the incidence of postoperative reocclusion will also contribute to patients' and physicians' decisions. Summary of the factors impacting prognosis in our systematic review had laid a foundation for the future research on development of a prediction model for patients with distal tubal pathology.

4.4. Strengths and limitations

This study benefits from the rigorous methods in the breadth of literature search and our assessment of risk of bias and certainty of evidence. We conducted subgroup analyses to compare different time points and types of surgery to explore the heterogeneity. However, potential limitations of the systematic review are the inconsistency and variability across eligibility criteria in the original studies and the variability in study designs, sample sizes, and definitions of the prognostic factors such as tubal disease severity and adhesion. A certain degree of clinical

Table 4
Influential factors studied in the included studies.

Study ID	Tubal stage	Adhesion	Previous hydrosalpinx	Duration of infertility	Anti-Mullerian Hormone	Age	Other pelvic surgery history	Other
Audebert 2014	Associated with worse prognosis	Associated with worse prognosis	Previous tubal plasty: associated with worse prognosis	Reported but not studied	Not studied	Not significant	Not studied	Chlamydia positive: Associated with worse prognosis Endometriosis: studied, but not significant
Bontis 1996	Associated with worse prognosis	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Canis 1991	Associated with worse prognosis	Associated with worse prognosis	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Daniell 1984	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Dlugi 1994	Not studied	Associated with worse prognosis	Subgroup data reported, but no analysis on it as a risk factor	Not studied	Not studied	Not studied	Not studied	Endometriosis, other factors (male factor and cervical factor): Patients with endometriosis and no other infertility factors had a significantly better cumulative pregnancy curve compared with patients without endometriosis or other factors as well as compared with patients with endometriosis but with other infertility factors
Dubuisson 1990	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Dubuisson 1995	Associated with worse prognosis Mucosa score was also studied: abnormal mucosa was associated with worse prognosis	Associated with worse prognosis	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Dunphy 1997	Tubal diameter was analyzed and associated with patient outcome, but no details were provided	Not studied	Not studied	Associated with patient outcome, but no details were provided	Not studied	Not studied	Not studied	Primary or secondary infertility was analyzed and associated with patient outcome, but no details were provided
Eyraud 1993	Associated with worse prognosis	Associated with worse prognosis	Not studied	Not significant	Not studied	Not significant	Not studied	Male factor and endometriosis: not significant
Filippini 1996	Associated with worse prognosis	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Kasia 1997	Associated with worse prognosis	Associated with worse prognosis	Not studied	Not significant	Not studied	Not significant		Primary or secondary infertility: not significant Chlamydia positive: not significant
Larvegne 1996	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Li 2013	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
McComb 2001	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Mettler 1979	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Milingos 2002	Associated with worse prognosis	Associated with worse prognosis	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Mossa 2005	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Oh 1996	Associated with worse prognosis	Associated with worse prognosis	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Prapas 1995	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied
Taylor 2001	Not studied	Dense adhesion associated with worse prognosis						Previous conception, gonorrhea, previous ectopic pregnancy, positive history for intrauterine device use, positive for pelvic inflammatory disease, unilateral surgery: can be combined to predict pregnancy outcomes
Yuan 2019	Associated with worse prognosis	Associated with worse prognosis	Not studied	Not studied	Not studied	Not studied	Not studied	Not studied

heterogeneity was expected because of the advances of the diagnostic and surgical techniques and the variabilities of the studies in terms of surgeon expertise and technologies across different countries and settings. The included studies also varied in the follow-up time. The short duration means earlier termination of follow-up for patients who had no outcome events occurred, which might underestimate pregnancy outcomes. The purpose for us to conduct meta-analyses on 1 year and 2 years of postoperative pregnancy rates was to mitigate this limitation. Another limitation is that we were unable to estimate the strength of associations between prognostic factors and pregnancy outcomes, other than pooled estimates of pregnancy outcomes for subgroups of patients with different tubal damage and adhesion severities.

5. Conclusion

Low certainty evidence suggested that laparoscopic surgery may restore the tubal function and cure infertility and should be considered as an alternative to IVF. The cumulative pregnancy rate, ectopic pregnancy rate, delivery rate, and miscarriage rate after laparoscopic surgeries were estimated to be 35.1%, 6.2%, 24.4%, and 4.6%. Tubal damage stage and adhesion were associated with worse pregnancy outcomes. The evidence is inconclusive regarding other prognostic factors. These findings will help inform experts in developing a prediction model for patients with distal tubal pathology.

Declaration of competing interest

None.

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