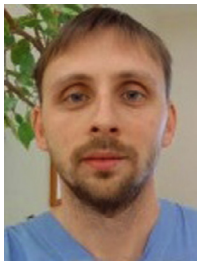
RBMO

REVIEW

Treatment of hydrosalpinx in relation to IVF outcome: a systematic review and meta-analysis



BIOGRAPHY

Dr Alexander Volodarsky-Perel completed his obstetrics–gynaecology residency in Shaare Zedek Medical Center, Israel, and is a senior physician in its IVF Unit. He is currently completing a fellowship in Reproductive Endocrinology and Infertility at McGill University, Canada. His main research focus is reproductive physiology, fertility preservation and decreased ovarian reserve.

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KEY MESSAGE

The most widely used treatment for hydrosalpinx is salpingectomy. The effect of salpingectomy on stimulation response during subsequent IVF cycle is unclear. Our meta-analysis showed no negative effect of salpingectomy on ovarian response parameters compared with other treatment options. Live birth and clinical pregnancy rates were higher in the salpingectomy group.

ABSTRACT

Salpingectomy is the most widely used treatment for hydrosalpinx. The effect of salpingectomy on the stimulation response during subsequent IVF treatment, however, remains unclear. The aim of this systematic review was to evaluate the ovarian response and pregnancy outcome of IVF treatment carried out after salpingectomy compared with other pre-IVF treatment options for hydrosalpinx. We conducted a literature search using *PubMed*, *Ovid MEDLINE*, *Google Scholar*, *ClinicalTrials.gov* and the *Cochrane Central Register of Controlled Trials*. Five randomized studies and nine observational studies were included in the systematic review and evaluated using Cochrane Collaboration's tool for randomized, Newcastle–Ottawa scale for observational studies and GRADE guidelines for certainty of evidence assessment. The mean number of retrieved oocytes was similar between the groups in randomized (mean difference [MD] = –0.03, 95% CI –0.75 to 0.70) and observational studies (MD = –0.15, 95% CI –2.32 to 2.02). Live birth (RR 1.59, 95% CI 1.17 to 2.16), clinical pregnancy (RR 1.27, 95% CI 1.02 to 1.57) and implantation rates (RR 1.55, 95% CI 1.16 to 2.08) were higher in the salpingectomy group in randomized studies. The present systematic review and meta-analysis showed that salpingectomy does not impair the ovarian response during subsequent IVF treatment.

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KEYWORDS

Hydrosalpinx
Hydrosalpinx aspiration
IVF
Salpingectomy
Sclerotherapy
Tubal occlusion

INTRODUCTION

The Fallopian tubes were named after Gabrielis Fallopius (Italy, 1523–1562), who initially described these structures accurately (*Phadnis and Irvine, 2013*). It was the Dutch scientist Reinier De Graaf (1641–1673), however, who developed a better understanding of the function of the Fallopian tube and depicted several pathological conditions of the tube, including tubal ectopic pregnancy.

> '…the eggs from which fetuses are to be generated pass from the 'testicles' through the tubes to the uterus and that a fetus is generated in a tube from no other cause than that an already fertilized egg gets caught for some reason or other in its transit. As such a fetus grows it prepares death for its mother'.

De Graaf also first described hydrosalpinx (*Ankum et al., 1996*). A substantial improvement in the knowledge of tubal function and pathology accelerated only after the introduction of IVF treatment 40 years ago (*Steptoe and Edwards, 1978*).

Tubal factors represent 25–35% of female factor infertility (*Honore et al., 1999*). One of the severe manifestations of tubal disease is hydrosalpinx, found in 10–30% of couples with infertility. Hydrosalpinx is a form of tubal damage that can be caused by intrinsic (ascending salpingitis) or extrinsic (peritonitis, endometriosis, pelvic surgery) factors (*Sotrel, 2009*). It is defined as a distally occluded, dilated, fluid-filled Fallopian tube (*Zegers-Hochschild et al., 2017*). The presence of hydrosalpinx or distal tubal occlusion affects fertility and IVF outcome (*Strandell et al., 2001*).

Hydrosalpinx has deleterious effects on IVF outcome, and several options to mitigate the effects of hydrosalpinx fluid on the embryo and implantation have been advocated. *Ducarme et al. (2006)* evaluated the management of hydrosalpinx among all registered IVF centres in France. Management varied from laparoscopic salpingectomy (67.6% of all centres), salpingectomy by laparotomy (1.8%), salpingostomy (21.6%), proximal tubal occlusion (9%), medical treatment with antibiotics (81.6%) or antibiotics with corticoids (18.4%), and ultrasound-guided aspiration (12.9%).

The most widely used treatment modality is salpingectomy. Concerns, however, about the negative effect of salpingectomy on ovarian reserve and on the stimulation response during subsequent IVF treatment have been raised (*Almog et al., 2011; Grynnerup et al., 2013*).

The purpose of this systematic review and meta-analysis was to assess the ovarian response and pregnancy outcome of IVF treatment carried out after salpingectomy compared with other pre-IVF treatment options of hydrosalpinx. We also conducted a comprehensive literature review of studies published in the last 40 years on the effect of hydrosalpinx on IVF outcome and hydrosalpinx before IVF treatment.

MATERIALS AND METHODS

Literature search

A systematic review based on a literature search using *PubMed*, *Ovid*, *MEDLINE*, *Google Scholar*, *ClinicalTrials.gov* and the *Cochrane Central Register of Controlled Trials* was conducted. No language or publication period restrictions were imposed.

The search strategy was based on the following medical subject heading terms and their combinations: 'hydrosalpinx', 'salpingostomy', 'salpingectomy' 'tubal occlusion' 'hysteroscopy' 'microinsert' 'Essure', 'hydrosalpinx aspiration', 'sclerotherapy', 'in-vitro fertilization', 'assisted reproductive technology', 'implantation'. The reference lists of identified studies were manually searched.

Selection criteria

All randomized controlled studies, cohort studies, case control studies and meeting abstracts on hydrosalpinx treatment that evaluated the stimulation response, IVF pregnancy rate and adverse events were included. Review articles, case series and case reports were excluded. Two authors (AV and TT) selected and evaluated studies independently. Any disagreements were resolved by a third author (WB). In cases of duplicate publication, the most recent and complete versions were selected.

Data extraction

The following data were obtained from all eligible studies: study design, year of publication, country, study period, age and number of patients, demographic data, hydrosalpinx treatment, total FSH stimulation dose, stimulation duration, number of retrieved oocytes, number of embryos per embryo transfer, implantation rate, clinical pregnancy rate (CPR) and live birth rate (LBR). The corresponding authors were contacted in cases of insufficient data.

The studies that evaluated the outcome of IVF treatment conducted after salpingectomy, compared with other pre-IVF treatments, were included in the meta-analysis. Primary outcome was number of retrieved oocytes. Secondary outcomes included LBR, CPR, implantation rate, total FSH dose, stimulation duration and the number of transferred embryos per cycle.

The systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) (*Moher et al., 2009*) and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines (*Stroup et al., 2000*). As all studies were extracted from previously published data, Institutional Review Board approval was not requested.

Data synthesis

Randomized controlled trials (RCTs) were assessed by the Cochrane Collaboration's tool for assessing the risk of bias (*Higgins et al, 2011*). Non-randomized studies were rated using the Newcastle–Ottawa scale. Additionally, the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used for certainty of evidence assessment of randomized and observational studies (*Guyatt et al., 2011*).

Continuous variables were expressed as a mean difference (MD) with 95% confidence intervals. Dichotomous results from each of the studies eligible for meta-analysis were expressed as relative risk (RR) with 95% CI. Mantel–Haenszel statistical method was used. The analysis of RCTs and observational studies was conducted separately, and subtotal results were presented in forest plots. In the meta-analysis of RCTs, data according to intention-to-treat (ITT) principle were used; LBR and CPR were calculated per number of randomized patients. Statistical heterogeneity was

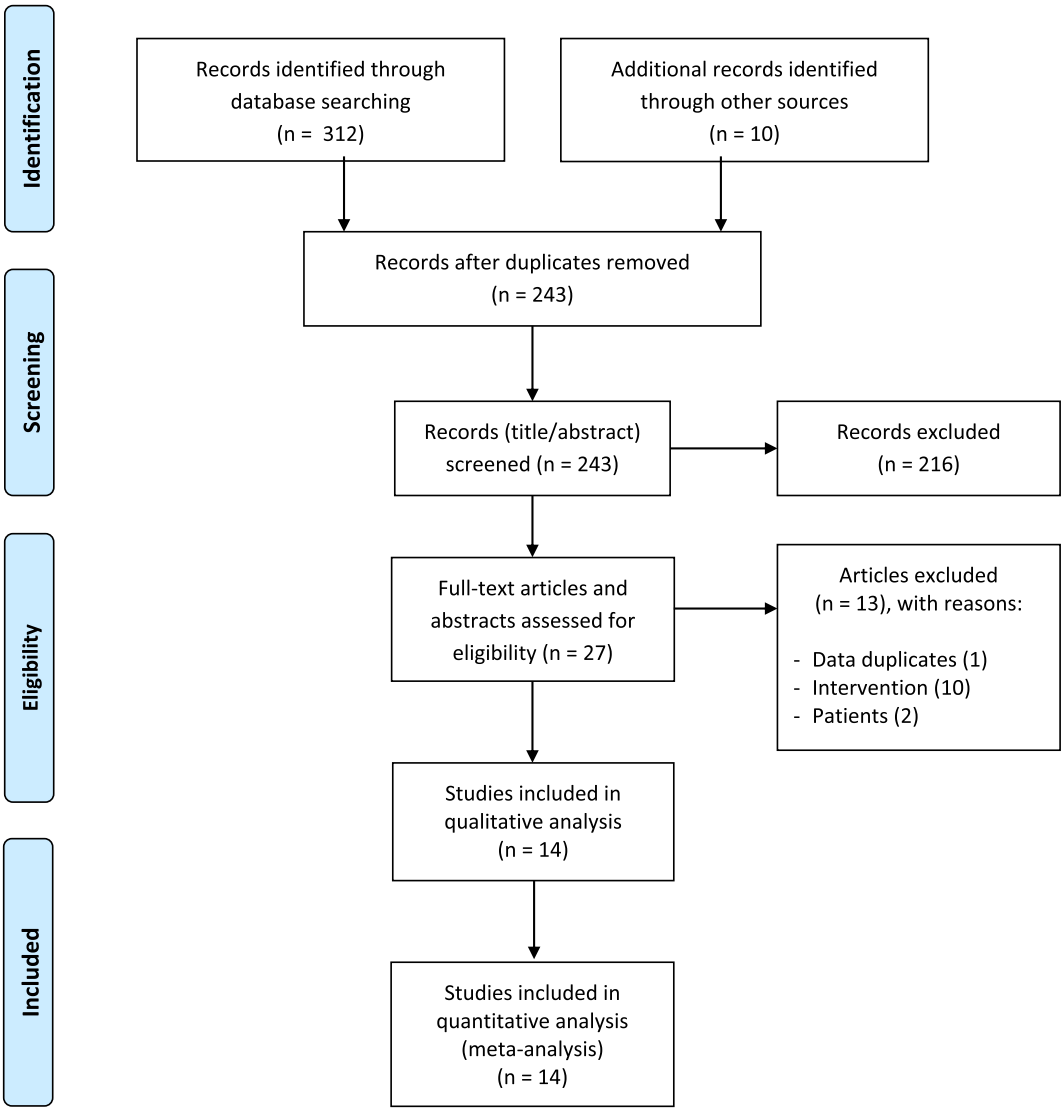

FIGURE 1 Literature search and selection based on PRISMA guidelines.
PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

evaluated by using the I-squared statistic method and considered absent if $P > 0.05$. I-squared values of 25%, 50% and 75% indicated low, moderate and high heterogeneity, respectively. A fixed-effects model was used in cases of no significant heterogeneity. A random-effects model was used when statistically significant heterogeneity was present. RevMan 5.3 Software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for meta-analysis.

RESULTS

Study selection

The PRISMA scheme for search and selection of literature is presented in FIGURE 1. A total of 322 articles fulfilled the search criteria. After duplicate records and title/abstract screen were removed, 27 records were selected for full-text review (TABLE 1). A total of 14 studies comparing IVF outcome after salpingectomy with other pre-IVF treatments of hydrosalpinx were included in the systematic review and were also eligible for our meta-analysis. They included five RCTs (*Kontoravdis et al., 2006; Moshin and Hotineanu, 2006; Fouda et al., 2015*; *Malhotra and Vignarajan, 2015*; *Dreyer et al., 2016*), two prospective cohort studies (*Matorras et al., 2013*; *Ni et al., 2013*) and seven retrospective cohort studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Gelbaya et al., 2006; Esinler et al., 2006; Nakagawa et al., 2008; Song et al., 2017; Na et al., 2012*). Date of publication ranged from 2000 to 2017. The number of cases varied between 17 and 482.

Data on total number of retrieved oocytes were insufficient in the study by *Malhotra and Vignarajan, 2015*. The corresponding authors were contacted twice using an Email address provided by the authors, but they did not respond. Thirteen studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Esinler et al., 2006*; *Gelbaya et al., 2006; Kontoravdis et al., 2006; Moshin and Hotineanu, 2006*; *Matorras et al., 2013*; *Na et al., 2012; Ni et al., 2013; Fouda et al., 2015*; *Malhotra and Vignarajan, 2015*; *Dreyer et al., 2016; Song et al., 2017*) included patients with uni- and bilateral hydrosalpinx. *Nakagawa et al. (2008)* evaluated patients with bilateral

TABLE 1 CHARACTERISTICS OF STUDIES SELECTED FOR FULL-TEXT REVIEW

Study	Country	Period	Design	Patients with hydrosalpinx (n)	Study group (n)	Control group (n)	Outcomes	Included or reason for exclusion
Salpingectomy								
Strandell et al., 1999	Sweden	1994–1998	RCT	204	Salpingectomy (116)	No intervention (88)	CPR, OPR, IR	No treatment in control group
Chanelles et al., 2011	France	2003–2007	RCS	81	Salpingectomy (46)	Salpingostomy (35)	CPR	No study and control groups comparison
Shelton et al., 1996	USA	1993–1994	RCS	15	Salpingectomy (15)	Pre-salpingectomy (15)	CRP, OPR	No treatment in control group
Orvieto et al., 2011	Israel	1995-2010	RCS	15	Salpingectomy (15)	Pre-salpingectomy (15)	CPR	No treatment in control group
Stewart et al., 2015	USA	2000–2013	RCS	55	Bilateral salpingectomy (14)	Unilateral salpingectomy (41)	LBR, ORR	Irrelevant control group
Bredkjaer et al., 1999	Denmark	1995-1997	RCCS	139	Salpingectomy (139)	No hydrosalpinx (139)	LBR, CPR, IR	Irrelevant control group
Laparoscopic proximal tubal ligation								
Stadtmauer et al., 2000	USA	1998–1999	RCS	60	LPTO (30)	Salpingectomy (15) No intervention (15) No hydrosalpinx (34)	CPR, IR, ORR	Included
Surrey and Schoolcraft, 2001	USA	NR	RCS	47	LPTO (15)	Salpingectomy (32) No hydrosalpinx (47)	CPR, IR, ORR	Included
Esinler et al., 2006	Turkey	NR	RCS	32	LPTO (16)	Salpingectomy (16)	LBR, CPR, IR, MR, ORR	Included
Kontoravdis et al., 2006	Greece	2000–2005	RCT	115	LPTO (50)	Salpingectomy (50) No intervention (15)	LBR, IR, CPR, OPR, MR, ORR	Included
Gelbaya et al., 2006	UK	2001–2004	RCS	168	LPTO /division/ (25)	Salpingectomy (40) No hydrosalpinx (103)	LBR, OPR, CPR, ORR, IR	Included
Nakagawa et al., 2008	Japan	2002–2006	RCS	17	LPTO /division/ (11)	Salpingectomy (6)	LBR, CPR, MR, ORR	Included
Ni et al., 2013	China	2007–2009	PCS	83	Bilateral LPTO (23)	Bilateral salpingectomy (26) Unilateral salpingectomty (34)	CPR, LBR, IR, ORR	Included
Malhotra and Vignarajan, 2015	India	2012–2014	RCT	75	LPTO (37)	Salpingectomy (38)	OPR, CPR, LBR, ORR, FR	Included
Moshin and Hotineanu, 2006	Moldova	NR	RCT	204	LPTO (78)	Salpingectomy (60) No intervention (66)	CPR, ORR,	Included
Kamal, 2012	Egypt	2009–2011	PCS	76	LPTO (19)	Salpingectomy (20) No hydrosalpinx (37)	OAPI, basal FSH, ORR.	Statistical difference in baseline parameters
Hysteroscopic tubal occlusion								
Matorras et al., 2013	Spain	2005–2010	PCS	63	HTO (15)	Salpingectomy (48) No hydrosalpinx (264)	CPR, ORR, FR	Included
Dreyer et al., 2016	Netherlands	2009–2014	RCT	85	HTO (42)	Salpingectomy (43)	OPR, IR, CPR, MR, LBR, ORR	Included
Ozgur et al., 2014	Turkey	2009–2012	RCS	102	HTO (23)	LPTO (76)	LBR, CPR	Irrelevant control group
Gonzalez et al., 2016	Spain	2008–2014	RCS	50	HTO (29)	Salpingectomy (21)	LBR, CPR, IR, MR, EPR,	Statistical difference in baseline parameters
Ultrasound-guided aspiration								
Sowter et al., 1997	UK	1991–1995	RCS	237	US aspiration (56)	No intervention (30)	OPR, CPR, IR	Irrelevant control group
Van Voorhis et al., 1998	United States	1993–1996	RCS	34	US aspiration (16)	No intervention (18)	OPR, CPR, IR	Irrelevant control group

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Table 1 – (continued)

Study	Country	Period	Design	Patients with hydrosalpinx (n)	Study group (n)	Control group (n)	Outcomes	Included or reason for exclusion
Fouda and Sayed, 2011	Egypt	2006–2010	RCT	110	US aspiration (55)	No intervention (55)	CPR, IR, OPR, ORR, MR	Irrelevant control group
Fouda et al., 2015	Egypt	2011–2014	RCT	160	US aspiration (80)	Salpingectomy (80)	LBR, CPR, IR, OPR, ORR, MR	Included
Ultrasound-guided sclerotherapy								
Song et al., 2017	China	2008–2014	RCS	482	Sclerotherapy (265)	Salpingectomy (108) US aspiration (109)	LBR, CPR, MR, IR, ORR	Included
Na et al., 2012	South Korea	2005–2012	RCS	97	Sclerotherapy (56)	Salpingectomy (41)	CPR, ORR, EPR	Included
Jiang et al., 2010	China	2005–2008	PCT	52	Sclerotherapy (33)	No intervention (19) No hydrosalpinx (47)	CPR, IR, ORR	Irrelevant control group, data duplication

CPR, clinical pregnancy rate; EPR, ectopic pregnancy rate; FR, fertilization rate; HTO, hysteroscopic tubal occlusion; IR, implantation rate; LBR, live birth rate; LPTO, laparoscopic proximal tubal occlusion; MR, miscarriage rate; OAPI, ovarian artery pulsatile index; OPR, ongoing pregnancy rate; ORR, oocyte retrieval rate; PCS, prospective cohort study; RCS, retrospective cohort study; RCCS, retrospective case-control study; RCT, randomized controlled trial; US, ultrasound.

hydrosalpinx. *Ni et al. (2013)* allocated patients with uni- and bilateral hydrosalpinx to the separate study groups. From this study, only the groups of patients who underwent bilateral tubal interruption and bilateral salpingectomy were included in our meta-analysis (*Ni et al., 2013*).

Quality assessment

The risk of bias assessment of included RCTs is shown in Supplementary Figure 1. Blinding of participants and personnel was not carried out in four studies (*Kontoravdis et al., 2006; Fouda et al., 2015*; *Malhotra and Vignarajan, 2015*; *Dreyer et al., 2016*) and was not carried out in one RCT (*Moshin and Hotineanu, 2006*). One study (*Kontoravdis et al., 2006*) did not report results according to the ITT principle. Three studies (*Moshin and Hotineanu, 2006; Fouda et al., 2015*; *Malhotra and Vignarajan, 2015*) did not present per protocol results. Only one study (*Dreyer et al., 2016*) presented the data according to the ITT and per protocol principles.

Overall quality of observational studies included in the meta-analysis was assessed using the Newcastle–Ottawa scale (Supplementary Table 1). All studies achieved scores seven to nine out of a maximum nine points; the main concerns were selecting non-exposed cohorts and study group allocation.

Supplementary Table 2 and Supplementary Table 3 show the GRADE certainty of evidence assessment of randomized and observational studies, respectively. The certainty of evidence for randomized studies was moderate to low owing to high risk of performance and reporting bias and high heterogeneity of data in stimulation duration and total FSH dose sub-analyses. Because of the bias-prone nature and the presence of significant heterogeneity of data in the mean number of retrieved oocytes, implantation rate, stimulation duration and number of transferred embryos sub-analyses, the certainty of evidence for included observational studies was low to very low.

IVF treatment outcome

Salpingectomy versus laparoscopic proximal tubal occlusion

IVF outcome in women with hydrosalpinx who underwent laparoscopic proximal tubal occlusion (LPTO) compared with salpingectomy was evaluated in three RCTs (*Kontoravdis et al., 2006; Moshin and Hotineanu, 2006*; *Malhotra and Vignarajan, 2015*) and six observational studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Gelbaya et al., 2006; Esinler et al., 2006; Nakagawa et al., 2008; Ni et al., 2013*). Analysis of the number of retrieved oocytes was conducted in two RCTs (*Moshin and Hotineanu, 2006; Kontoravdis et al., 2006*) and all six observational studies. Our meta-analysis showed no statistical difference in the number of retrieved oocytes between salpingectomy and LPTO groups in RCTs (MD = 0.35, 95% CI –1.03 to 1.74) and observational studies (MD = –0.46, 95% CI –2.47 to 1.55).

Live birth rate was evaluated in one RCT (*Kontoravdis et al., 2006*) and four observational studies (*Gelbaya et al., 2006; Esinler et al., 2006; Nakagawa et al., 2008; Ni et al., 2013*) and was similar between the groups (RR 1.13; 95% CI 0.85 to 1.50). Clinical pregnancy rate was assessed in all nine studies included in the current analysis (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Esinler et al., 2006; Gelbaya et al., 2006; Kontoravdis et al., 2006; Moshin and Hotineanu, 2006; Nakagawa et al., 2008; Ni et al., 2013*; *Malhotra and Vignarajan, 2015*) and was also similar (RR 1.00, 95% CI 0.82 to 1.21). Implantation rate was presented in one RCT (*Kontoravdis et al., 2006*) and four observational studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Gelbaya et al., 2006; Ni et al., 2013*). Meta-analysis of observational studies showed similar implantation rate between the groups (RR 1.06, 95% CI 0.79, 1.42) (FIGURE 2).

Analysis of observational studies (*Surrey and Schoolcraft, 2001; Gelbaya et al., 2006; Esinler et al., 2006; Ni et al., 2013*) demonstrated longer stimulation duration in the LPTO group (MD = –0.50, 95% CI –0.81 to –0.19). Total FSH dose was evaluated in two RCTs (*Kontoravdis et al., 2006*; *Malhotra and Vignarajan, 2015*) and three observational studies (*Esinler et al., 2006; Gelbaya et al., 2006; Ni et al., 2013*) and was similar between the groups (MD = 7.09, 95% CI –164.93 to –179.10). Mean number of transferred embryos were presented in six studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Moshin and Hotineanu, 2006; Kontoravdis et al., 2006; Esinler et al., 2006; Ni et al., 2013*) and was also similar (MD = –0.12; 95% CI –0.43 to 0.20).

Salpingectomy versus hysteroscopic tubal occlusion

One RCT (*Dreyer et al., 2016*) and one observational study (*Matorras et al., 2013*) assessed IVF outcome after hysteroscopic tubal occlusion (HTO) compared with salpingectomy. Both included studies used Essure microinsert for hysteroscopic tubal occlusion. The number of retrieved oocytes was similar between the groups (MD = 3.50, 95% CI –3.46 to 10.45) in total analysis of both studies. The total FSH dose, stimulation duration, implantation rate and LBR were reported only in one study (*Dreyer et al., 2016*). The HTO group was characterized by longer stimulation with lower implantation rate and LBR. Clinical pregnancy rate was presented in both included studies and was similar between the groups (MD = 1.68, 95% CI 1.01 to 2.78) (FIGURE 3).

Salpingectomy versus ultrasound-guided hydrosalpinx aspiration

One RCT (*Fouda et al., 2015*) and one observational study (*Song et al., 2017*) compared IVF outcome after salpingectomy versus ultrasound-guided aspiration. No difference in the number of retrieved oocytes was found between the groups (MD = –1.17, 95% CI –2.63 to 0.29). Total analysis of two included studies showed higher LBR (MD = 1.94, 95% CI 1.40 to 2.68), CPR (MD = 1.64, 95% CI 1.24 to 2.17) and implantation rate (MD = 1.67, 95% CI 1.27 to 2.21) in the salpingectomy group. Those parameters were similar between the groups in the only included RCT (*Fouda et al., 2015*). The mean number of transferred embryos was similar between the groups (MD = 0.04, 95% CI –0.06 to 0.14) (FIGURE 4).

Salpingectomy versus ultrasound-guided hydrosalpinx sclerotherapy

Outcome of IVF in patients who underwent salpingectomy compared with sclerotherapy was evaluated in two observational studies (*Na et al., 2012, Song et al., 2017*). The number of retrieved oocytes was evaluated in both studies and was similar between the groups (MD = 3.13, 95% CI –8.21 to 1.96) Data on LBR, implantation rate, stimulation duration, total FSH dose and number of embryos per transfer were reported in one study (*Song et al., 2017*), and no difference was found between the two groups. Clinical pregnancy rate was evaluated in both studies and was also similar (MD = 1.14, 95% CI 0.92 to 1.41) (FIGURE 5).

Salpingectomy versus non-salpingectomy treatments

Outcome of IVF after salpingectomy was additionally compared with all other hydrosalpinx treatment modalities, including LPTO, HTO, ultrasound-guided aspiration and sclerotherapy (non-salpingectomy treatment group). As the study by *Song et al. (2017)* included three groups (salpingectomy, sclerotherapy and ultrasound-guided aspiration), only the comparison between patients who underwent salpingectomy and sclerotherapy was included in the current analysis.

The mean number of retrieved oocytes was evaluated in 13 studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Esinler et al., 2006; Gelbaya et al., 2006; Kontoravdis et al., 2006; Moshin and Hotineanu, 2006; Nakagawa et al., 2008*; *Matorras et al., 2013*; *Na et al., 2012; Ni et al., 2013; Fouda et al., 2015; Dreyer et al., 2016; Song et al., 2017*) and was similar between the groups in RCTs (MD = –0.03, 95% CI –0.75 to 0.70) and observational studies (MD = –0.15, 95% CI –2.32 to 2.02).

Live birth rate was assessed in eight studies (*Esinler et al., 2006; Gelbaya et al., 2006; Kontoravdis et al., 2006; Nakagawa et al., 2008; Ni et al., 2013; Fouda et al., 2015; Dreyer et al., 2016; Song et al., 2017*) and was higher in the salpingectomy group when only RCTs were evaluated (RR 1.59; 95% CI 1.17, 2.16). Clinical pregnancy rate was evaluated in 14 studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Esinler et al., 2006; Gelbaya et al., 2006; Kontoravdis et al., 2006; Moshin and Hotineanu, 2006; Nakagawa et al., 2008*; *Matorras et al., 2013*; *Na et al., 2012; Ni et al., 2013; Fouda et al., 2015*; *Malhotra and Vignarajan, 2015*; *Dreyer et al., 2016; Song et al., 2017*) was also higher in the salpingectomy group in RCTs (RR 1.27, 95% CI 1.02 to 1.57) and similar in observational studies (RR 1.08, 95% CI 0.91 to 1.27). Implantation rate was presented in eight studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Gelbaya et al., 2006; Kontoravdis et al., 2006; Ni et al., 2013; Fouda et al., 2015; Dreyer et al., 2016; Song et al., 2017*), and was higher in the salpingectomy group in RCTs (RR 1.55; 95% CI 1.16 to 2.08) and similar in observational studies (RR 1.11; 95% CI 0.92 to 1.33).

Stimulation duration was presented in nine studies (*Surrey and Schoolcraft, 2001; Esinler et al., 2006; Gelbaya et al., 2006; Kontoravdis et al., 2006; Ni et al., 2013; Fouda et al., 2015*; *Malhotra and Vignarajan, 2015*; *Dreyer et al., 2016; Song et al., 2017*), and was similar in RCTs (MD = –0.31, 95% CI –0.99 to 0.36) and longer in observational studies (MD = –0.40; 95% CI –0.69 to –0.11) in the non-salpingectomy group. Total FSH dose was evaluated in eight studies (*Esinler et al., 2006; Gelbaya et al., 2006; Kontoravdis et al., 2006; Ni et al., 2013; Fouda et al., 2015*; *Malhotra and Vignarajan, 2015*; *Dreyer et al., 2016; Song et al., 2017*), and was higher in the non-salpingectomy group in RCTs (MD = –159.01, 95% CI –289.21 to –28.80) and similar in observational studies (MD = 65.85, 95% CI –57.73 to 189.42).

The number of transferred embryos per cycle was presented in 10 studies (*Stadtmauer et al., 2000; Surrey and Schoolcraft, 2001; Esinler et al., 2006; Kontoravdis et al., 2006; Moshin and Hotineanu, 2006*; *Matorras et al., 2013*; *Ni et al., 2013; Fouda et al., 2015; Dreyer et al., 2016; Song et al., 2017*) and was similar between salpingectomy and non-salpingectomy groups in RCTs (MD = –0.03, 95% CI –0.11, 0.04) and observational studies (MD = 0.00, 95% CI –0.33, 0.33) (FIGURE 6).

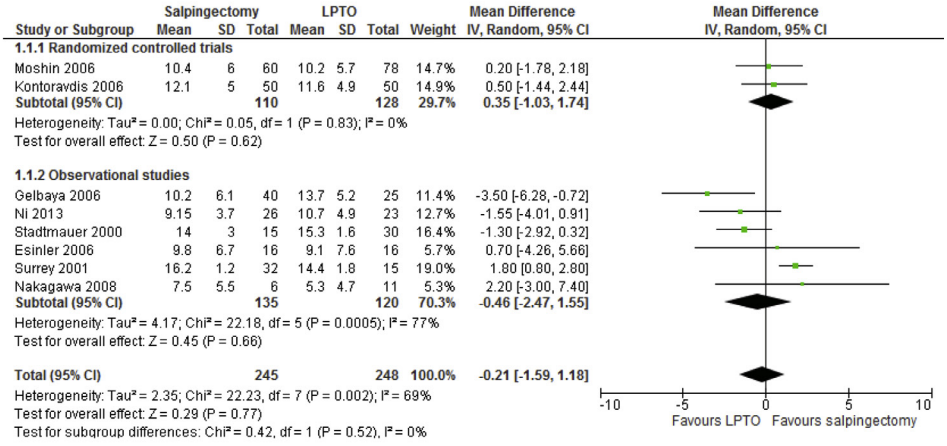
DISCUSSION

Forty years of IVF experience has shown that the presence of hydrosalpinx impairs IVF outcome. Yet, optimal pre-IVF treatment remains unclear. The most widely used option is salpingectomy. In theory, it might affect ovarian blood flow and reduce ovarian response during subsequent IVF cycles (*Almog et al., 2011; Grynnerup et al., 2013*). The results of our systematic review and meta-analysis showed that the number of retrieved oocytes and total FSH dose between the salpingectomy group compared with the non-salpingectomy treatment group were similar in both RCTs and observational studies. The live birth, clinical pregnancy and implantation rates in the salpingectomy group were higher than in the non-salpingectomy treatment group.

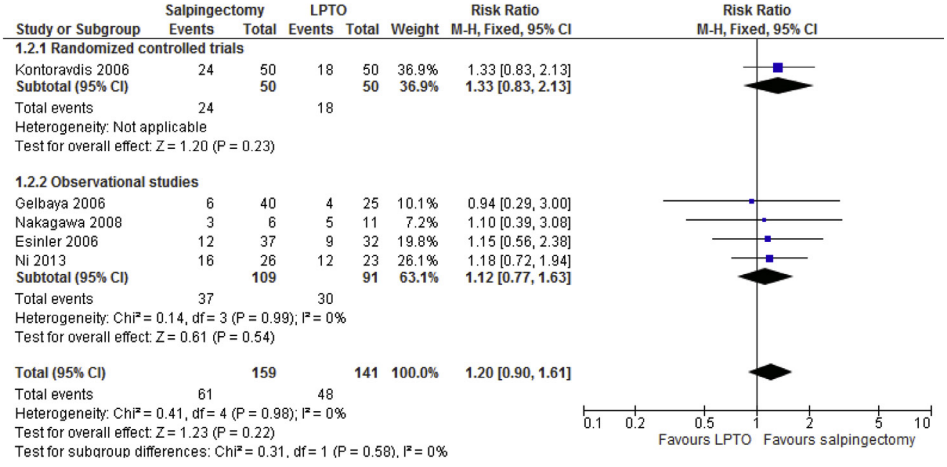
Effect of hydrosalpinx on IVF outcome

The presence of hydrosalpinx before IVF treatment adversely affects

1. Mean number of retrieved oocytes



2. Live birth rate per IVF cycle started*



3. Clinical pregnancy rate per IVF cycle started*

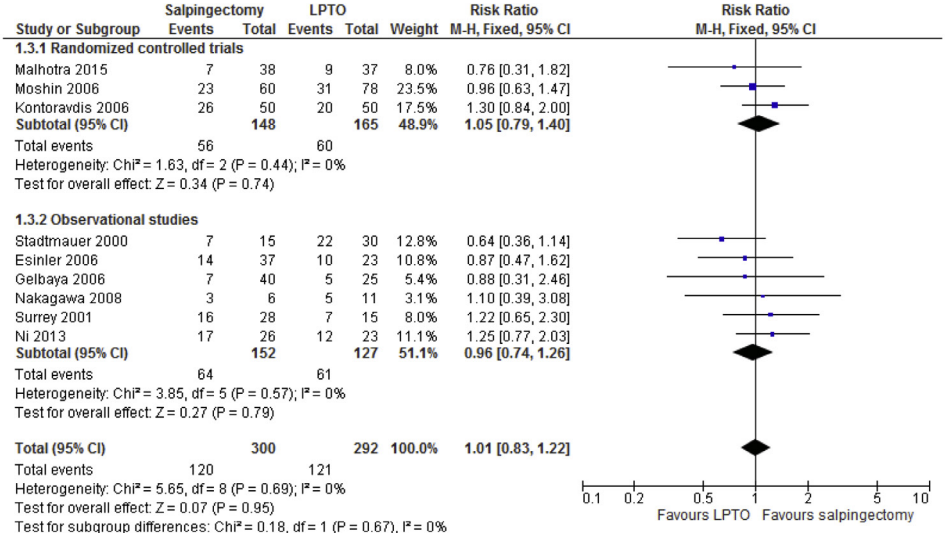
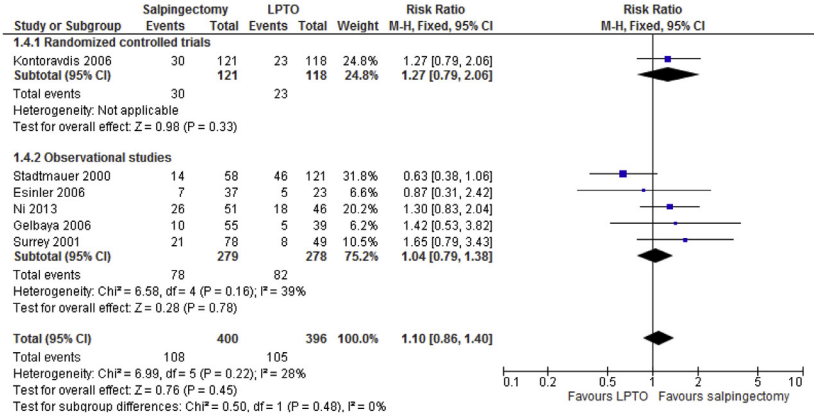
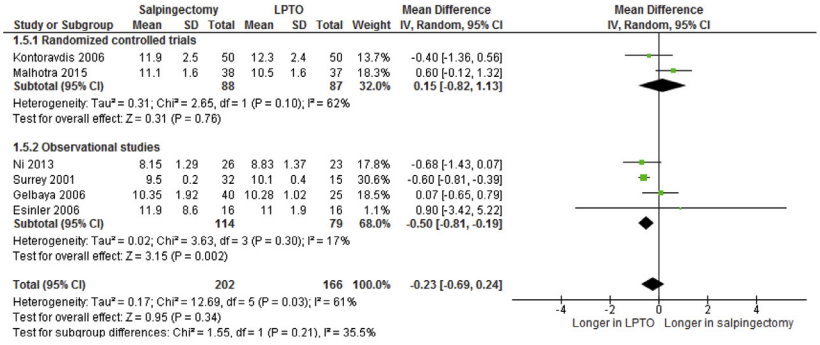


FIGURE 2 Salpingectomy versus laparoscopic proximal tubal ligation (LPTO) (IVF treatment outcome). * Per randomized patient for randomized controlled trials; **per total number of transferred embryos.

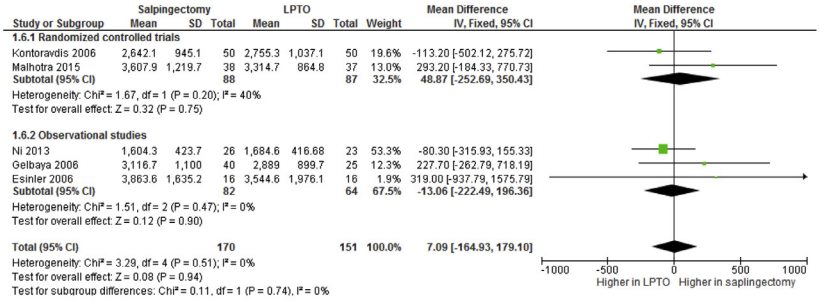
4. Implantation rate



5. Stimulation duration (days)



6. Total FSH dose (IU)



7. Mean number of transferred embryos

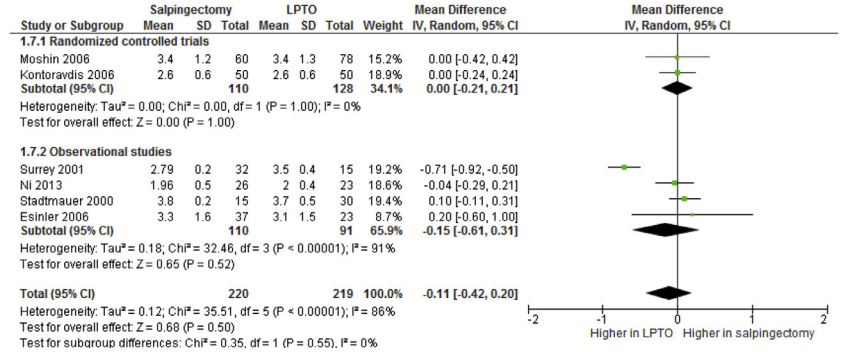
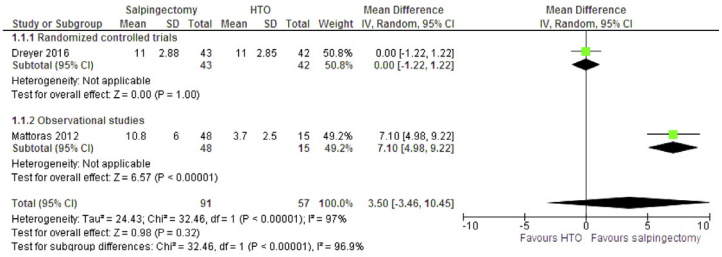
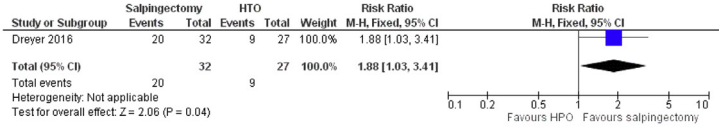


FIGURE 2 *(Continued)*

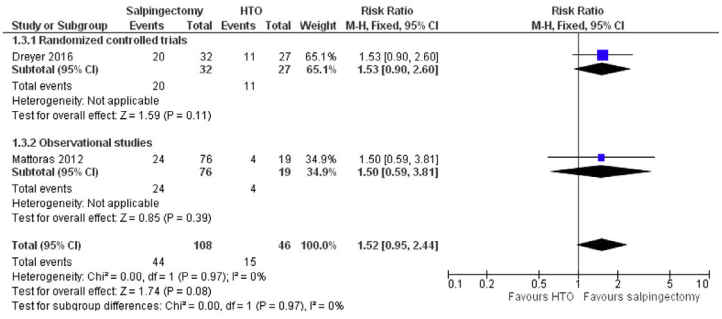
1. Mean number of retrieved oocytes



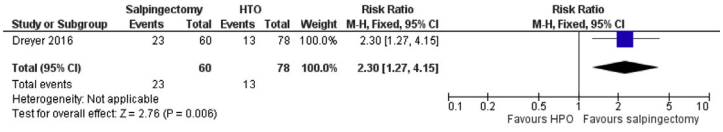
2. Live birth rate per IVF cycle started*



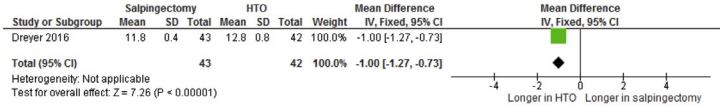
3. Clinical pregnancy rate per IVF cycle started*



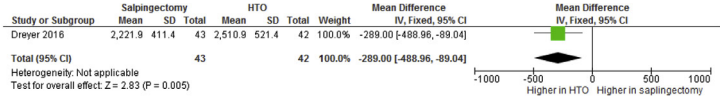
4. Implantation rate



5. Stimulation duration (days)



6. Total FSH dose (IU)



7. Mean number of transferred embryos

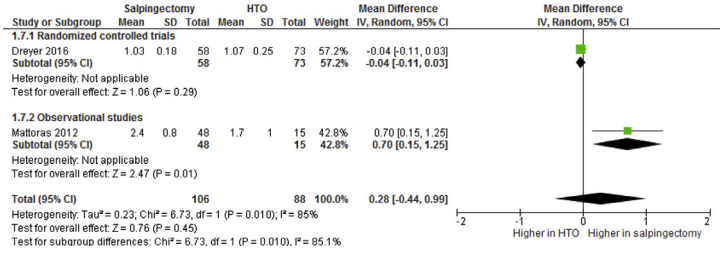
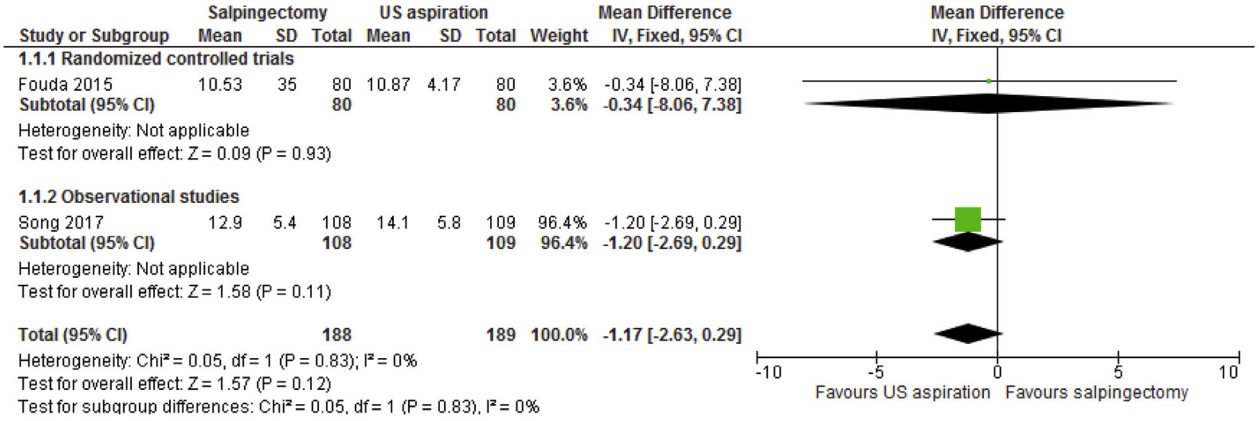
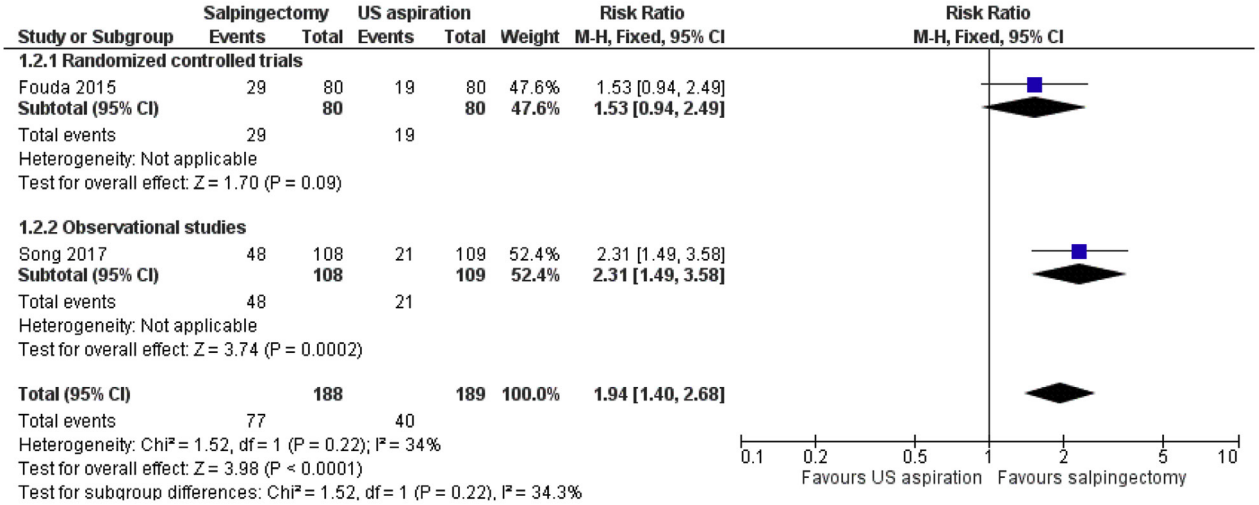


FIGURE 3 Salpingectomy versus hysteroscopic tubal occlusion (HTO) (IVF treatment outcome).*Per randomized patient for RCTs; **per total number of transferred embryos.

1. Mean number of retrieved oocytes



2. Live birth rate per IVF cycle started*



3. Clinical pregnancy rate per IVF cycle started*

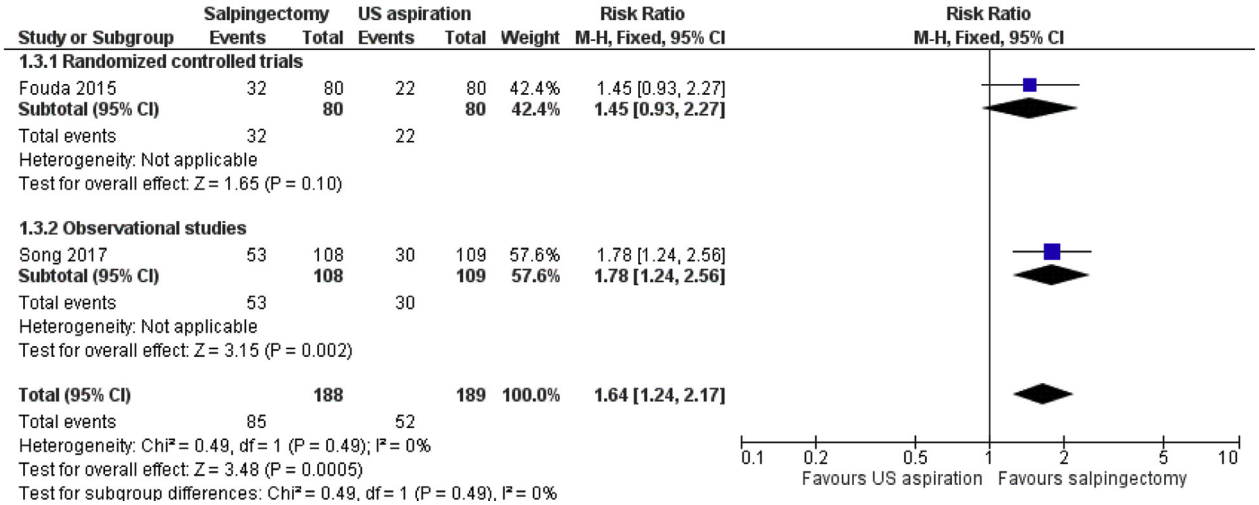
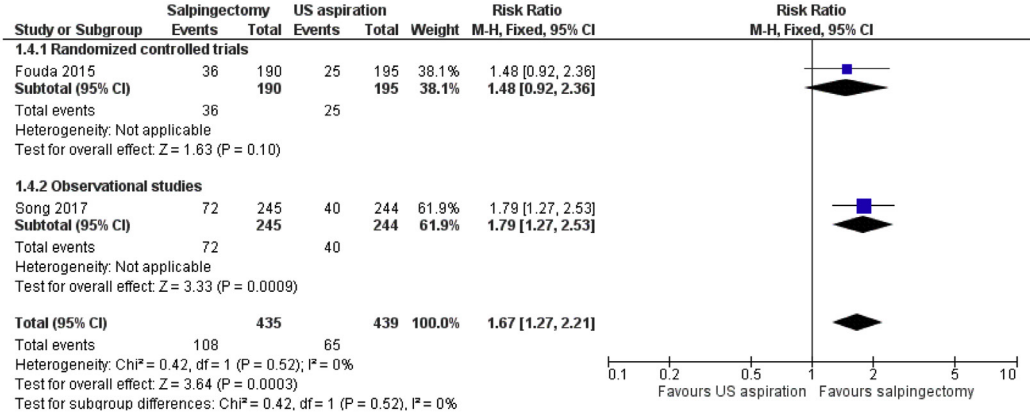
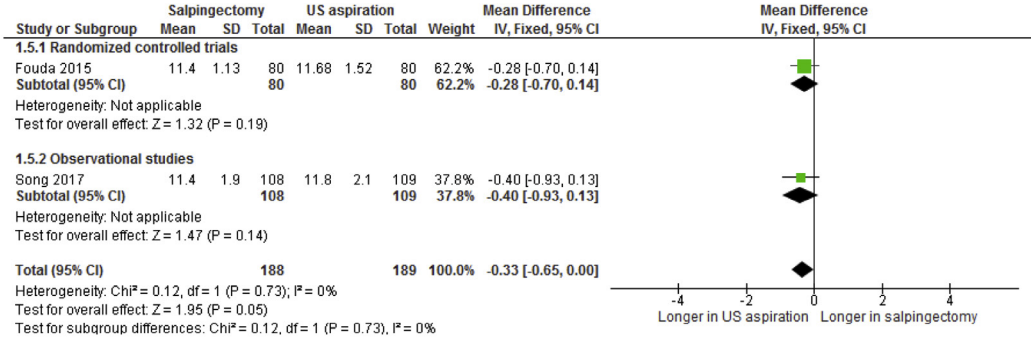


FIGURE 4 Salpingectomy versus ultrasound aspiration (IVF treatment outcome). *per randomized patient for RCTs; **per total number of transferred embryos.

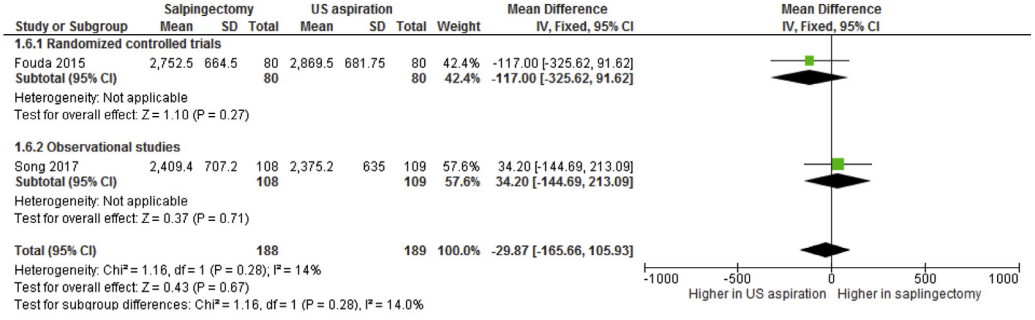
4. Implantation rate



5. Stimulation duration (days)



6. Total FSH dose (IU)



7. Mean number of transferred embryos

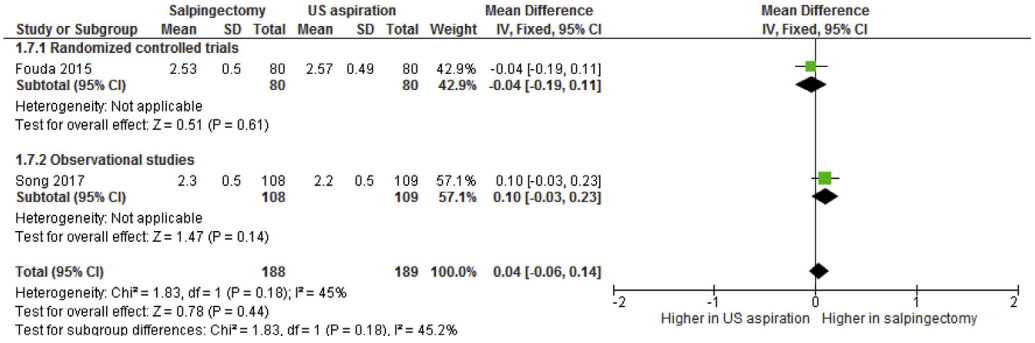
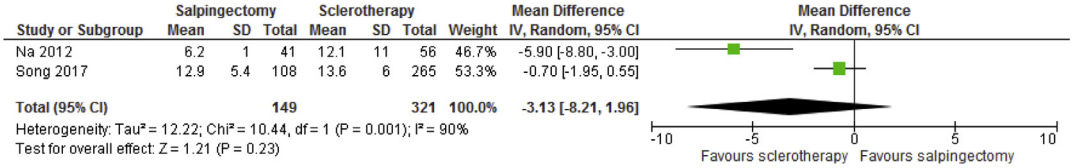


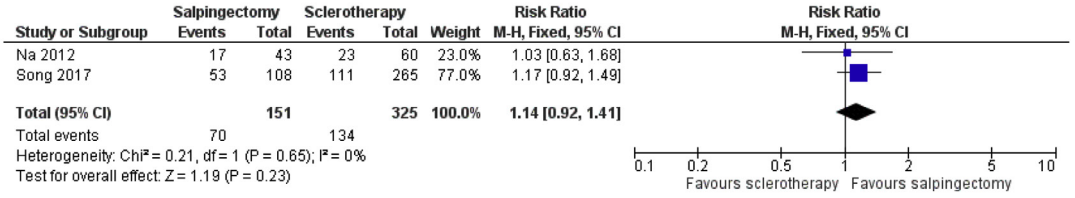
FIGURE 4 *(Continued)*

1. Mean number of retrieved oocytes



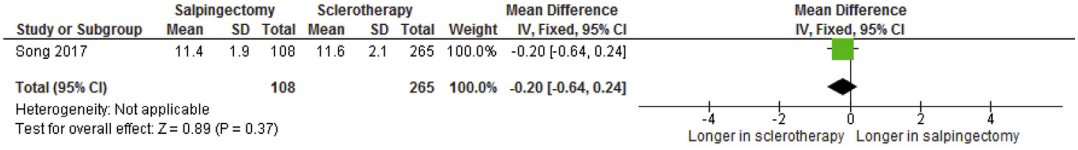
2. Live birth rate per IVF cycle started

3. Clinical pregnancy rate per IVF cycle started

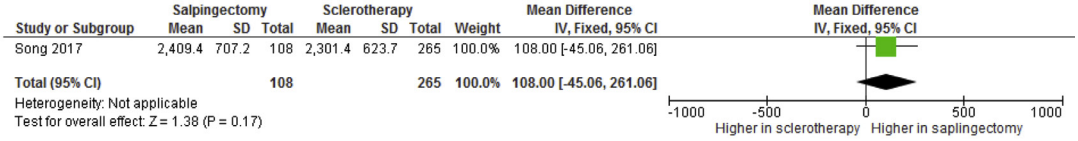


4. Implantation rate

5. Stimulation duration (days)



6. Total FSH dose (IU)



7. Mean number of transferred embryos

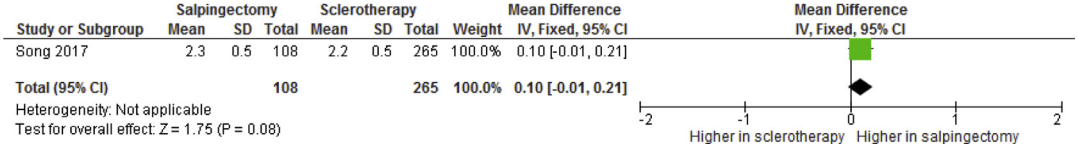
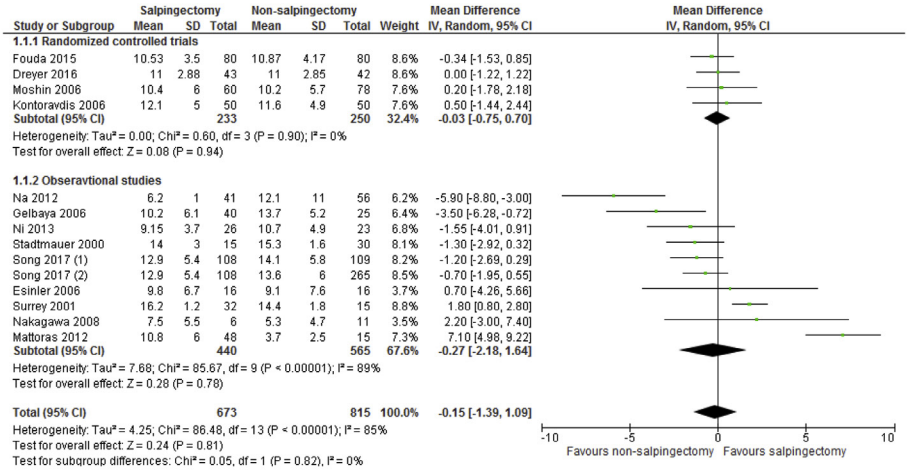
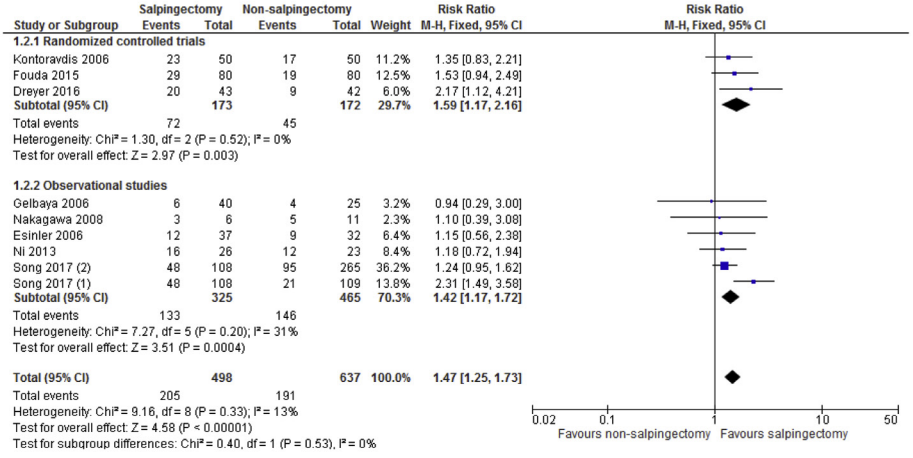


FIGURE 5 Salpingectomy versus sclerotherapy (IVF treatment outcome). *Per total number of transferred embryos.

1. Mean number of retrieved oocytes



2. Live birth rate per IVF cycle started*



3. Clinical pregnancy rate per IVF cycle started*

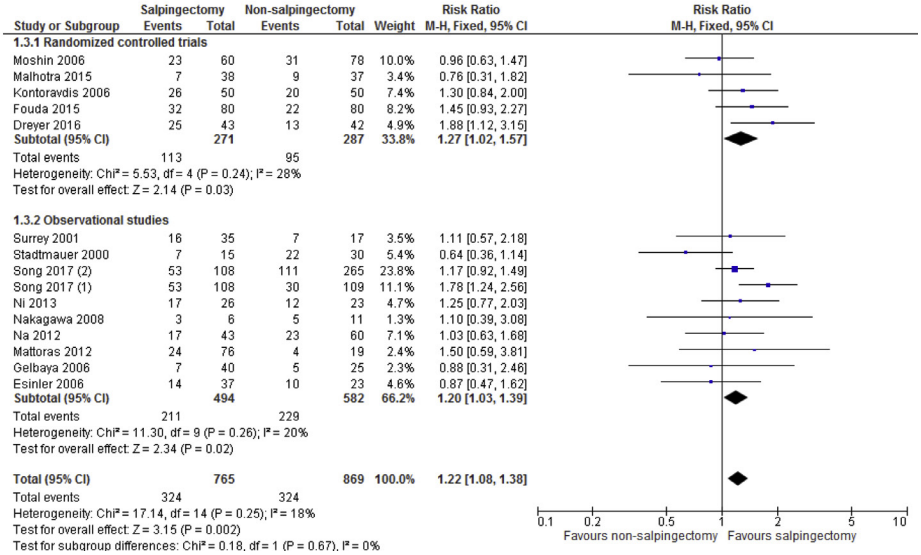
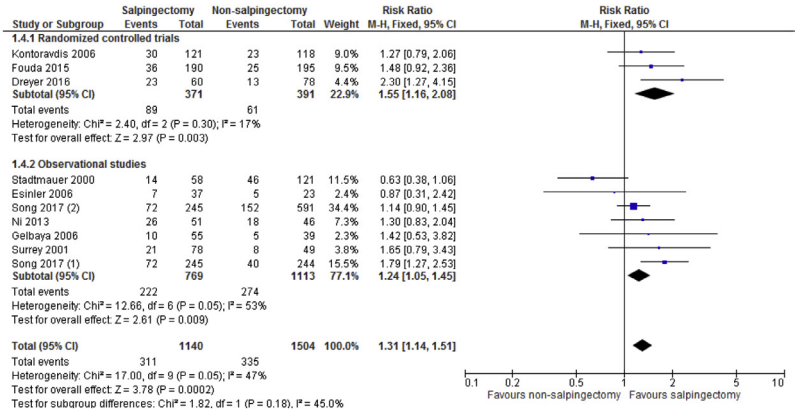
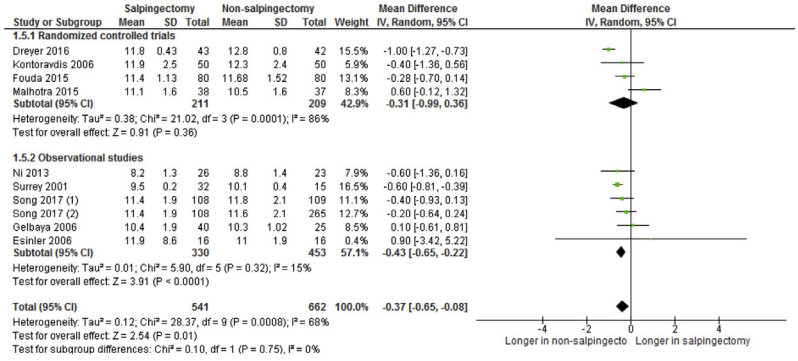


FIGURE 6 Salpingectomy versus non-salpingectomy treatment (IVF treatment outcome).*Per randomized patient for RCTs; **per total number of transferred embryos.

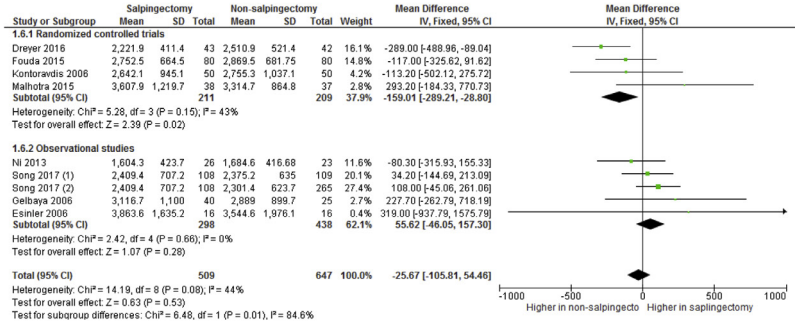
4. Implantation rate



5. Stimulation duration (days)



6. Total FSH dose (IU)



7. Mean number of transferred embryos

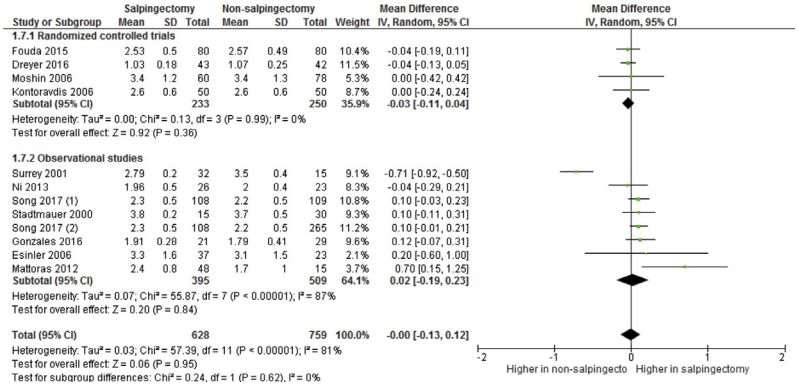


FIGURE 6 *(Continued)*

pregnancy rates and increases the risk of spontaneous miscarriage (*Strandell et al., 1994; Vandromme et al., 1995; Blazar et al., 1997*). In a meta-analysis of 1144 IVF cycles in women with hydrosalpinx and 5569 others without hydrosalpinx, the implantation and pregnancy rates were about 50% lower in women with hydrosalpinx (*Zeyneloglu et al., 1998*). The exact mechanism remains unclear. This could, however, be related to mechanical effects of hydrosalpinx fluid, toxic effects on the gamete or embryo and alteration of endometrial receptivity (*Ozmen et al., 2007*).

In one study, the investigators examined biochemical components, microorganisms and cytokine concentrations in the hydrosalpinx fluid of 33 women who underwent laparoscopic surgery. Compared with blastocyst culture medium, hydrosalpinx fluid had higher pH and $HCO_3(-)$ ($P < 0.05$ and $P < 0.01$, respectively) and lower K^+, Ca^{2+}, Mg^{2+}, and glucose levels ($P < 0.01$, $P < 0.05$, $P = 0.006$ and $P = 0.007$, respectively) (*Bao et al., 2017*).

Results of studies evaluating the effects of hydrosalpinx fluid on embryo development have been mixed. In a study of 183 frozen donor embryos, no difference was observed in in-vitro development of human embryos in hydrosalpinx fluid at concentrations of 50 and 100%, and in standard medium (*Strandell et al., 1998*). Another study of animal models evaluated the development of 587 two-cell murine embryos in fetal calf serum with RPM1 medium or in endometrial co-culture system with varying concentrations of hydrosalpinx fluid (0, 1%, 10%, 50%, 75%, and 100%). For each stage of embryogenesis, the investigators found reduced development with increasing concentrations of hydrosalpinx fluid. When an endometrial co-culture system was used, development was not inhibited until exposure reached a minimum of 75% hydrosalpinx fluid. This could be related to a detoxifying effect of the endometrium (*Spandorfer et al., 1999*).

Excessive intrauterine fluid during implantation process shown in a mouse model could be another reason for abnormal implantation leading to embryo growth retardation, miscarriage and increased pregnancy loss, similar to the adverse effects observed in women with hydrosalpinx (*Lu et al., 2013*).

The presence of hydrosalpinx could also affect uterine and ovarian blood flows. In a study of 120 women with or without hydrosalpinx, investigators found significantly lower endometrial vascularization ($P = 0.002$), flow ($P = 0.041$), vascularization flow ($P = 0.018$) indices as well as lower ovarian vascularization ($P = 0.011$) and vascularization flow ($P = 0.015$) indices in the hydrosalpinx group. The endometrial thickness, uterine artery pulsatility and resistance index, ovarian artery pulsatility and resistance index, endometrial volume, ovarian volume and flow index, however, were not significantly different between the two groups. The investigators concluded that hydrosalpinx is associated with impaired endometrial and ovarian blood flows, which may adversely affect endometrial receptivity and oocyte quality (*El-Mazny et al., 2016*).

Hydrosalpinx treatment before IVF

Salpingectomy

The beneficial effects of pre-IVF salpingectomy have been shown in randomized studies. In a Cochrane meta-analysis (*Johnson et al., 2010*) involving 646 women in three RCTs (*Déchaud et al, 1998; Strandell et al, 1999; Kontoravdis et al, 2006*), investigators reported a higher ongoing pregnancy rate in the pre-IVF treatment group compared with those not treated beforehand. The benefits seem to be higher when the hydrosalpinx is bilateral, visible on ultrasound, or both (*Strandell et al, 1999*).

Salpingectomy removes the chronically infected hydrosalpinx decreasing the risk of infection after oocyte retrieval, adnexal torsion and increasing the accessibility of the ovary. It is a surgical procedure, however, and could be challenging, especially in the presence of dense periadnexal adhesions. Salpingectomy could also affect the ovarian blood flow and reduces the ovarian response during consequent IVF cycles (*Almog et al., 2011; Grynnerup et al., 2013*). Yet, results of studies on this subject have been mixed.

In a prospective study involving 134 cycles, the investigators evaluated the effects of various tubal surgery on ovarian reserve and the subsequent IVF and embryo transplantation outcome in women with tubal infertility. They found no significant differences in ovarian reserve and response to gonadotrophin and IVF and embryo transplantation outcome among all groups (*Ni et al., 2013*). Another prospective study (*Grynnerup et al., 2013*) involving 71 women showed that serum AMH levels in the salpingectomy group (16.1 [5.2–54] pmol/l) were lower than those in the control group (23.4 [3.5-50], pmol/l; $P = 0.04$). The salpingectomy group in the study, however, included only 16 patients. A meta-analysis including 12 retrospective and six prospective studies did not reveal any significant differences in the peak oestradiol level, the total gonadotrophin dose used for stimulation and number of oocytes retrieved between salpingectomy ($n = 657$) and control ($n = 825$) groups. The indication of salpingectomy in their study was hydrosalpinx removal before IVF or for the treatment of tubal ectopic pregnancy. The number of pregnancies before and after salpingectomy did not differ significantly (OR 1.180, 95% CI 0.854 to 1.630) (*Yoon et al., 2016*).

Another meta-analysis including 25 studies showed lower numbers of oocytes retrieved after unilateral salpingectomy (inverse variance [IV] −0.17; 95% CI −0.27 to −0.06) and bilateral salpingectomy (IV −0.20, 95% CI −0.32 to −0.08) compared with the control group. In addition, a significant reduction was found between the number of oocytes retrieved from the ipsilateral and contralateral ovary (IV 0.25, 95% CI −0.40 to −0.10). Bilateral salpingectomy can also lead to increased FSH levels (IV 0.39, 95% CI 0.20 to 0.59) (*Fan and Ma, 2016*). The increase in FSH and decrease in AMH levels suggest reduced ovarian reserve. The subtotal estimates for randomized and observational studies, however, were not presented in this meta-analysis. Additionally, the quality of included studies was generally poor.

We recommend carrying out pre-IVF salpingectomy close to the tube to avoid compromising the blood supply to the ovary (**FIGURE 7**). This hypothesis, however, has not been clinically tested.

In the present meta-analysis, IVF outcome after salpingectomy was compared with non-salpingectomy treatment options. No adverse effect of salpingectomy on the number of retrieved oocytes, stimulation duration and total FSH dose was found. Live birth

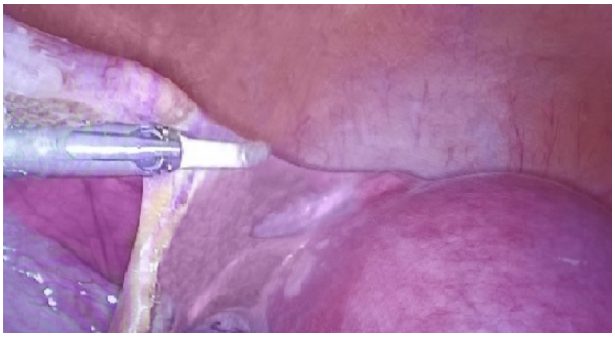


FIGURE 7 Salpingectomy performed close to the tube.

rate, CPR and implantation rate were higher in the salpingectomy group in RCTs.

Laparoscopic proximal tubal occlusion

Another technique to prevent hydrosalpinx fluid entering the uterine cavity is by occluding the proximal portion of the Fallopian tube at laparoscopy. A meta-analysis showed that ongoing IVF pregnancy rates of proximal tubal occlusion (RR 3.22, 95% CI 1.27 to 8.14) and salpingectomy (RR 2.24, 95% CI 1.27 to 3.95) were superior to no intervention (*Tsiami et al., 2016*). *Kontoravdis et al. (2006)* compared the efficacy of the two treatment methods prospectively. They included 106 patients with unilateral or bilateral hydrosalpinx and reported similar ongoing pregnancy rates in salpingectomy and proximal tubal occlusion groups (OR 1.6, 95% CI 0.7 to 3.6). These were significantly higher than in the no intervention group (OR, 12.5, 95% CI 1.5 to 103.1). The results according to the ITT principle, however, were not reported in this randomized trial (*Kontoravdis et al., 2006*). A meta-analysis of eight studies demonstrated a similar IVF clinical pregnancy rate (39.6% versus 41.6%; RR 0.98, 95% CI 0.79 to 1.21) and live birth rate (31.7% versus 29.7%; RR 1.07, 95% CI 0.76 to 1.51) between laparoscopic salpingectomy and proximal tubal occlusion (*Xu et al., 2017*).

Occlusion of the proximal tube can be carried out with electrocoagulation or with clips. It seems that the use of electrocoagulation impairs ovarian blood supply. This is reflected in decreased antral follicle count (AFC) 10 months after surgery. In a series of 88 women, AFC in the electrocoagulation group was 10.5 ± 2.3 and in the mechanical clip group was 11.9 ± 2.1 (P = 0.003) (*Goynumer et al., 2009*). As endoscopic clips are designed for normal uterine tubes, however, there is a risk of clip dislodgement, when it is applied on a significantly dilated tube (*Varma and Gupta, 2004*).

In our meta-analysis, LPTO was as effective as salpingectomy in number of retrieved oocytes, LBR, CPR, implantation rate and total FSH dose. Laparoscopic proximal tubal occlusion is technically less demanding (*Tulandi and Marzal, 2012*) and may be considered a valid alternative to salpingectomy in hydrosalpinx treatment, especially in women with severe periadnexal adhesions preventing access to the distal tube.

Hysteroscopic tubal occlusion

Hysteroscopic placement of micro insert occluding the proximal part of the tube before IVF treatment has been advocated. This procedure is particularly useful for women who are poor laparoscopic candidates (*Tulandi and Marzal, 2012; Ozgur et al., 2014*). One of the devices is Essure (Bayer Pharma AG, Germany), which was approved by the US Food and Drug Federation for tubal sterilization. The device and the resulting fibrosis of the tubal lumen occluded the tube (*Matorras et al., 2013*).

The first reported IVF live birth after Essure placement in an obese woman with hydrosalpinx and extensive pelvic adhesions was reported in 2005 (*Rosenfield et al., 2005*). Subsequently, *Dreyer et al. (2016)* conducted a two-centre randomized study comparing the efficacy of hysteroscopic proximal tubal occlusion with Essure (n = 42) and laparoscopic salpingectomy (n = 43) in women undergoing IVF and intracytoplasmic sperm injection. The ongoing pregnancy rate per patient after hysteroscopic proximal occlusion (26.2%) was lower than that after laparoscopic salpingectomy (55.8%) (absolute difference: 29.6%, 95% CI 7.1 to 49.1; RR 0.47; 95% CI 0.27 to 0.83). The investigators reported a protocol violation rate of up to 24% explained by the long waiting period of the scheduled surgery and IVF treatment (*Dreyer et al., 2016*). A systematic review of 115 women pretreated with Essure placement before IVF showed 38.6% pregnancy rate (95% CI 30.9 to 46.8%) and 27.9% live birth rate (95% CI 21.1 to 35.8%) (*Arora et al., 2014*).

In a recent meta-analysis, investigators evaluated the IVF outcome of patients with hydrosalpinx treated with Essure, laparoscopic salpingectomy and proximal tubal occlusion. The LBR and CPR after Essure treatment were significantly lower than those after laparoscopic surgery (salpingectomy and proximal tubal occlusion), with a CPR of 34.1% versus 44.0% (RR 0.71; 95% CI 0.51 to 0.98) and an LBR of 22.2% versus 37.4% (RR 0.57; 95% CI 0.35 to 0.91) (*Xu et al., 2017*).

Essure placement has been associated with pelvic pain necessitating removal of the device (Lannon and Lee, 2007). The incidence of acute pelvic pain after Essure placement was 8.1%, and persistent pain at 3 months was 4.2% (*Yunker et al., 2015*). This could be related to the enlargement of the hydrosalpinx or an allergy to nickel. Other concerns include pregnancy-related Essure dislocation, embryotoxic effect of nickel, and negative implantation effect of trailing coils (*Arora et al., 2014; Khati et al., 2014*). This device has been withdrawn from the market in some European countries, USA and Canada. The use of Essure as pre-IVF treatment is off label.

In the present meta-analysis, a comparable number of retrieved oocytes was found between the salpingectomy and HTO groups. Longer stimulation with lower LBR and implantation rate was demonstrated in the HTO group. The number of studies eligible for the meta-analysis, however, was limited.

Ultrasound guided aspiration of hydrosalpinx

Ultrasound-guided aspiration of hydrosalpinx fluid before IVF treatment is a simple and inexpensive procedure. Two randomized trials evaluated IVF treatment outcome of patients who underwent hydrosalpinx aspiration

compared with no intervention. One study showed a similar clinical pregnancy rate (31.3% versus 17.6%; RR 1.8; 95% CI 0.8 to 4.3). The study, however, was terminated before achieving the required sample owing to recruitment issues, and was, therefore, underpowered to examine the trial end-points (*Hammadieh et al., 2008*). Another trial demonstrated higher clinical and ongoing pregnancy rates in the aspiration group (OR 3.69, 95% CI 1.23 to 11.05) (*Fouda and Sayed, 2011*). *Fouda et al. (2015)* conducted another randomized trial comparing the efficacy of ultrasound-guided hydrosalpinx aspiration at the time of oocyte retrieval, and salpingectomy in 160 women with ultrasound visible hydrosalpinx. The ongoing pregnancy rates in the salpingectomy group and aspiration group were similar (38.67% versus 25.0%; OR 1.89, 95% CI 0.94 to 3.8). Rapid re-accumulation of hydrosalpinx fluid, however, tended to occur in the aspiration group. The ongoing pregnancy rate per transfer was significantly higher in salpingectomy group (38.7%) than in a subgroup of patients with fluid re-accumulation (15.4%) (*Fouda et al., 2015*).

Our meta-analysis revealed similar numbers of retrieved oocytes and total FSH dose in the salpingectomy and ultrasound aspiration groups. In both studies included in this analysis, ultrasound-guided aspiration was carried out on the day of oocyte retrieval, which means that IVF stimulation was started in the presence of hydrosalpinx in the aspiration group. Hydrosalpinx may also re-accumulate during stimulation if aspiration is carried out before the start of the IVF cycle. In contrast, IVF treatment in the salpingectomy group was started after excision of the hydrosalpinx. This fact could affect the evaluation of LBR and CPR, which were significantly higher in the salpingectomy group in a meta-analysis of both included studies (*Fouda et al., 2015; Song et al., 2017*).

Sclerotherapy of hydrosalpinx

Ultrasound-guided sclerotherapy has been advocated to minimize entry of hydrosalpinx fluid into the uterine cavity before embryo transfer. The purpose is to decrease recurrence of hydrosalpinx after aspiration and to increase the IVF pregnancy rate. First, the hydrosalpinx fluid is aspirated and 98% ethanol equal to a half volume of the aspirated fluid is injected into the dilated tube and left inside the tube for 5–10 min before removal. Antibiotic prophylaxis is prescribed to all the patients during the procedure and for 3 days after. Two weeks later, ultrasound is evaluated. Sclerotherapy is considered to be successful when the Fallopian tube contains no fluid or the remaining fluid is less than 10% of the original volume (*Jiang et al., 2010*).

In a prospective study including 52 women with hydrosalpinx, the investigators reported a higher IVF clinical pregnancy rate in women pretreated with sclerotherapy (42.9%) than in the non-pretreated group (4.5%). The outcome of the sclerotherapy group was similar to that in the control group with non-hydrosalpinx tubal factor infertility (54.0%). The main limitation of this study was the small number of patients in the sclerotherapy (n = 33) and in the non-treatment (n = 19) group (*Jiang et al., 2010*). In a retrospective study of 339 women, the blood flow parameters (pulsatility index and resistance index) were significantly higher in the untreated hydrosalpinx group compared with the sclerotherapy group and control group without hydrosalpinx (*Zhang et al., 2014*). The investigators concluded that hydrosalpinx sclerotherapy before IVF could improve endometrial receptivity and pregnancy rate, and might serve as an effective alternative to salpingectomy for patients with hydrosalpinx.

In a systematic review and meta-analysis, *Cohen et al. (2017)* reported similar CPR between the sclerotherapy and the salpingectomy groups (OR 0.79, 95% CI 0.54 to 1.17) carried out before IVF. The miscarriage rates in the sclerotherapy and salpingectomy groups were comparable (14.4% and 9.4%, respectively) (*Song et al., 2017*).

Potential complications of hydrosalpinx sclerotherapy include abdominal pain, ethanol leakage into the abdominal cavity, ethanol intoxication, pelvic adhesions and infection (*Shokeir, 2014*). Recurrence of hydrosalpinx occurs in around 20% of patients (*Zhang et al., 2014*).

Our meta-analysis of two observational studies (*Na et al., 2012; Song et al., 2017*) showed similar ovarian response parameters, LBR and CPR between salpingectomy and sclerotherapy groups.

Reconstructive surgery

The role of reconstructive surgery for hydrosalpinx is limited. No studies have compared ovarian response after salpingectomy and reconstructive tubal surgery.

The treatment options include neosalpingostomy and fimbrioplasty. Depending on the severity of the hydrosalpinx, the rate of pregnancy can be low if the tube is rigid and thick without mucosal folds, and up to 50% when the tubal damage is minimal (*Tulandi and Marzal, 2012*). The degree of tubal damage is best evaluated at surgery. In a prospective study assessing the efficacy of laparoscopic neosalpingostomy in 61 women with hydrosalpinx, the cumulative intrauterine pregnancy rates after 1 year of surgery were 13.6% in patients with only distal tubal obstruction and 23% in those with mild degree of tubal disease and periadnexal adhesions. At 24 months, the cumulative pregnancy rates were 20.5% and 29% respectively (*Milingos et al., 2000*). In women with severe disease, the intrauterine pregnancy rate could be as low as 5%. The recurrence rate of hydrosalpinx was 77% and the extrauterine pregnancy rate was 2.5% to 16.5% (*Taylor et al. 2001*).

Tubal surgery can still be considered for selected women younger than 35 years, with mild tubal disease and no other co-existing infertility factors, and for those who cannot or refuse to undergo IVF treatment (*Daniilidis et al., 2017*). Because of the uncertainty of tubal damage without surgery and the poor results of salpingostomy, IVF is generally a better alternative. Regardless of the surgical approach, the results of salpingostomy remain poor (*Taylor et al., 2001*).

Strengths and limitations

To the best of our knowledge, this was the first systematic review and meta-analysis evaluating the ovarian response during IVF treatment after salpingectomy compared with other pre-IVF hydrosalpinx treatments. The subgroup meta-analyses comparing salpingectomy with other hydrosalpinx treatment options separately was also conducted. We evaluated risks of bias using Newcastle–Ottawa scale and Cochrane Collaboration's tool. In sub-analyses where high heterogeneity was observed, a random-effects model was used. Additionally, certainty of evidence of included randomized and

observational studies was in accordance with the GRADE approach.

The main limitation of the present meta-analysis was the limited number of studies comparing IVF outcome after salpingectomy and other hydrosalpinx treatments, especially the hysteroscopic tubal occlusion, ultrasound-guided aspiration and sclerotherapy.

Publication period of the included studies ranged from 2000 to 2017. This can provide an additional limitation, as this period reflects significant changes in IVF treatment and embryological protocols. As both study and control groups of each study were treated at the same period, however, the results of IVF outcomes analysed in the meta-analysis are still reliable.

The certainty of evidence was low to very low for observational studies and moderate-to-low for RCTs. *Kontoravdis et al. (2006)* did not report the results according to ITT analysis. In our meta-analysis, however, we presented live birth and clinical pregnancy rates per number of randomized patients for all included RCTs. During the systematic review, we found only one study that compared ovarian reserve parameters after different pre-IVF hydrosalpinx treatments (*Ni et al., 2013*). In non-randomized studies, the non-salpingectomy treatment group included patients with contraindications to laparoscopy and patients with severe pelvic adhesions, which can additionally affect the IVF outcome of the non-salpingectomy treatment group. Only one study (*Dreyer et al., 2016*) provided comprehensive information about fresh and frozen embryo transfers rates. Separate subgroups of day-3 and day-5 embryo transfers were not presented in any of included studies.

The results of quality assessment suggest that a well-designed prospective study comparing IVF outcomes after salpingectomy and other hydrosalpinx treatment options is needed.

In conclusion, 40 years ago, women with non-functioning Fallopian tubes were considered sterile. The history of the first 'test tube' baby born to the couple who had tubal infertility for 9 years has minimized the role of reconstructive tubal surgery. Yet, surgery remains important in women with hydrosalpinx in this IVF era. Pre-IVF salpingectomy significantly increases the pregnancy rate and could be carried out easily by laparoscopy. Proximal tubal occlusion could be carried out as an alternative to salpingectomy, especially in the presence of severe adhesions surrounding the distal tube. In women who may be at risk of abdominal surgery, hysteroscopic tubal occlusion with Essure has been advocated. Yet, some women with Essure have complained of abdominal pain necessitating removal of the device or the uterus. Hydrosalpinx sclerotherapy is a relatively new technique that can be used before IVF. The present meta-analysis showed that salpingectomy does not impair the ovarian response during subsequent IVF treatment. Salpingectomy was associated with a higher IVF live birth, clinical pregnancy and implantation rates compared with other hydrosalpinx treatment options. Further well-designed prospective studies are required to clarify this matter.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.rbmo.2019.04.012.

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